Three-Electron S_N2 Reactions of Arylcyclopropane Cation Radicals. 2. Steric and Electronic Effects of Substitution[1]

J. P. Dinnocenzo,* H. Zuilhof, D. R. Lieberman, T. R. Simpson, and M. W. McKechney

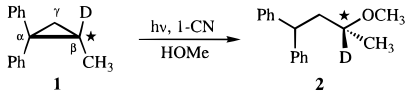
Contribution from the Department of Chemistry, University of Rochester, Rochester, New York 14627-0216

Received September 4, 1996[⊗]

Abstract: The nucleophilic substitution reactions on substituted arylcyclopropane cation radicals were studied by a combination of methods including product studies, time-resolved laser flash photolysis, kinetic isotope effects, and quantum chemical calculations. The reactions were found to proceed stereospecifically with inversion of configuration, with high regioselectivity for nucleophilic attack at the more substituted carbon atom, and with very small steric effects. Electronic effects on the nucleophilic substitution regiochemistry and the rate constants were found to be substantial for substituents on the cyclopropane moiety and on the aryl ring.

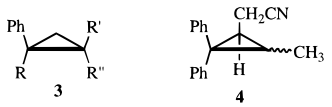
Introduction

Recent studies on the reactions of nucleophiles with arylcyclopropane cation radicals have shown some interesting differences in the structure−reactivity relationships of three-electron vs. four-electron nucleophilic substitutions. For example, the 1-cyanonaphthalene(1-CN)-photosensitized reaction of (*S*)-1-methyl-2,2-diphenyl[1-^{2}H]cyclopropane (**1**) with methanol provides optically active (*R*)-ether **2** as the only product (eq 1).[2] The reaction is proposed to proceed through the intermediacy of $\mathbf{1}^{\bullet+}$, which undergoes selective, nucleophilic attack of methanol at C_β rather than C_γ, i.e., at the more highly substituted carbon atom. This unusual regioselectivity was first observed by Rao and Hixson for the photosensitized oxidation of *trans*-1-methyl-2-phenylcyclopropane with methanol[3] and contrasts strongly with that observed in classical four-electron S_N2 reactions, where substitution generally occurs preferentially at the least hindered carbon atom.



1 **2** (1)

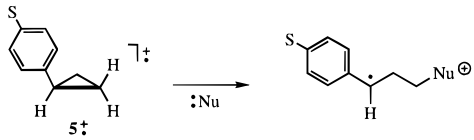
In this paper, we present a systematic study of substituent effects on three-electron S_N2 reactions of arylcyclopropane cation radicals. The effects of alkyl substituents on the cyclopropyl moiety were investigated using monophenyl- and diphenylalkylcyclopropanes **3** and **4** to probe how the number, the steric size, and the electronic properties of substituents affect the reaction regiochemistry. Time-resolved nanosecond laser flash photolysis was used to measure the substituent effects on the rate constants for reaction of the cyclopropane cation radicals with nucleophiles. In addition, secondary kinetic isotope effects were measured to probe the distribution of positive charge in the substitution transition states. These experimental studies were complemented by quantum chemical calculations on selected arylcyclopropane cation radicals and their transition states for nucleophilic substitution by methanol.



3 **4**

(R = H, Ph; R', R" = H, alkyl)

Finally, electronic effects of aryl substitution on the reactivities of para-substituted phenylcyclopropane cation radicals (**5**) with nucleophiles were measured by time-resolved nanosecond laser flash photolysis (eq 2).



5$^{\bullet+}$ (2)

Results

A. Syntheses. *Cis*- and *trans*-1-methyl-2-phenylcyclopropane were prepared from the reaction of *trans*-4-phenyl-3-buten-2-one with hydrazine followed by thermal decomposition of the resulting 2-pyrazoline.[4] 1,1-Dimethyl-2-phenylcyclopropane was prepared via the reaction of benzyl chloride/lithium tetramethylpiperidide with isobutylene.[5] The 1,1-diphenyl-2-alkylcyclopropanes and 1,1-dimethyl-2,2-diphenylcyclopropane were synthesized by photolysis of diphenyldiazomethane in the presence of the appropriate alkene.[6]

cis-3-Methyl-2,2-diphenylcyclopropaneacetonitrile (**6**) was prepared in four steps from 1,1-diphenylpropene as shown in Scheme 1. Reaction of 1,1-diphenylpropene with ethyl diazoacetate under rhodium catalysis gave a diastereoisomeric mixture of *cis*- and *trans*-3-methyl-2,2-diphenylcyclopropanecarboxylate esters. After chromatographic separation of the diastereoisomers, the *cis*-3-methyl-2,2-diphenylcyclopropanecarboxylate

⊗ Abstract published in *Advance ACS Abstracts,* January 15, 1997.

(1) (a) Taken in part from the doctoral thesis of T.R.S., University of Rochester, 1995. (b) A preliminary account of this work has been published: Dinnocenzo, J. P.; Lieberman, D. R.; Simpson, T. R. *J. Am. Chem. Soc.* **1993**, *115*, 366.

(2) Dinnocenzo, J. P.; Simpson, T. R.; Zuilhof, H.; Todd, W. P.; Heinrich, T. Preceding paper in this issue (*J. Am. Chem. Soc.* **1997**, *119*, 987.

(3) Rao, V. R.; Hixson, S. S. *J. Am. Chem. Soc.* **1979**, *101*, 6458.

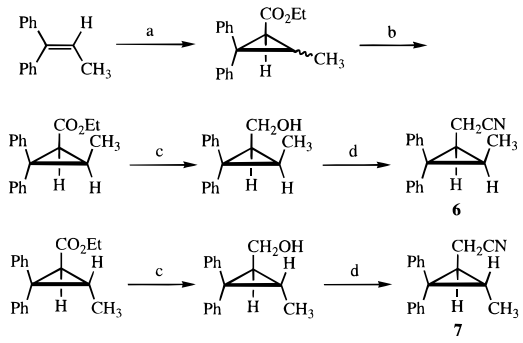
(4) (a) Casey, C. P.; Polichnowski, S. W.; Shusterman, A. J.; Jones, C. R. *J. Am. Chem. Soc.* **1979**, *101*, 7282. (b) In our hands the reaction yielded between 0 and 26%. In general, we have found other procedures to be somewhat more reproducible: Denmark, S. E.; Christenson, B. L.; Coe, D. M.; O'Connor, S. P. *Tetrahedron Lett.* **1995**, *36*, 2215.

(5) Olofson, R. A.; Dougherty, C. M. *J. Am. Chem. Soc.* **1973**, *95*, 581.

(6) Baron, W. J.; Hendrick, M. E.; Jones, M., Jr. *J. Am. Chem. Soc.* **1973**, *95*, 6286.

S0002-7863(96)03112-5 CCC: $14.00

Scheme 1[a]



[a] (a) N_2═$CHCO_2Et$, $Rh_2(O_2C(CH_2)_4CH_3)_4$ (b) chrom. sep. (c) $LiAlH_4$. (d) (i) *p*-TsCl, (ii) *n*-Bu_4NCN.

ester was reduced to the alcohol, reacted with tosyl chloride, and then treated with cyanide to give **6**. *trans*-3-Methyl-2,2-diphenylcyclopropaneacetonitrile (**7**) was prepared analogously from the *trans*-3-methyl-2,2-diphenylcyclopropanecarboxylate ester.

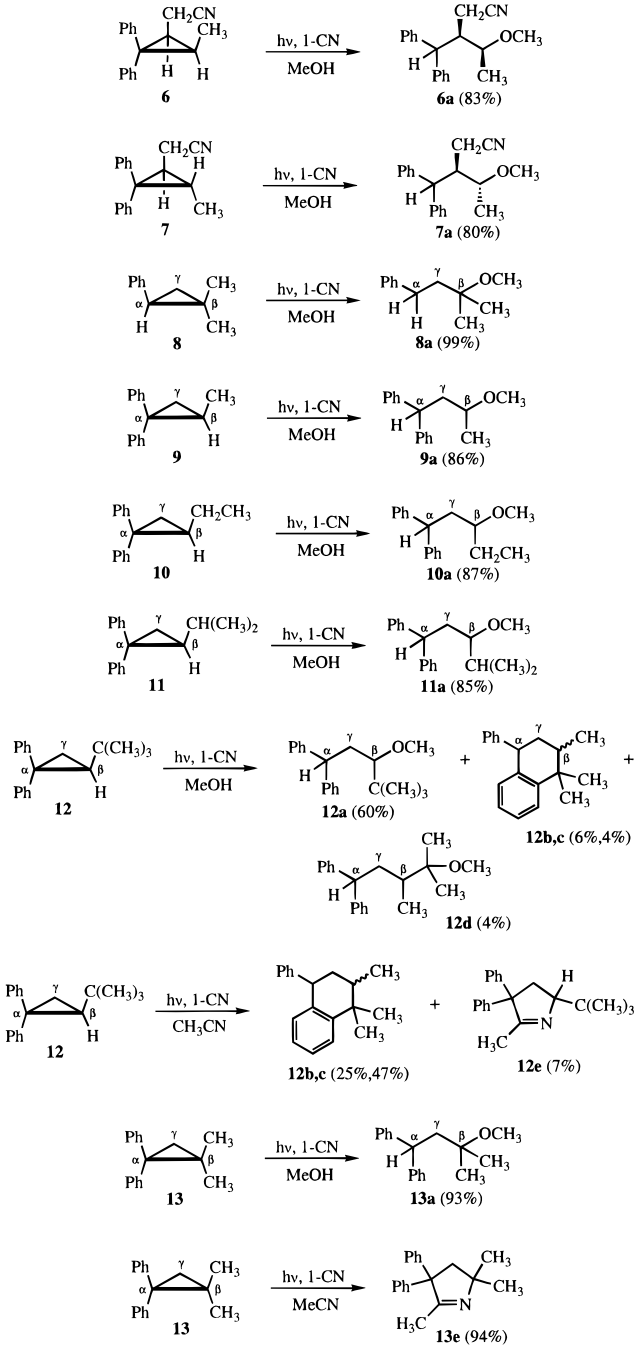
The para-substituted phenylcyclopropanes were synthesized by modified Simmons−Smith cyclopropanation[7] of the corresponding para-substituted styrenes (see Experimental Section).

B. Photooxidations. Photooxidations of cyclopropanes **6**−**13** in methanol or acetonitrile were performed in rigorously degassed solutions containing 1-cyanonaphthalene (1-CN) as a photosensitizer. Reported yields refer to reactions run on a small scale and were determined by gas chromatography (GC).[8] Reactions were run on a larger scale for preparative isolation of the photoproducts. The results are presented in Scheme 2.

Photooxidation of cyclopropane **6** and **7** gave products of nucleophilic attack by methanol with complete inversion of configuration. Cyclopropane **6** gave as its sole detectable product the *syn* substitution product **6a**, while **7** gave only the corresponding *anti* product **7a**. These results show that nucleophilic attack by methanol is not only stereospecific but also regioselective, in agreement with earlier observations.[1−3] This was also observed for cyclopropanes **8**−**11** which react with methanol selectively at the more hindered carbon atom, giving the methanol-addition products **8a**−**11a**. For **12**, the photooxidation in methanol gave in addition to the major nucleophilic substitution product **12a**, the tetralin-derivatives **12b**−**c**, and 4-methoxy-3,4-dimethyl-1,1-diphenylpentane (**12d**). To determine the regioselectivity of methanol substitution on **12**, the product of methanol substitution at C_γ was independently synthesized (*vide infra*). GC analysis showed that the reaction was >99.9% regioselective for substitution at C_β vs.C_γ. In dry acetonitrile, photooxidation of **12** gave tetralin-derivatives **12b**−**c** and cyclic imine **12e**. Cyclopropane **13** provided the substitution product **13a** in methanol. As done for **12**, the product of methanol substitution at C_γ of **13** was independently prepared. GC analysis revealed that the photooxidation reaction was >99.99% regioselective. Finally, photooxidation of **13** in dry acetonitrile gave cyclic imine **13e**.

C. Independent Synthesis of Photoproducts. The stereochemistries of the products from the photooxidations of cyclopropanes **6** and **7** in methanol were determined by chemical correlation. First, methanol-addition products **6a** and **7a** were

Scheme 2



reduced with sodium in the presence of Fe(III)acetylacetonate[9] to give *syn*-ether **6a′** and *anti*-ether **7a′**, respectively. These products were then correlated by ^{1}H NMR and GC to compounds independently synthesized as shown in Scheme 3. Reaction of *cis*-2-epoxybutane with diphenylmethyllithium followed by methylation of the resulting alcohol gave *syn*-ether **6a′**. Analogously, *trans*-2-epoxybutane provided *anti*-ether **7a′**.

The structure of photoproduct **8a** was determined by independent synthesis via the base-catalysed methylation of α,α-dimethylbenzenepropanol. The structures of the remaining photooxidation products were deduced by spectroscopic methods (see Experimental Section).

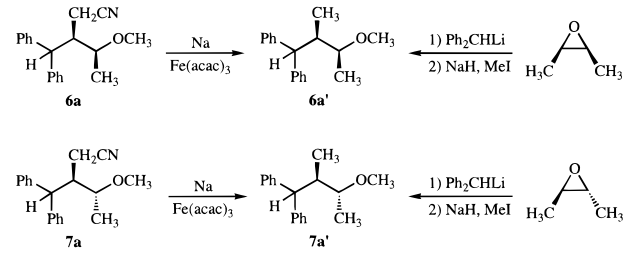
In order to determine the regioselectivities for methanol substitution at C_β vs. C_γ in the photooxidations of cyclopropanes **12** and **13**, it was necessary to independently prepare the

(7) (a) S = MeO, Me: Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron* **1968**, *24*, 53. (b) S = F, Cl: Denmark, S. E.; Edwards, J. P. *J. Org. Chem.* **1991**, *56*, 6974. (c) S = C(═O)Me: Levina, R. Ya.; Gembitskii, P. A.; Kostin, V. N.; Shostakovskii, S. M.; Treshchova, E. G. *Zh. Obshch. Khim.* **1963**, *33*, 365. (d) S = OC(═O)Me: Horrom, B. W.; Mazdiyasni, H. *OPPI Briefs* **1992**, *6*, 696.

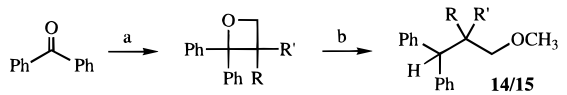
(8) See preceding paper in this issue (*J. Am. Chem. Soc.* **1997**, *119*, 987) for general description of the reaction procedure.

(9) Tamelen, E. E. van; Rudler, H.; Bjorkland, C. *J. Am. Chem. Soc.* **1971**, *93*, 7113.

Scheme 3



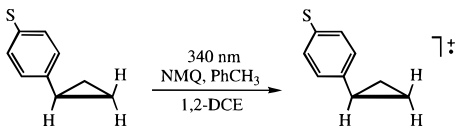
Scheme 4[a]



[a] (a) RR′C═CH_2, hν. (b) (i) Li/Bu^t-PhPh-Bu^t; (ii) MeI. (**14**, R = R′ = Me; **15**, R = Bu^t, R′ = H).

products that would be formed by substitution at C_γ since they could not be detected in the crude reaction mixtures by ^{1}H NMR analyses. Ether **14**, which would be formed by C_γ substitution on **13**$^{\bullet+}$, was prepared by the Paterno−Büchi reaction of benzophenone with isobutylene[10] followed by reductive cleavage of the oxetane and methylation of the resulting alcohol (Scheme 4). Ether **15**, the product of C_γ substitution on **12**$^{\bullet+}$, was prepared in an analogous fashion starting from benzophenone and 3,3-dimethyl-1-butene.

D. Kinetics of Nucleophilic Substitution. Hammett Study. A Hammett study was performed to study the electronic characteristics of the transition states for the S_N2 reaction of arylcyclopropane cation radicals with methanol and pyridine as nucleophiles. The cation radicals were produced by photoinduced electron transfer using *N*-methylquinolinium hexafluorophosphate (NMQ) as a photooxidant and toluene as a cosensitizer (eq 3).[11] The UV-vis spectra of the cation radicals were measured by picosecond laser flash photolysis (Figure 1). The reactivity of the cyclopropane cation radicals with nucleophiles (eq 2) in 1,2-dichloroethane (1,2-DCE) was studied using nanosecond laser transient absorption spectroscopy. In the presence of nucleophiles the decay of the cation radical signals followed pseudo-first-order kinetics. The pseudo-first-order rate constants for disappearance of the cation radicals were determined by fitting the decay profiles at 540 nm with monoexponential functions. In all cases, plots of the rate constants vs. nucleophile concentration showed good linearity. The slopes of the plots gave the bimolecular rate constants, k_{MeOH} and k_{pyr}, for reactions with methanol and pyridine, respectively. The results are presented in Table 1. Hammett plots of these data vs σ^+ and Arnold's $\sigma_\alpha^\bullet$ substituent constants are shown in Figure 2.[12]



(3)

Effect of Alkyl Substituents on the Cyclopropyl Moiety. The cation radicals of the arylcyclopropanes **8**−**13** and **16**−**18** were generated by photoinduced electron transfer as described above. All of the cation radicals gave strong absorption peaks in the visible region which were recorded by either picosecond

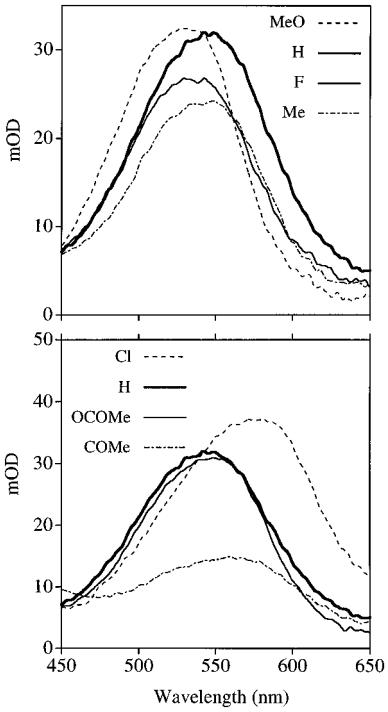


Figure 1. UV-vis spectra of the cation radicals of para-substituted phenylcyclopropanes in 1,2-dichloroethane at 23 °C.

Table 1. Rate Constants (in M^{-1} s^{-1}) for the Reaction of Para-Substituted Phenylcyclopropane Cation Radicals with Methanol (k_{MeOH}) and Pyridine (k_{pyr}) in 1,2-Dichloroethane at 23 °C

substituent	σ^+	k_{MeOH}	k_{pyr}
MeO	−0.78	≤ 1.0×10^5	$3.0 (\pm 0.5) \times 10^6$
Me	−0.31	$1.2 (\pm 0.3) \times 10^6$	$6.1 (\pm 0.7) \times 10^8$
OC(═O)Me	−0.18	$1.7 (\pm 0.1) \times 10^6$	$5.2 (\pm 0.2) \times 10^8$
F	−0.07	$9.7 (\pm 0.1) \times 10^6$	$3.2 (\pm 0.4) \times 10^9$
H	0.0	$1.5 (\pm 0.1) \times 10^7$	$3.9 (\pm 0.1) \times 10^9$
Cl	+0.11	$8.4 (\pm 0.2) \times 10^6$	$1.7 (\pm 0.1) \times 10^9$
C(═O)Me	+0.41	$2.9 (\pm 0.3) \times 10^7$	$4.0 (\pm 0.4) \times 10^9$

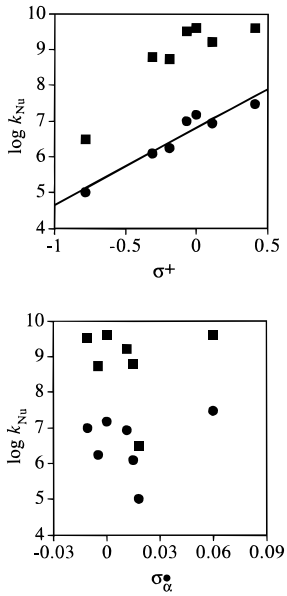


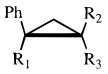
Figure 2. Hammett plots: log k_{Nu} for the reaction of arylcyclopropane cation radicals with nucleophiles (squares = pyridine; circles = methanol) in 1,2-dichloroethane at 23 °C, versus σ^+ and $\sigma_\alpha^\bullet$.

(10) Arnold, D. R.; Hinman, R. L.; Glick, A. H. *Tetrahedron Lett.* **1964**, *5*, 1425.

(11) (a) Todd, W. P.; Dinnocenzo, J. P.; Farid, S.; Goodman, J. L.; Gould, I. R. *J. Am. Chem. Soc.* **1991**, *113*, 3601. (b) Dockery, K. P.; Dinnocenzo, J. P.; Farid, S.; Goodman, J. L.; Gould, I. R.; Todd, W. P. *J. Am. Chem. Soc.* **1997**, *119*. In press.

(12) (a) σ^+: Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165. (b) $\sigma_\alpha^\bullet$: Wayner, D. D. M.; Arnold, D. R. *Can J. Chem.* **1984**, *62*, 1164. (c) σ^+ (COMe) is a calculated value (see ref 12a).

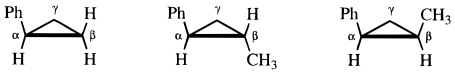
Table 2. Rate Constants (in M^{-1} s^{-1}) for Phenyl- and Diphenylcyclopropane Cation Radicals **8**$^{\bullet+}$−**13**$^{\bullet+}$ and **16**$^{\bullet+}$−**19**$^{\bullet+}$ with Methanol in Dichloromethane at 23 °C



compd	R_1	R_2	R_3	k_{MeOH}
19$^{\bullet+}$	Ph	H	H	1.7×10^7 [a]
9$^{\bullet+}$	Ph	Me	H	1.5×10^8
10$^{\bullet+}$	Ph	Et	H	8.3×10^7
11$^{\bullet+}$	Ph	Pr^i	H	3.0×10^7
12$^{\bullet+}$	Ph	Bu^t	H	4.8×10^6
13$^{\bullet+}$	Ph	Me	Me	3.2×10^8
16$^{\bullet+}$	H	H	H	1.0×10^7 [a]
17$^{\bullet+}$	H	H	Me	3.1×10^7
18$^{\bullet+}$	H	Me	H	3.1×10^8
8$^{\bullet+}$	H	Me	Me	1.5×10^8

[a] Statistically corrected (k_{obsd}/2).

or nanosecond transient absorption methods.[2] The kinetics of their reactions with methanol were determined by monitoring the decay profiles of the cation radicals at the respective λ_{max} by using nanosecond laser flash methods as described above. The bimolecular rate constants (k_{MeOH}) are presented in Table 2.



E. Kinetic Isotope Effects. The 1-cyanonaphthalene-photosensitized reactions of phenylcyclopropane (**16**) and *trans*-1-methyl-2-phenylcyclopropane (**17**) with *n*-butanol (*n*-C_4H_9OH) and nonadeuteriobutanol (*n*-C_4D_9OH) were studied to determine β-secondary kinetic isotope effects (KIEs). These KIEs provide information on the buildup of positive charge on the nucleophile in the transition states.[13] For both **16** and **17** the sole products are those derived from butanol substitution (Scheme 5). For **17**, *n*-butanol substitution occurs exclusively at C_β, which is the same substitution regiochemistry observed in the photosensitized reaction of **17** with methanol. The products of reaction of **16** and **17** with *n*-C_4H_9OH vs. *n*-C_4D_9OH (**16a**−**b** and **17a**−**b**) were baseline separable by capillary GC, so that the KIEs could be determined from the product ratios.[14] The measured KIEs for **16** and **17** at 20.0 ± 0.5 °C were 0.9798 ± 0.0033 and 0.9419 ± 0.0032, respectively. An analogous experiment was attempted with 1,1-dimethyl-2-phenylcyclopropane (**8**). In this case, however, several minor products were formed in addition to the major substitution product. Since such a result can complicate an accurate determination of the KIE in several ways, this experiment was not pursued further.

F. Quantum Chemical Calculations: Arylcyclopropane Cation Radicals. The data in Scheme 2 show that alkyl groups exert a powerful directing effect on the regiochemistry of reaction of substituted arylcyclopropane cation radicals with nucleophiles. To assess how alkyl substituents at C_β affect the reactant cation radical structures, quantum chemical calculations were performed on phenylcyclopropane cation radical (**16**$^{\bullet+}$), *trans*-1-methyl- (**17**$^{\bullet+}$), *cis*-1-methyl- (**18**$^{\bullet+}$), and 1,1-dimethyl-2-phenylcyclopropane (**8**$^{\bullet+}$) cation radical. All calculations were performed with the density functional hybrid-method B3LYP with the 6-31G(d) basis set.[15] The advantages of this method for calculating cation radical structures and energies have recently been discussed.[16] Selected bond lengths and group charges for the cation radicals are shown in Table 3.

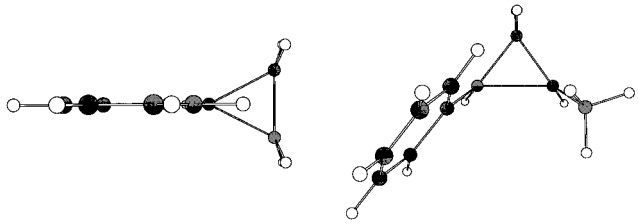


Figure 3. B3LYP/6-31G* optimized structures (bond lengths in Å) for the cation radicals of phenylcyclopropane (**16**$^{\bullet+}$; left) and *cis*-1-methyl-2-phenylcyclopropane (**18**$^{\bullet+}$; right).

Table 3. Selected Bond Lengths (Å) and Group Charges (Q) for B3LYP/6-31G(d) Calculated Alkylarylcyclopropane Cation Radicals

compd	$r(C_\alpha-C_\beta)$	$r(C_\alpha-C_\gamma)$	$r(C_\beta-C_\gamma)$	$r(C_\alpha-C_{Ph})$	Q(Ph)	$Q(C_\beta)$	$Q(C_\gamma)$
16$^{\bullet+}$	1.591	1.591	1.450	1.431	0.681	0.187	0.187
17$^{\bullet+}$	1.723	1.523	1.463	1.428	0.592	0.290	0.158
18$^{\bullet+}$	1.789	1.511	1.469	1.426	0.570	0.310	0.155
8$^{\bullet+}$	1.943	1.450	1.483	1.422	0.491	0.406	0.121

Based on the data in Table 3, it is clear that phenylcyclopropane cation radical is structurally distinct from the three alkyl-substituted cation radicals. Following the notation of Hudson *et al.*,[17] **16**$^{\bullet+}$ is a 2L1N isomer (two lengthened C−C bonds, one normal C−C bond) while **17**$^{\bullet+}$, **18**$^{\bullet+}$, and **8**$^{\bullet+}$ are 1L2N isomers (one lengthened C−C bond, two normal C−C bonds). Several geometric features are most prominently different in these species. First, it is seen that the addition of methyl groups at C_β results in a significant increase in $r(C_\alpha-C_\beta)$ and that the incremental increase is roughly additive with each methyl group. Concurrent with this are decreases in $r(C_\alpha-C_\gamma)$ and $r(C_\alpha-Ph)$ and increases in $r(C_\beta-C_\gamma)$. Second, as shown in Figure 3, the orientation of the phenyl ring with respect to the cyclopropane ring changes significantly with alkyl substitution. In **16**$^{\bullet+}$, the phenyl group bisects the cyclopropane ring, as expected for a 2L1N structure. For all three alkyl-substituted cation radicals, the orientation is similar to that shown for **18**$^{\bullet+}$, where the plane of the phenyl ring is nearly completely aligned with the $C_\alpha-C_\gamma$ bond. Thus in **16**$^{\bullet+}$, two cyclopropane C−C σ bonds profit from partial overlap with the π-orbitals on the phenyl ring, while for the alkyl-substituted cation radicals the π-orbitals overlap maximally with the long $C_\alpha-C_\beta$ bond. As shown in Table 3, the geometric changes due to alkyl-substitution result in significant redistribution of the positive charge. For example, the phenyl group charge, Q(Ph), in **16**$^{\bullet+}$ is 0.68. This decreases upon 2,2-dimethyl substitution to only 0.49 in **8**$^{\bullet+}$. Simultaneously, there are large increases in $Q(C_\beta)$ and small decreases in $Q(C_\gamma)$ upon alkyl-substitution at C_β.

Calculations of the vibrational frequencies confirmed that all of the calculated cation radical structures were energy minima. The calculated expectation values of $\langle S^2 \rangle$ ranged from 0.762−0.765, in good agreement with that expected for a pure doublet state (0.750). That the cation radicals are predicted to have structures with bonded cyclopropane rings is consistent with the stereochemical and kinetic evidence obtained from experiment. Confirmation is also provided by approximate estimates

(13) (a) Sunko, D. E.; Hehre, W. J. *Prog. Phys. Org. Chem.* **1983**, *14*, 205. (b) Lee, I. *Chem. Soc. Rev.* **1995**, *24*, 223.

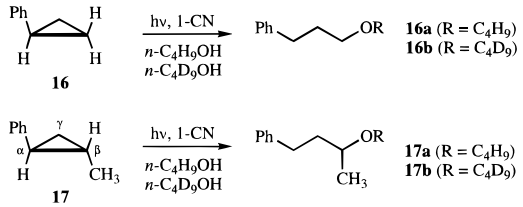
(14) For other examples of this technique to determine kinetic isotope effects, see: (a) De Vaal, P.; Lodder, G.; Cornelisse, J. *J. Phys. Org. Chem.* **1992**, *5*, 581. (b) Zuilhof, H.; Van Gelderen, F. A.; Cornelisse, J., Lodder, G. Submitted for publication.

(15) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623.

(16) Zuilhof, H.; Dinnocenzo, J. P.; Reddy, C.; Shaik, S. *J. Phys. Chem.* **1996**, *100*, 15774.

(17) Hudson, C. E.; Giam, C. S.; McAdoo, D. J. *J. Org. Chem.* **1993**, *58*, 2017.

Scheme 5



Scheme 6

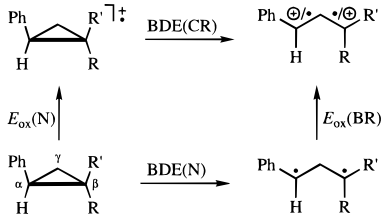


Table 4. Oxidation Potentials (V vs. SCE) and Bond Dissociation Energies (kcal/mol) for Neutral **16**, **17**, **18**, and **8** as well as Their Cation Radicals

compd	E_{ox}(N)	BDE(N)	E_{ox}(BR)	BDE(CR)
16	1.94	46	0.37	10
17	1.73	43	0.37	11
18	1.71	42	0.37	11
8	1.65	41	0.09	5

of the bond dissociation energies of the cation radicals as determined from the thermodynamic cycle shown in Scheme 6.[1b,18] The results of these calculations as well as the associated thermodynamic data are given in Table 4.[19,20] It includes the oxidation potentials of the cyclopropanes, E_{ox}(N), the estimated bond dissociation energies of the neutral cyclopropanes, BDE(N), and the oxidation potentials of the 1,3-biradicals produced by homolytic cleavage of the $C_\alpha-C_\beta$ bond, E_{ox}(BR). For **16**$^{\bullet+}$, **17**$^{\bullet+}$, and **18**$^{\bullet+}$, E_{ox}(BR) was approximated by the oxidation potential reported for the 1-phenylethyl radical (0.37 V).[20d] For **8**$^{\bullet+}$, E_{ox}(BR) was taken as the oxidation potential for the *tert*-butyl radical (0.09 V).[20d] Thus for **8**$^{\bullet+}$, the apportionment of spin and charge in the ring-opened cation radical is different than in the other three cation radicals. This is the principal reason that **8**$^{\bullet+}$ has a significantly lower BDE(CR). The other three cation radicals have similar BDE(CR) values due to approximately offsetting effects of alkyl-substitution on E_{ox}(N) and BDE(N).

G. Quantum Chemical Calculations: Transition States for Nucleophilic Substitution. Quantum chemical calculations were performed to evaluate the effect of alkyl substitution on the structures and energies of the transition states for nucleophilic substitution by methanol. Due to the high computational demands of these calculations, semiempirical (AM1 and PM3) methods were employed.[21] In all cases, force constant calculations were performed to ensure that the optimized geometries were indeed transition states for the nucleophilic substitution reactions. Selected geometric and electronic features of the transition states for reaction of phenylcyclopropane cation radical as well as cation radicals with alkyl substituents at C_β are listed in Table 5.

In view of the high regioselectivity observed for the nucleophilic reaction arylcyclopropane cation radicals at the more substituted carbon atom, transition state energies were also calculated for reaction with methanol at the less substituted carbon atom in order to obtain the differential activation enthalpies, $\Delta\Delta H^{\ddagger}$. The calculated values are shown in Table 6. These data will be discussed in detail below.

Discussion

Product Studies. Previous steady-state and transient kinetics experiments have shown that the photooxidation of arylcyclopropanes in the presence of nucleophiles such as methanol are consistent with the reaction mechanism shown in Figure 4.[2] The key feature of this mechanism in the context of the present discussion is the S_N2 reaction between the cyclopropane cation radicals and methanol.

We begin by discussing the results from photooxidation of cyclopropanes **8**−**13**. All of the cyclopropanes undergo clean photooxidation in methanol to give products from nucleophilic substitution at C_β, except for **12**, which additionally gives several rearrangement products. These will be discussed later. Based on the product studies and the reaction mechanism, we conclude that the cation radicals of cyclopropanes **8**−**13** show a strong preference for nucleophilic substitution at the more hindered carbon atom, i.e., at C_β rather than C_γ. No substitution is observed at C_α, which would be expected if the reaction occurred by an S_N1 mechanism.[2,19] The regiochemical selectivities determined in the cases of **12** (>99.99%) and **13** (>99.9%) show that the energetic preferences must be significant, since neopentyl and tertiary substitutions at C_β are favored over primary substitutions at C_γ. The results can be rationalized by assuming that the alkyl groups at C_β stabilize positive charge in the substitution transition states and that this stabilization overwhelms the opposing steric effects. This hypothesis is also consistent with results from the photooxidations of cyclopropanes **6** and **7**. Here, the substituents at C_β and C_γ are comparable sterically but not electronically.[12a] In each of these cases nucleophilic substitution is observed only at the carbon atom bearing the more electron-donating methyl group. The fact that the nucleophilic substitutions also proceed with complete inversion of configuration provides additional evidence for an S_N2 mechanism.

Photooxidation of cyclopropane **12** in methanol provides, in addition to the nucleophilic substitution product **12a**, products

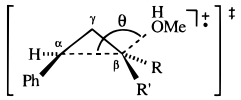
(18) Wayner, D. D. M.; Parker, V. D. *Acc. Chem. Res.* **1993**, *26*, 287.

(19) (a) Oxidation potentials of the neutrals, E_{ox}(N), were obtained from the equilibrium constants for electron transfer between reference aromatic compounds and the cyclopropanes as studied by picosecond laser flash transient absorption spectroscopy (Lingenfelter, T. G.; Simpson, T. R.; Dinnocenzo, J. P. Manuscript in preparation). (b) Bond dissociation energies of the neutrals, BDE(N), were estimated based on group additivity relationships. For **16**, BDE(N) was obtained by taking the C−C BDE of cyclopropane (59 kcal/mol)[20a] and correcting it for the effect of phenyl substitution by adding the difference between the C−H BDEs for Ph-CHMe-H (85 kcal/mol)[20b] and $MeCH_2$-H (98 kcal/mol).[20b] For **17**, BDE(N) was obtained by taking the C−C BDE of **16** (46 kcal/mol) and correcting it for the effect of methyl substitution by adding the difference between the C−H BDEs for Me_2CH-H (95 kcal/mol)[20b] and $MeCH_2$-H (98 kcal/mol).[20b] For **18**, BDE(N) was obtained by taking the C−C BDE of **17** (43 kcal/mol) and correcting it for the effect of having the substituents in a cis configuration by adding the difference between the heats of formation for *trans*-1,2-dimethylcyclopropane (−1 kcal/mol)[20c] and *cis*-1,2-dimethylcyclopropane (0 kcal/mol).[20c] For **8**, BDE(N) was obtained by taking the C−C BDE of **16** (46 kcal/mol) and correcting it for the effect of geminal dimethyl substitution by adding the difference between the C−H BDEs for Me_3C−H (93 kcal/mol)[20b] and $MeCH_2$-H (98 kcal/mol).[20b] (c) The oxidation potential of the biradical, E_{ox}(BR), was estimated by taking the lower oxidation potential of the two radical sites. $E_{1/2}$ for the 1-phenylethyl radical (0.37 V)[20d] was used for **16**, **17**, and **18**. $E_{1/2}$ for the *tert*-butyl radical (0.09 V)[20d] was used for **8**.

(20) (a) Doering, W. v. E. *Proc. Natl. Acad. Sci. U.S.A.* **1981**, *78*, 5279. (b) McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493. (c) Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. In *Gas-Phase Ion and Neutral Thermochemistry*; Lide, D. R. J., Ed.; *J. Phys. Chem. Ref. Data* **1988**, *17*, Supplement no. 1. (d) Wayner, D. D. M.; McPhee, D. J.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 132. (e) Wayner, D. D. M., personal communication.

(21) (a) AM1: Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart. J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902. (b) PM3: Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209, 221.

Table 5. Selected Transition State Data for the Reaction of Several 1-Alkyl-2-phenylcyclopropane Cation Radicals with Methanol



R,R′	method	$r^{\ddagger}(C_\alpha-C_\beta)$ (Å)	$r^{\ddagger}(C_\beta-O)$ (Å)	θ	$Q^{\ddagger}$(Ph)	$Q^{\ddagger}(C_\beta)$	$Q^{\ddagger}$(HOMe)	$\Delta H^{\ddagger}$ (kcal/mol)
H,H	AM1	2.24	2.10	139.9	0.29	0.39	0.12	3.0
Me,H	AM1	2.34	1.97	137.6	0.22	0.50	0.18	4.2
H,Me	AM1	2.34	1.98	130.5	0.21	0.46	0.17	4.1
Bu^t,H	AM1	2.35	2.01	132.9	0.21	0.52	0.16	3.2
Me,Me	AM1	2.43	1.88	129.3	0.11	0.54	0.23	8.6
H,H	PM3	2.22	1.95	143.0	0.27	0.36	0.21	10.0
Me,H	PM3	2.32	1.89	140.7	0.24	0.45	0.24	11.2
H,Me	PM3	2.32	1.87	135.2	0.21	0.41	0.26	9.7
Bu^t,H	PM3	2.34	1.93	136.0	0.22	0.45	0.22	7.5
Me,Me	PM3	2.42	1.83	133.4	0.18	0.47	0.29	14.0

Table 6. Calculated $\Delta\Delta H^{\ddagger}$ ($\Delta H^{\ddagger}(C_\gamma) - \Delta H^{\ddagger}(C_\beta)$, kcal/mol) for Reaction of 1-Alkyl-2-phenyl- or 1,1-Dialkyl-2-phenylcyclopropane Radical Cations with Methanol at C_γ vs. C_β

substituents	AM1	PM3
cis-Me	5.8	5.8
trans-Me	10.5	9.0
trans-Bu^t	6.3	5.0
2,2-Me_2	15.5	13.3

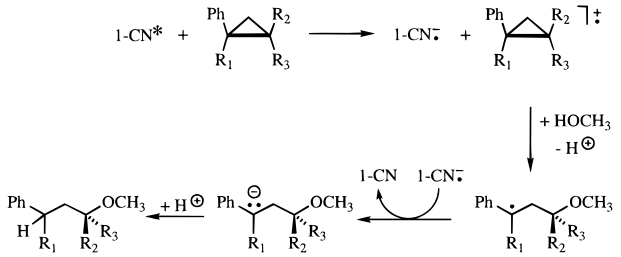


Figure 4. Mechanism for the photooxidation of arylcyclopropanes in the presence of methanol.

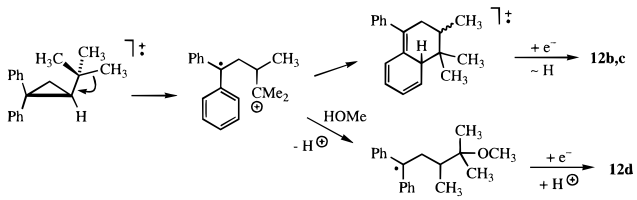


Figure 5. Proposed mechanism for formation of **12b**−**d**.

12b−**c** and **12d**. As shown in Figure 5, the latter products can be rationalized by an alkyl-migration mechanism analogous to that proposed for the solvolysis of neopentyl derivatives[22] and for rearrangements of other strained ring cation radicals.[23] Although an alternative S_N1-type mechanism in which **12**$^{\bullet+}$ undergoes fragmentation of the $C_\alpha-C_\beta$ bond, followed by either nucleophilic capture or neopentyl rearrangment, cannot be ruled out, the observed products argue against it. If unimolecular fragmentation of the $C_\alpha-C_\beta$ bond occurred, then it should give a distonic cation radical in which the radical is localized at C_β and the positive charge at C_α.[19c] This distonic cation radical should lead to nucleophilic capture at C_α, which is not observed. For this reason we postulate that the ring-closed cation radical

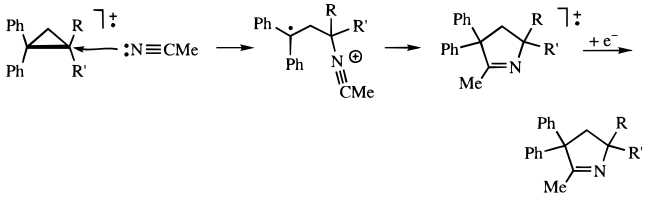


Figure 6. Proposed mechanism for the reaction of diphenylcyclopropane cation radicals with CH_3CN.

of **12** undergoes nucleophilic attack by methanol at C_β in competition with neopentyl rearrangement that is concerted with ring-opening of the cation radical.

Reactions of strained-ring cation radicals with CH_3CN to form cyclic imines such as **12e** have been previously reported in several cases.[24] The reaction of CH_3CN with **12**$^{\bullet+}$ differs from these only in that we suggest it proceeds by an S_N2 mechanism (Figure 6). This mechanistic proposal is based on the regiochemistry of nucleophilic substitution, which is analogous to that observed for the reaction of **12**$^{\bullet+}$ with methanol. As described above, an S_N1 mechanism leads to the prediction that nucleophilic substitution should occur at C_α, which is not observed. The distonic cation radical produced from nucleophilic attack by CH_3CN can form the imine product in several ways. It can undergo ring closure as shown in Figure 6, followed by reduction with either the sensitizer anion radical or **12**. The latter process would lead to a chain reaction which has previously been shown to be feasible.[24a] Alternatively, the distonic cation radical could be reduced by the sensitizer anion radical to produce a biradical which undergoes ring closure to **12e**. Our present data do not distinguish between these possibilities. A cyclic imine is also formed from the photooxidation of cyclopropane **13** in CH_3CN. In this case, the reaction regiochemistry can be explained by either an S_N2 or an S_N1 mechanism. An S_N1 mechanism cannot be ruled out here because ring-opening of **13**$^{\bullet+}$ is expected to give a distonic cation radical with the positive charge at C_β,[19c] and thus nucleophilic capture would be expected to occur there, as observed.

Kinetics. Based on the reaction regioselectivities described above, the three-electron S_N2 reactions of arylcyclopropane cation radicals **8**$^{\bullet+}$−**13**$^{\bullet+}$ appear to be dominated by electronic rather than steric effects. The steric effects that are present can be estimated by comparing the second-order rate constants for reaction of **9**$^{\bullet+}$−**12**$^{\bullet+}$ with methanol. As seen from the data in Table 2, the rate constants decrease along this series. We attribute this to a steric effect. It is worth noting, however,

(22) (a) Dauben, W. G.; Chitwood, J. L. *J. Am. Chem. Soc.* **1968**, *90*, 6876. (b) Ando, T.; Morisaki, H. *Tetrahedron Lett.* **1979**, *20*, 121. (c) Shiner, V. J., Jr.; Reib, R. C. *Tetrahedron Lett.* **1979**, *20*, 121. (d) Shiner, V. J., Jr.; Tai, J. J. *J. Am. Chem. Soc.* **1981**, *103*, 436. (e) Yamataka, H.; Ando, T. *J. Am. Chem. Soc.* **1982**, *104*, 1808. (e) Yamataka, Y.; Ando, T.; Nagase, S.; Hanamura, M.; Morokuma, K. *J. Org. Chem.* **1984**, *49*, 631.

(23) (a) Adam W.; Walter, H.; Chen, G.-F.; Williams, F. *J. Am. Chem. Soc.* **1992**, *114*, 3007. (b) Weng, H.; Sheik, Q.; Roth, H. D. *J. Am. Chem. Soc.* **1995**, *117*, 10655.

(24) (a) Zona, T. A.; Goodman, J. L. *J. Am. Chem. Soc.* **1993**, *115*, 4925. (b) Arnold, D. R.; Du, X. *Can. J. Chem.* **1994**, *72*, 403. (c) ref. 23b.

that the effects are much smaller than those observed in comparable four-electron S_N2 reactions. For example, the Me/Bu^t ratio in the three-electron S_N2 reaction is only 31, whereas in typical four-electron substitutions it is ca. 10^5!![25] Based on the small steric effects measured for the three-electron substitutions, it seems plausible that electronic factors can overwhelm the steric effects, thus explaining nucleophilic attack at the more substituted carbon atom. Possible reasons for the small steric effects will be discussed below.

It is also interesting to compare rate constants for reaction of methanol with the cation radicals of 1,1-diphenyl- (**19**), 1,1-diphenyl-2-methyl- (**9**), and 1,1-dimethyl-2,2-diphenylcyclopropane (**13**), which reveal the effects of mono- and dimethyl-substitution at C_β. As shown by the data in Table 2, the substitution rate constants increase with increasing alkyl substitution, a trend opposite that found in typical four-electron S_N2 reactions. Although the origin of this trend is more difficult to evaluate because both electronic and steric factors change, it is clear that steric effects do not dominate these nucleophilic substitution reactions. We considered the possibility that the increase in rate constants observed with increasing alkyl substitution at C_β might be due to an internal steric effect, namely release of strain upon nucleophilic substitution between the phenyl groups at C_α and the cis-alkyl group(s) at C_β. To test this hypothesis, the rate constants for reaction of the analogous monophenylcyclopropane cation radicals (**16**$^{\bullet+}$, **17**$^{\bullet+}$, **18**$^{\bullet+}$, **8**$^{\bullet+}$) with methanol were measured. As described above, **8**$^{\bullet+}$ reacts with methanol exclusively at C_β; **17**$^{\bullet+}$ and **18**$^{\bullet+}$ have been previously shown to do so as well.[3] The rate data in Table 2 show that addition of a single methyl group at C_β leads to an increase in the rate constant for reaction with methanol. The effect is slightly larger for a cis-methyl group than a trans-methyl group. Addition of a second methyl group leads to either a small increase or decrease in rate constant relative to one methyl group depending on whether comparison is made to the trans- or cis-methyl derivatives. Based on these data we conclude that there may be a small internal steric component to the rate increase observed in the diphenylcyclopropane cation radical series. A clear interpretation of the data is complicated, however, by the prediction that the cation radical structures change significantly upon alkyl substitution (see below).

Cation Radical Structures. The most striking observation regarding the calculated structures for the arylcyclopropane cation radicals are the large structural changes that accompany alkyl-substitution at C_β (Table 3). Most notably, $r(C_\alpha-C_\beta)$ increases significantly upon alkyl-sustitution at C_β. This stands in marked contrast to the corresponding neutral cyclopropanes whose structures are comparatively insensitive to substitution. The likely origin of the structural changes can be deduced from the group charges listed in Table 3. It is seen that alkyl-substitution leads to a significant increase in $Q(C_\beta)$ and corresponding decreases in Q(Ph) and $Q(C_\gamma)$. It is reasonable to conclude from these data that the structural changes are driven by the ability of the alkyl groups to stabilize positive charge in the cation radicals.

The data in Table 3 also reveal that phenylcyclopropane cation radical is predicted to have a structure with two lengthened cyclopropane C−C bonds, whereas the alkyl-substituted derivatives have one lengthened bond. The calculated 2L1N structure for phenylcyclopropane cation radical is somewhat unusual for cyclopropane cation radicals which generally prefer 1L2N structures.[17,26] For this reason, it seemed of interest to determine to what degree a 2L1N structure was preferred in this case. This was assessed by fixing the plane of the phenyl ring such that it was colinear with the $C_\alpha-C_\gamma$ bond. As mentioned above, this structural feature is common to all of the alkyl-substituted phenylcyclopropane cation radicals, which have 1L2N structures. When optimized with this one constraint, the resulting phenylcyclopropane cation radical structure had one long cyclopropane bond: $r(C_\alpha-C_\beta) = 1.671$ Å. The other cyclopropane bond lengths ($r(C_\alpha-C_\gamma) = 1.526$ Å; $r(C_\beta-C_\gamma) = 1.430$ Å) were found to be comparable to those in the alkyl-substituted phenylcyclopropane cation radicals. Although the 1L2N structure for phenylcyclopropane cation radical is not predicted to be a minimum, its energy is only 1.0 kcal/mol above the 2L1N minimum. Thus it is clear that the potential energy surface for distortion of the phenylcyclopropane cation toward a long-bond structure is quite soft. Further rotation of the phenyl group causes a much steeper increase in the energy of the cation radical, however. For example, rotation by 90° leads to the transition state for rotational isomerization which is 12.0 kcal/mol higher in energy than the ground state, bisected structure.

Transition State Structures and Energies. Selected structural and electronic parameters for the AM1 and PM3 calculated transition states for backside nucleophilic attack of methanol on phenylcyclopropane cation radical are shown in Table 5. Several common trends are seen in the data. First, both methods predict $r(C_\alpha-C_\beta)$ to increase significantly on going from the reactants to the transition state. Second, both methods predict the $C_\alpha-C_\beta-O$ angle (θ) to be ca. 140°—far from the 180° angle nominally found in most conventional four-electron S_N2 reactions. Third, nucleophilic attack by methanol results in a substantial increase in $Q(C_\beta)$ from reactants to transition state (from 0.19 to ca. 0.4). The increase in $Q(C_\beta)$ comes largely at the expense of Q(Ph), which decreases from 0.68 to ca. 0.28. The large shift in positive charge away from the phenyl group provides an understanding of why the rate constants for nucleophilic sustitution on para-substituted phenylcyclopropane cation radicals correlate reasonably well with Hammett σ^+ substituent constants and why ρ is positive. Electron-donating substituents make it more difficult to transfer positive charge out of the phenyl group toward both C_β and the nucleophile upon substitution, which results in increased reaction barriers.

As shown in Table 5, both computational methods predict that alkyl substitution results in reasonably smooth changes in all of the transition state parameters except the activation energies. For example, $r^\ddagger(C_\beta-O)$ is predicted to continually decrease upon increasing alkyl-substitution. This change is understandably accompanied by increases in both $Q^\ddagger(C_\beta)$ and $Q^\ddagger$(HOMe). These trends suggest that the transition states generally become "later" with increasing alkyl-substitution. The increase in $r^\ddagger(C_\alpha-C_\beta)$ with increasing alkyl-substitution seems to be in accord with this conclusion. This measure of reaction progress must be analyzed cautiously, however, because the *reactant* $r(C_\alpha-C_\beta)$ distances also increase significantly upon alkyl-substitution (see Table 3). In fact, the $\Delta r(C_\alpha-C_\beta)$ variations for the ground state cation radicals exceed $\Delta r^\ddagger(C_\alpha-C_\beta)$ for the transition states. Other ground state cation radical parameters are also considerably affected by alkyl-substitution [e.g., $Q(C_\beta)$ and Q(Ph)]. For this reason, the estimation of progress along the reaction coordinate cannot be based solely on trends in the transition state properties.

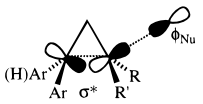
The increases in $Q^\ddagger(C_\beta)$ and $Q^\ddagger$(HOMe) with increasing alkyl-substitution show that substituents significantly polarize the transition states. These predictions are in agreement with the β-secondary kinetic isotope effects measured for the reaction

(25) Streitwieser, A. *Solvolytic Displacement Reactions*; McGraw-Hill: New York, 1962; p 13.

(26) Krogh-Jespersen, K.; Roth, H. D. *J. Am. Chem. Soc.* **1992**, *114*, 8388, and references therein.

of phenylcyclopropane cation radical (**16**$^{\bullet+}$) and *trans*-1-methyl-2-phenylcyclopropane cation radical (**17**$^{\bullet+}$) with *n*-BuOH vs d_9-*n*-BuOH. Inverse isotope effects are observed in both experiments, consistent with charge buildup on the nucleophile in the transition states. Reaction of **17**$^{\bullet+}$ shows a more inverse isotope effect, consistent with the greater $Q^{\ddagger}$(Nu) predicted in this case.

As mentioned above, the $C_\alpha-C_\beta-O$ angle (θ) for nucleophilic attack of methanol on phenylcyclopropane cation radical is significantly less than 180°. The reaction of cyclopropane cation radical ($C_3H_6^{\bullet+}$) with nucleophiles is also calculated to have a nucleophilic attack angle of <180°.[27] The origin of the deviation from a colinear displacement can be traced to the electronic mechanism of nucleophilic substitution. Using a valence bond model, the reaction barriers for three-electron S_N2 reactions on σ-cation radicals have been previously analyzed in terms of the crossing of two states that are related by single electron transfer from the nucleophile to the σ^* orbital of the bond undergoing nucleophilic attack.[28] The avoided crossing interaction of these states is proportional to the overlap between the nucleophile lone pair orbital and σ^*. The $C_\alpha-C_\beta-Nu$ angle which maximizes this overlap, and thereby minimizes the activation barrier, is expected to occur for θ <180° for the reaction of cyclopropane cation radicals with nucleophiles, as schematically illustrated below.



As shown in Table 5, both $r^{\ddagger}(C_\beta-O)$ and θ are calculated to decrease with increasing alkyl-substitution at the carbon atom undergoing nucleophilic displacement. The fact that θ decreases on going from *trans*-1-methyl-2-phenylcyclopropane cation radical to *trans*-1-*tert*-butyl-2-phenylcyclopropane cation radical, while $Q^{\ddagger}(C_\beta)$ and $Q^{\ddagger}$(HOMe) remain relatively unaffected, suggests that θ is at least partially controlled by steric factors. Consistent with this interpretation, methanol substitution on 1,1-dimethyl-2-phenylcyclopropane cation radical shows the smallest θ. It should be noted that the steric consequences of the trends in $r^{\ddagger}(C_\beta-O)$ and θ oppose each other. The decrease in $r^{\ddagger}(C_\beta-O)$ with alkyl-substitution increases the steric interactions between the nucleophile and the substituents attached to C_β. In contrast, the simultaneous decrease in θ decreases the steric interactions. Consequently, based on the calculations, it is difficult to predict the direction or magnitudes of the steric effects from the structural changes in the transition states. Thus it is not surprising that the calculated activation enthalpies for the corresponding nucleophilic substitution show no clear trend. For example, addition of a single alkyl group at C_β is predicted to have a modest effect on $\Delta H^{\ddagger}$, regardless of whether the substituent is cis or trans, large or small. However, addition of a second alkyl group is predicted to raise $\Delta H^{\ddagger}$ significantly.

The calculated $\Delta H^{\ddagger}$ values listed in Table 5 show a significant method dependence. $\Delta H^{\ddagger}$ calculated for reaction of phenylcyclopropane cation radical with methanol using PM3 is 7.0 kcal/mol higher than that calculated using AM1. A similar trend is seen in the remaining $\Delta H^{\ddagger}$ values. It is clear that the $\Delta H^{\ddagger}$ values calculated with PM3 are too large to be consistent with the experimental rate constants. Despite the absolute differences between the AM1 and PM3 data, the predicted trends in $\Delta H^{\ddagger}$ with alkyl-substitution at C_β are reasonably similar. The results are best described as in modest agreement with experiment, however. For example, addition of one methyl group at C_β is predicted to have little effect on $\Delta H^{\ddagger}$, consistent with the experimental rate data (Table 2). However, addition of a second methyl group is predicted to lead to a large increase in $\Delta H^{\ddagger}$ and thus a large decrease in rate constant. This is not observed experimentally. Further work will be required to understand the discrepancy.

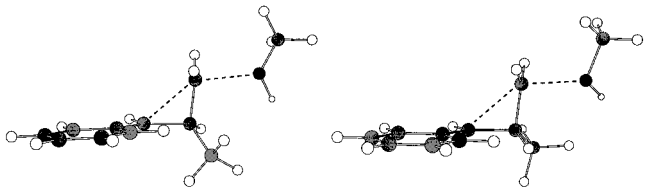


Figure 7. Transition states for nucleophilic substitution by methanol at C_γ on the cation radicals of *cis*-1-methyl-2-phenylcyclopropane (left) and *trans*-1-methyl-2-phenylcyclopropane (right)

Table 6 lists the calculated differential activation enthalpies for reaction of alkyl-substituted phenylcyclopropane cation radicals with methanol at C_β vs. C_γ. Here both computational methods give consistent results and good agreement with experiment. In all cases, a high regioselectivity for reaction at C_β is predicted and observed. An unanticipated result from these calculations is the prediction that the energetic preference for reaction of *cis*-1-methyl-2-phenylcyclopropane cation radical at C_β vs. C_γ is significantly greater than for the isomeric trans-cation radical. The likely origin of this effect can be seen by comparing the transition state structures for substitution at C_γ for the cis- and trans-cation radicals (Figure 7). Note that conjugation of the $C_\alpha-C_\gamma$ bond undergoing nucleophilic cleavage with the phenyl group leads to an eclipsing interaction between one of the ortho-phenyl hydrogens and the methyl group in the cis-isomer which is absent in the trans-isomer. As a result, substitution at C_γ in the cis-isomer is disfavored both sterically and electronically. Unfortunately, the prediction cannot be tested in these particular cases because both experimental regioselectivities are larger than can be accurately measured. Nonetheless, this may provide a new structural element which could be useful for controlling the regioselectivity of other nucleophilic substitutions.

Conclusions

The nucleophilic substitution reactions of arylcyclopropane cation radicals with alkyl-substitutents on the cyclopropane moiety proceed in good yields by an S_N2 mechanism on the ring-closed cation radicals. Substitution takes place at the most highly substituted carbon atom with a high degree of regioselectivity, even when the carbon is tertiary or neopentyl. Steric effects measured for alkyl substituents attached to the carbon atom undergoing substitution are very small. The preference for nucleophilic attack at the more substituted site is ascribed to the electron-donating ability of the alkyl-substituents which stabilize positive charge in the substitution transition states. This electronic effect is supported by experimental data (isotope effects and competitive substituent effects) and by computational results.

Experimental Section

The general techniques and apparatus are described in the experimental section of the preceding paper (*J. Am. Chem. Soc.* **1997**, *119*, 987).[2]

Ethyl *cis*- and *trans*-3-Methyl-2,2-Diphenylcyclopropanecarboxylate. Ethyl diazoacetate (1.20 mL, 11.4 mmol) was added over 6 h by means of a syringe pump to solution containing 1,1-diphenylpropene (25.72 mg , 132 mmol),[29] rhodium hexanoate dimer (38.28 mg, 57

(27) Shaik, S.; Reddy, A. C.; Ioffe, A.; Dinnocenzo, J. P.; Danovich, D.; Cho, J. K. *J. Am. Chem. Soc.* **1995**, *117*, 3205.

(28) Shaik, S. S.; Dinnocenzo, J. P. *J. Org. Chem.* **1990**, *55*, 3434.

μmol),[30] hexane (30 mL), and diethyl ether (10 mL). After 2 h, the resulting solution was concentrated. Column chromatography using hexane as an eluent (until the excess diene was eluted), followed by hexane:ethyl acetate (98:2) gave a mixture of the title compounds as a colorless oil (2.76 g, 86%). Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.00; H, 7.17. The isomers were separated by medium pressure liquid chromatography.

Ethyl *cis*-3-Methyl-2,2-diphenylcyclopropanecarboxylate. (1.44 g, 45%): ^{1}H NMR ($CDCl_3$): δ 7.32−7.10 (m, 9.74 H), 4.16−4.03 (m, 2.03 H), 2.40 (d, J = 8.9, 0.98 H), 2.12−2.03 (m, 1.05 H), 1.45 (d, J = 6.6, 3.14 H), 1.21 (t, J = 7.1, 3.07 H).

Ethyl *trans*-3-Methyl-2,2-diphenylcyclopropanecarboxylate. (0.77 g, 24%): ^{1}H NMR ($CDCl_3$): δ 7.35−7.09 (m, 10.04 H), 3.93−3.85 (m, 1.93 H), 2.43 (m, 0.97 H), 2.28 (d, J = 5.6 Hz, 0.97 H), 1.01−0.96 (m, 6.09 H).

***cis*-3-Methyl-2,2-diphenylcyclopropanemethanol.** A solution of ethyl *cis*-3-methyl-2,2-diphenylcyclopropanecarboxylate (2.27 g, 8.08 mmol) in tetrahydrofuran (3 mL) was added dropwise over 1 h to a stirred suspension of lithium aluminum hydride (271 mg, 7.14 mmol) and tetrahydrofuran (30 mL). After refluxing for 2.5 h, water (5 mL) was carefully added. The mixture was transferred into a separatory funnel along with diethyl ether (50 mL) and a 70 mL of a 5% HCl solution. The layers were separated and the aqueous phase was extracted with ether (3 × 70 mL). The combined organic layer was washed with water, dried, concentrated, and distilled (140−145 °C, 0.03 mm Hg) to give a light yellow oil (1.76 g, 92%). ^{1}H NMR ($CDCl_3$): δ 7.36−7.06 (m, 9.85 H), 3.92−3.87 (m, 1.03 H), 3.55 (dd, J = 10.2, 5.4, 1.03 H), 1.84−1.70 (m, 2.19 H), 1.33 (brs, 0.99 H), 1.16 (d, J = 6.3, 2.91 H). Anal. Calcd for $C_{17}H_{18}O_1$: C, 85.67; H, 7.61. Found: C, 85.41; H, 7.61.

***trans*-3-Methyl-2,2-diphenylcyclopropanemethanol.** This material was prepared using the same procedure as above except ethyl *trans*-3-methyl-2,2-diphenylcyclopropanecarboxylate (1.98 g, 7.07 mmol) was used. The resulting product was distilled (140−145 °C, 0.03 mmHg) to give a clear light yellow oil (1.44 g, 85%). ^{1}H NMR ($CDCl_3$): δ 7.35−7.13 (m, 10.04 H), 3.51 (dd, J = 11.3, 6.0, 0.97 H), 3.30 (dd, J = 11.3, 7.9, 0.99 H), 1.74−1.62 (m, 2.03 H), 1.31 (broad s, 1.00 H), 0.93 (d, J = 5.9, 2.96 H). Anal. Calcd for $C_{17}H_{18}O_1$: C, 85.67; H, 7.61. Found: C, 85.54; H, 7.64.

***cis*-3-Methyl-2,2-diphenylcyclopropaneacetonitrile (6).** *p*-Toluenesulfonyl chloride (0.778 g, 4.1 mmol) was added in several portions to a solution of *cis*-3-methyl-2,2-diphenylcyclopropanemethanol (0.896 g, 3.8 mmol) and pyridine (9.0 mL) which was maintained at −10 °C. After 15 min, the solution was warmed to 4° for 12 h. The reaction mixture was then poured into a separatory funnel containing ice-cold methylene chloride (100 mL). The organic layer was washed successively with 20 mL portions of cold water, cold 5% HCl, cold 5% sodium bicarbonate, and cold brine. It was then dried and concentrated to give 0.33 g of a light yellow oil. This material was immediately placed in a flask containing a solution of tetra-*n*-butylammonium cyanide (3.66 g, 13.6 mmol) in DMSO (15 mL). After 2 h the solution was poured into a separatory funnel with pentane (100 mL) and water (50 mL). After separation of the layers, the aqueous layer was extracted with pentane (3 × 30 mL). The combined organic layers were washed with brine, dried, and concentrated to give a yellow oil which gave after column chromatography (97:3 hexane:ethyl acetate) a white solid (339 mg, 36%). ^{1}H NMR ($CDCl_3$): δ 7.40−7.09 (m, 10.12 H), 2.46 (dd, J = 17.3, 1.00 H), 2.21 (dd, J = 17.3, 7.3, 1.04 H), 1.92−1.84 (m, 0.97 H), 1.80−1.72 (m, 0.99 H), 1.18 (d, J = 6.6, 2.87 H). ^{13}C NMR ($CDCl_3$): δ 146.72, 137.20, 131.09, 128.79, 128.15, 126.77, 125.81, 119.24, 37.38, 24.49, 22.98, 15.22, 10.80. Anal. Calcd for $C_{18}H_{17}N_1$: C, 87.41; H, 6.93. Found: C, 87.21; H, 6.88.

***trans*-3-Methyl-2,2-diphenylcyclopropaneacetonitrile (7)**. This material was prepared using the same procedure as above except *trans*-3-methyl-2,2-diphenylcyclopropanemethanol was used instead. Purification of the crude product by column chromatography (90:10 hexane:ethyl acetate) gave a white solid (0.27 g, 52%). ^{1}H NMR ($CDCl_3$): δ 7.34−7.18 (m, 10.23 H), 2.23−2.01 (m, 2.08 H), 1.71−1.60 (m, 1.91 H), 0.97 (d, J = 6.0, 2.77 H). ^{13}C NMR ($CDCl_3$): δ 141.64, 141.55, 129.86, 128.72, 128.39, 126.88, 126.51, 119.35, 41.25, 25.79, 22.80, 18.56, 14.89. Anal. Calcd for $C_{18}H_{17}N_1$: C, 87.41; H, 6.93. Found: C, 87.11; H, 6.99.

(2*R,3*R**)-3-Methyl-4,4-diphenyl-2-butanol.** Under an argon atmosphere, lithium (154 mg, 22 mmol) was added to a solution of biphenyl (1.54 g, 10 mmol) and 1,1,2,2-tetraphenylethane (3.35 g, 10 mmol)[29] in tetrahydrofuran (85 mL). After 2 h, the reaction mixture was refluxed for 45 min and then cooled to −10 °C. *trans*-2,3-Epoxybutane (1.21 mL, 14 mmol) in tetrahydrofuran (15 mL) was added dropwise over 45 min. The reaction mixture was warmed to room temperature for 2.5 h and then several drops of water were carefully added. Extractive workup followed by column chromatography (starting with methylene chloride followed by ether) gave a clear colorless oil (2.29 g, 69%). ^{1}H NMR ($CDCl_3$): δ 7.43−7.11 (m, 9.99 H), 3.87 (d, J = 11.5, 0.93 H), 3.79−3.72 (m, 1.01 H), 2.38−2.27 (m, 0.95 H), 1.25 (brs, 1.09 H), 1.17 (d, J = 6.5, 3.06 H), 0.84 (d, J = 6.7, 2.97 H).

(2*S,3*R**)-3-Methyl-4,4-diphenyl-2-butanol.** This material was prepared using the same procedure as above except *cis*-2,3-epoxybutane was used. Column chromatography (85:15 methylene chloride:ethyl aceate) gave a clear colorless oil (97%). ^{1}H NMR ($CDCl_3$): δ 7.32−7.12 (m, 10.41 H), 3.79−3.71 (m, 0.94 H), 3.58 (d, J = 11.1, 1.02 H), 2.72−2.60 (m, 0.99 H), 1.41 (broad s, 1.01 H), 1.08 (d, J = 6.3, 2.77 H), 0.82 (d, J = 6.7, 2.77 H).

(2*R,3*R**)-3-Methoxy-2-methyl-1,1-diphenylbutane (7a′).** (2*R**, 3*R**)-3-Methyl-4,4-diphenyl-2-butanol (406 mg, 1.7 mmol) in tetrahydrofuran (2 mL) was added dropwise over 20 min by means of a syringe pump to a mixture of sodium hydride (51 mg, 2.1 mmol), methyl iodide (156 μL, 355 mg, 2.5 mmol), and tetrahydrofuran (6 mL) maintained at 46 °C. After 30 min, additional methyl iodide (50 μL, 114 mg, 0.8 mmol) was added. After 2.5 h, the reaction mixture was cooled to room temperature, and several drops of water were carefully added. Extractive workup followed by column chromatography (95:5 hexane:ethyl acetate) gave a clear colorless oil which formed a white solid on standing (345 mg, 80%). ^{1}H NMR ($CDCl_3$): δ 7.34−7.11 (m, 10.33 H), 3.56 (d, J = 11.4, 0.98 H), 3.25 (s, 2.86 H) 3.24−3.16 (m, 0.97 H), 2.88−2.76 (m, 1.01 H), 1.01 (d, J = 6.3, 2.90 H), 0.78 (d, J = 6.7, 2.95 H). Anal. Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.78; H, 8.68.

(2*S,3*R**)-3-Methoxy-2-methyl-1,1-diphenylbutane (6a′).** This material was prepared using the same procedure as above except (2*S**,3*R**)-3-methyl-4,4-diphenyl-2-butanol was used. Chromatography (98:2 hexane:ethyl acetate) gave a clear colorless oil which formed a white solid on standing in the freezer (60%). ^{1}H NMR ($CDCl_3$): δ 7.33−7.10 (m, 10.43 H), 3.94 (d, J = 11.5, 0.91 H), 3.14−3.07 (m, 3.77 H) 2.30−2.21 (m, 0.93 H), 1.09 (d, J = 6.3, 3.01 H), 0.83 (d, J = 6.8, 2.95 H). Anal. Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 85.02; H, 8.71.

Reduction of Products from the 1-Cyanonaphthalene-Sensitized Photooxidations of *cis*-3-Methyl-2,2-diphenylcyclopropaneacetonitrile (6) and *trans*-3-Methyl-2,2-diphenylcyclopropaneacetonitrile (7) in Methanol. Reductive decyanation[9] of the product obtained from the photooxidation of *cis*-3-methyl-2,2-diphenylcyclopropaneacetonitrile gave a product which showed an identical GC rentention time and ^{1}H NMR spectrum to independently synthesized **6a′**, prepared as described

(29) Simes, B. E.; Rickborn, B.; Fluornoy, J. M. Berlman, I. B. *J. Org. Chem.* **1988**, *53*, 4613.

(30) Johnson, S. A.; Hunt, H. R.; Neumann, H. M. *Inorg. Chem.* **1963**, *2*, 960.

(31) (a) Miller, J. B. *J. Org. Chem.* **1959**, *24*, 560. (b) Smith, L. I.; Howard, K. L. *Organic Synthesis* Wiley: New York, 1959; Collect Vol. 3, p 351.

(32) Walborsky, H. M.; Murari, M. P. *Can. J. Chem.* **1984**, *62*, 2464.

(33) (a) Pretch, E.; Clerc, T.; Seibl, J.; Simon, W. *Tables of Spectral Data for Structure Determination of Organic Compounds*; Springer-Verlag: Berlin, 1983; p I-190. (b) Socrates, G. *Infrared Characteristic Group Frequencies*, Wiley-Interscience: Chichester, 1980; p 55. (c) Meyers, A. I.; Ritter, J. J. *J. Org. Chem.* **1958**, *23*, 1918.

(34) MOPAC93; Dr. J. J. P. Stewart & Fujitsu Ltd., Tokyo, 1993.

(35) (a) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Petterson, G. A.; Montgomery, J. A.; Raghavari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Repogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. *Gaussian 94, versions C.3 & D.1*; Gaussian, Inc.: Pittsburgh, PA, 1995.

above. Analogously, application of the reaction to the product obtained from photooxidation of *trans*-3-methyl-2,2-diphenylcyclopropaneacetonitrile gave a product which showed an identical GC rentention time and ^{1}H NMR spectrum to independently synthesized **7a′**, prepared as described above.

3-Methoxy-3-methyl-1-phenylbutane (8a). A solution of α,α-dimethylbenzenepropanol (0.289 g, 1.76 mmol) in tetrahydrofuran (2 mL) was added over 5 min to a suspension of sodium hydride (54.5 mg, 2.27 mmol), methyl iodide (160 μL, 2.57 mmol), and tetrahydrofuran (6 mL) maintained at 40 °C. After 30 min, additional methyl iodide (100 μL, 1.61 mmol) was added. After 1.5 h, extractive workup gave a light yellow oil which, after chromatography (90:10 hexane: ethyl acetate), gave a colorless liquid (0.285 g, 94% yield). ^{1}H NMR ($CDCl_3$): δ 7.30−7.20 (m, 4.59 H), 3.26 (s, 2.87 H), 2.69−2.64 (m, 2.03 H), 1.83−1.77 (m, 2.01 H), 1.24 (s, 6.50 H).

2-*tert*-Butyl-1,1-diphenylcyclopropane (12). Diphenyldiazomethane[31] (0.978 g, 5.03 mmol) was reacted with 3,3-dimethyl-1-butene (26.12 g, 310 mmol) following a literature procedure.[6] Removal of the volatiles followed by extraction with pentane gave an orange oil which after vacuum distillation (0.01 mmHg, 78−82 °C) afforded 0.666 g (53%) of a clear oil. ^{1}H NMR ($CDCl_3$): δ 7.16−7.51 (m, 10.23 H), 1.68 (m, 0.93 H), 1.58 (m, 0.98 H), 1.11 (dd, J = 9.4, 4.6, 0.98 H), 0.87 (s, 8.88 H). Anal. Calcd for $C_{19}H_{22}$: C, 91.14; H, 8.86. Found: C, 91.30; H, 8.86.

3-Methoxy-2,2-dimethyl-1,1-diphenylpropane (14). Lithium (16.5 mg, 2.38 mmol) was added to a solution of 4,4′-di-*tert*-butylbiphenyl (681 mg, 2.56 mmol) in THF (6 mL) at 0 °C. After 3 h, the solution was cooled to −78 °C, and 3,3-dimethyl-2,2-diphenyloxetane[10] (0.250 g, 1.05 mmol) in THF (650 μL) was added dropwise. After 3 h, the solution was warmed to room temperature. After 10 h, extractive work-up followed by chromatography (90:10 hexane:ethyl acetate) gave a light yellow oil shown to be 2,2-dimethyl-3,3-diphenyl-1-propanol (0.182 g, 69%). ^{1}H NMR ($CDCl_3$): δ 7.47 (d, J = 7.4, 4 H), 7.16−7.33 (m, 6 H), 4.07 (s, 1 H), 3.35 (d, J = 6.0, 2 H), 1.38 (t, J = 6.0, 0.9 H), 1.03 (s, 6.1 H). A solution of the alcohol (59 mg, 0.25 mmol) in THF (0.31 mL) was added dropwise over 25 min to a solution of NaH (0.100 g, 4.2 mmol) and iodomethane (57 mg, 0.42 mmol) in THF (800 μL) maintained at 45 °C. Extractive work-up followed by column chromatography (90:10 hexane:ethyl acetate) gave 12 mg of the title compound **14**. ^{1}H NMR ($CDCl_3$): δ 7.47 (d, J = 7.4, 4H), 7.17−7.35 (m, 6H), 4.17 (s, 1H), 3.27 (s, 2.8 H), 2.95 (s, 1.8H), 1.04 (s, 1H). HRMS (CI) calcd for $C_{18}H_{23}O$ (M + 1): 255.1748. Found: 255.1748.

2-*tert*-Butyl-3-methoxy-1,1-diphenylpropane (15). Reaction of benzophenone with 3,3-dimethyl-1-butene following a literature procedure[10] gave 3-*tert*-butyl-2,2-diphenyloxetane. ^{1}H NMR ($CDCl_3$): δ 7.17−7.58 (m, 10H), 4.65 (dd, J = 9, 8, 1 H), 4.54 (dd, J = 9, 8, 1 H), 3.61 (t, J = 9, 1 H), 0.72 (s, 9 H). Reduction with lithium as described above gave 2-*tert*-butyl-3,3-diphenyl-1-propanol. ^{1}H NMR ($CDCl_3$): δ 7.16−7.41 (m, 10 H), 4.20 (d, J = 9, 0.9 H), 3.60−3.75 (m, 1.9 H), 2.31−2.38 (m, 0.9 H), 0.92 (s, 9.3 H). Methylation as described above gave the title compound **15** (7%). ^{1}H NMR ($CDCl_3$): δ 7.07−7.44 (m, 10 H), 4.19 (d, J = 9, 1 H), 3.14−3.30 (m, 2 H), 2.84 (s, 3 H), 2.26−2.35 (m, 1 H), 0.88 (s, 9 H). HRMS (CI) calcd for $C_{20}H_{27}O$ (M + 1): 283.2061. Found: 283.2063.

***Trans*- and *cis*-1-methyl-2-phenylcyclopropane (17)** and **(18)** were synthesized according to the procedure of Casey *et al*.[4a] Distillation of the crude reaction mixture (3.37 g; 75%) afforded a mixture of the title compounds **17** and **18** as a colorless oil (1.18 g, 26%). The isomers were separated by preparative GC (10′ × 1/4″ Apiezon L + 2% KOH on Chromosorb W-AW 80/100).

***trans*-1-Methyl-2-phenylcyclopropane (17).** ^{1}H NMR ($CDCl_3$): δ 7.25−7.03 (m, 5.34 H), 1.61−1.55 (m, 0.92 H), 1.20 (d, J = 5.8, 2.92 H), 1.11−1.02 (m, 0.92 H), 0.92−0.86 (m, 0.95 H), 0.78−0.72 (m, 0.95 H).

***cis*-1-Methyl-2-phenylcyclopropane (18).** ^{1}H NMR ($CDCl_3$): δ 7.31−7.16 (m, 5.07 H), 2.13−2.06 (m, 0.96 H), 1.20−1.11 (m, 0.95 H), 1.03−0.95 (m, 1.03 H), 0.81 (d, J = 6.2, 2.95 H), 0.62−0.57 (m, 0.99 H).

Photooxidations. General Procedure. A Pyrex photolysis vessel was charged with a solution containing the cyclopropane, 1-cyanonaphthalene, and internal standard in methanol, except for the preparative reactions which contained no internal standard. The solution was degassed by three freeze−pump−thaw cycles and then sealed with a hand torch. The sealed tube was placed in a Rayonet photoreactor and irradiated with nominal 300 nm light bulbs. The reaction mixture was subsequently analyzed by GC, in which the retention times were compared with those of independently synthesized materials where available. All reported yields are based on GC analysis of the analytical reactions which were run in duplicate. A portion (typically 3−6 mg) of the major products were isolated by preparative GC (column: 6′ × 3/8″ 17% XF-1150 on Anachrom Q, except when noted otherwise) and analyzed by ^{1}H NMR, GC, and other techniques as described.

Photooxidation of *cis*-3-Methyl-2,2-diphenylcyclopropaneacetonitrile (6) in Methanol. A degassed solution of **6** (154 mg, 623 μmol) and 1-cyanonaphthalene (67 mg, 438 μmol) in methanol (12.0 mL) was irradiated for 73 h. Concentration followed by column chromatography (85:15 hexane:ethyl acetate) gave a light yellow oil (145 mg, 83%), **6a**. ^{1}H NMR ($CDCl_3$): δ 7.38−7.16 (m, 10.05 H), 4.12 (d, J = 11.8, 1.00 H), 3.27−3.18 (m, 1.03 H), 3.17 (s, 2.94 H), 2.64−2.57 (m, 0.95 H), 2.46 (dd, J = 17.1, 7.2, 1.00 H), 2.30 (dd, J = 17.4, 2.8, 1.01 H), 1.23 (d, J = 6.2, 3.03 H). ^{13}C NMR ($CDCl_3$): δ 141.66, 141.57, 128.77, 128.67, 127.57, 127.28, 126.79, 126.54, 119.03, 75.65, 55.82, 52.74, 41.51, 14.80, 13.18. Anal. Calcd for $C_{19}H_{21}N_1O_1$: C, 81.68; H, 7.58. Found: C, 81.53; H, 7.37.

Photooxidation of *trans*-3-Methyl-2,2-diphenylcyclopropaneacetonitrile (7) in Methanol. The same procedure as above was followed except **7** was used. Column chromatography (85:15 hexane: ethyl acetate) gave a light yellow oil (80%), **7a**. ^{1}H NMR ($CDCl_3$): δ 7.39−7.16 (m, 10.29 H), 3.90 (d, J = 12.3, 0.97 H), 3.40−3.33 (m, 0.98 H), 3.26 (s, 2.86 H), 3.06−2.98 (m, 1.01 H), 2.52 (dd, J = 17.1, 3.1, 1.02 H), 2.21 (dd, J = 17.1, 6.6, 1.01 H), 1.15 (d, J = 6.5, 2.86 H). ^{13}C NMR ($CDCl_3$): δ 142.84, 142.35, 129.08, 128.80, 128.03, 127.95, 126.95, 126.67, 119.97, 74.55, 56.41, 53.88, 45.65, 17.27, 14.89. Anal. Calcd for $C_{19}H_{21}N_1O_1$: C, 81.68; H, 7.58. Found: C, 81.32; H, 7.54.

Photooxidation of 1,1-Dimethyl-2-phenylcyclopropane (8) in Methanol. A degassed solution of **8** (25.0 mg, 0.163 mmol)[6] and 1-cyanonaphthalene (4.3 mg, 28.1 μmol) in methanol (50 μL) was irradiated for 1.25 h. GC analysis showed the retention time of the major product (99%) to be identical to that of independently synthesized 3-methoxy-3-methyl-1-phenylbutane (**8a**). A portion of this product was isolated by column chromatography (90:10 hexane:ethyl acetate) and gave a colorless liquid whose ^{1}H NMR was identical to that of **8a**. ^{1}H NMR ($CDCl_3$): δ 7.30−7.20 (m, 5.07 H), 3.26 (s, 3.04 H), 2.69−2.64 (m, 1.97 H), 1.83−1.77 (m, 2.00 H), 1.24 (s, 5.92 H).

Photooxidation of 2-Methyl-1,1-diphenylcyclopropane (9) in Methanol. Analytical scale: A degassed solution of **9** (10 mg, 48 μmol),[6] 1-cyanonaphthalene (2.6 mg, 17 μmol), and tetraethylene glycol dimethyl ether (15 μL, internal standard) in methanol (600 μL) was irradiated for 28 h. GC analysis showed 99% conversion and formation of one product (86%; **9a**). Preparative scale: A degassed solution of **9** (125 mg, 600 μmol) and 1-cyanonaphthalene (46.5 mg, 310 μmol) in methanol (9 mL) was irradiated for 39 h. GC analysis showed formation of 83% of product and 13% remaining cyclopropane. Purification by column chromatography (neutral alumina; 95:5 hexane: ether) gave 29 mg (22% yield) of oil which was spectrally identical to a sample of 3-methoxy-1,1-diphenylbutane (**9a**).[32]

Photooxidation of 2-Ethyl-1,1-diphenylcyclopropane (10) in Methanol. Analytical scale: Same conditions as for **9** except irradiation time was 16 h. GC analysis showed >99% conversion and formation of one product (87%; **10a**). Preparative scale: Same conditions as for **9**. GC analysis showed formation of 82% product and 14% remaining cyclopropane. Column chromatography as described for **9**, gave 79 mg (58%) of pure material, which was characterized to be 3-methoxy-1,1-diphenylpentane (**10a**). ^{1}H NMR ($CDCl_3$): δ 7.17−7.35 (m, 9.85 H), 4.23 (t, J = 7.9, 0.98 H), 3.27 (s, 3.00 H), 2.99 (m, 0.98 H), 2.21 (dd, J = 8.1, 6.0, 2.03 H), 1.57 (dq, J = 7.4, 5.2, 2.03 H), 0.91 (t, J = 7.4, 3.14 H). HRMS (EI) Calcd for $C_{18}H_{22}O$ (M^+): 254.1671. Found: 254.1671.

Photooxidation of 2-Isopropyl-1,1-diphenylcyclopropane (11) in Methanol. Analytical scale: Same conditions as for **10**. GC analysis showed >99% conversion and formation of one product (85%; **11a**). Preparative scale: A degassed solution of **11** (49.1 mg, 208 μmol) and

1-cyanonaphthalene (8.0 mg, 52 μmol) in methanol (1 mL) was irradiated for 12 h. GC analysis showed formation of 82% product and 14% remaining cyclopropane. Column chromatography as described for **9** gave 29 mg (31%) pure material, which was characterized to be 3-methoxy-4-methyl-1,1-diphenylpentane (**11a**). ^{1}H NMR ($CDCl_3$): δ 7.14−7.34 (m, 9.86 H), 4.22 (dd, J = 10.9, 4.9, 0.94 H), 3.26 (s, 2.82 H), 2.82 (m, 1.00 H), 2.20 (m, 1.06 H), 2.04 (ddd, J = 13.8, 8.2, 4.9), 1.92 (m, 2.05 H including δ 2.04 peak), 0.88 (2 d, J = 6.7, 6.7, 6.3 H).

Photooxidation of 2-*tert*-Butyl-1,1-diphenylcyclopropane (12) in Methanol. Analytical scale: Same conditions as for **9** except irradiation time was 40 h. GC analysis showed 86% conversion and formation of four products: **12a** (60%), **12b** (6.1%), **12c** (3.6%) and **12d** (3.7%). GC analysis showed that relative to **12a**, <0.1% of the independently synthesized **15** was present in the crude reaction mixture. Preparative scale: A degassed solution of **12** (1.80 g, 7.19 mmol) and 1-cyanonaphthalene (440 mg, 2.87 mmol) in methanol (50 mL) was irradiated for 91 h. The crude material was purified by flash column chromatography (95:5 hexane:ether) to give 80 mg of pure **12a**. Purification of **12d** was achieved by using preparative GC (10% OV-1 on Chromosorb W/AW). Compounds **12b** and **12c** were isolated from the reaction in acetonitrile (*vide infra*).

12a: ^{1}H NMR ($CDCl_3$): δ 7.15−7.35 (m, 9.88 H), 4.24 (dd, J = 11.8, 4.1, 0.99 H), 3.35 (s, 2.90 H), 2.68 (dd, J = 10.2, 1.4, 0.99 H), 2.37 (ddd, J = 14.0, 11.6, 1.4, 0.99 H), 1.99 (ddd, J = 14.4, 10.3, 3.9, 0.99 H), 0.90 (s, 9.26 H).

12d: ^{1}H NMR ($CDCl_3$): δ 7.13−7.70 (m, 10.83 H), 4.00 (dd, J = 12.1, 3.4, 1.00 H), 2.96 (s, 2.71 H), 2.44 (t, J = 11.8, 1.00 H), 1.59 (m, 2.07 H), 1.08 (2 s, 5.56 H), 0.93 (d, J = 6.7, 2.85 H).

Photooxidation of 2-*tert*-Butyl-1,1-diphenylcyclopropane (12) in Acetonitrile. Analytical scale: Same conditions as for **12**. GC analysis showed 100% conversion and formation of three products: **12b** (25%), **12c** (47%), and **12e** (7%). Preparative scale: A degassed solution of **12** (253 mg, 1.02 mmol) and 1-cyanonaphthalene (39.4 mg, 260 μmol) in acetonitrile (4.5 mL) was irradiated for 37 h. The products were isolated by flash chromatography followed by preparative GC (6′ × 1/4″10% Apiezon L + 2% KOH on Chromosorb W/AW 80/100).

12b: ^{1}H NMR ($CDCl_3$): δ 7.46 (d, J = 7.7, 0.95 H), 7.18−7.29 (m, 4.43 H), 7.02−7.09 (m, 2.37 H), 6.89 (d, J = 7.7, 0.95 H), 4.22 (t, J = 5.4, 0.95 H), 2.00−2.06 (m, 1.03 H), 1.55−1.91 (m, 2.06 H), 1.40 (s, 3.09 H), 1.22 (s, 3.17 H), 0.94 (d, J = 6.8, 3.01 H). HRMS (EI) Calcd for $C_{19}H_{22}$ (M^+): 250.1722. Found, 250.1710.

12c: ^{1}H NMR ($CDCl_3$): δ 7.44 (d, J = 7.9, 0.95 H), 7.14−7.33 (m, 5.67 H), 6.97 (t, J = 7.4, 0.95 H), 6.73 (d, J = 7.8, 0.87 H), 4.08 (dd, J = 10.9, 6.4, 0.95 H), 1.78−1.92 (m, 3.15 H), 1.40 (s, 3.15 H), 1.23 (s, 3.23 H), 0.94 (d, J = 6.3, 3.08 H).

12e: ^{1}H NMR ($CDCl_3$): δ 7.15−7.38 (m, 9.67 H), 3.60 (m, 1.09 H), 2.54 (dd, J = 13.2, 6.4, 1.09 H), 2.38 (dd, J = 13.2, 9.9, 1.09 H), 1.92 (d, J = 2.1, 2.92 H), 1.02 (s, 9.12 H). Decoupling at δ 1.9 simplifies δ 3.6 to a dd with J = 9.8 and 6.4 Hz; these couplings correspond to those between the methine hydrogen and the two diastereotopic methylene hydrogens. IR ($CDCl_3$): 1643 cm^{-1} (C═N stretch).[33] HRMS (EI) Calcd for $C_{21}H_{25}N$ (M^+): 291.1987. Found, 291.1963.

Photooxidation of 1,1-Diphenylcyclopropane (13) in Methanol. Analytical scale: Same conditions as for **9** except irradiation time was 27 h. GC analysis showed 100% conversion and formation of one product, **13a** (93%). GC analysis showed that relative to **13a**, <0.01% of independently synthesized **14** was present in the crude reaction mixture. Preparative scale: A degassed solution of **12** (20.6 mg, 92.8 μmol) and 1-cyanonaphthalene (3.5 mg, 23 μmol) in methanol (750 μL) was irradiated for 13 h. Purification of the crude by preparative GC (6′ × 1/4″ 10% Apiezon L + 2% KOH on Chromosorb W/AW 80/100) gave **13a**. ^{1}H NMR ($CDCl_3$): δ 7.14−7.37 (m, 10.56 H), 4.17 (t, J = 6.3, 1.04 H), 3.12 (s, 2.88 H), 2.36 (d, J = 6.4, 1.92 H), 1.05 (s, 5.60 H).

Photooxidation of 1,1-Dimethyl-2,2-diphenylcyclopropane (13) in Acetonitrile. Analytical scale: Same conditions as for **13**. GC analysis showed 100% conversion and formation of one product, **13e** (94%). Preparative scale: A degassed solution of **13** (0.226 g, 1.02 mmol) and 1-cyanonaphthalene (63 mg, 23 μmol) in acetonitrile (15 mL) was irradiated for 83 h. Purification of the crude reaction product by flash column chromatography (80:20 hexane:benzene) gave 124 mg of **13e**. ^{1}H NMR ($CDCl_3$): δ 7.18−7.34 (m, 10.28 H), 2.61 (s, 2.00 H), 1.85 (s, 2.88 H), 1.28 (s, 5.84 H). IR ($CDCl_3$): 1647 cm^{-1} (C═N stretch).[33] HRMS (EI) Calcd for $C_{19}H_{21}N$ (M^+): 263.1674. Found 263.1635. Calcd for $C_{18}H_{18}N$ ($M^+ - 15$): 248.1439. Found: 248.1471.

Kinetic Isotope Effects. Phenylcyclopropane (0.20 g), 1-cyanonaphthalene (0.04 g), *n*-butanol (1.00 g) and 1,1,2,2,3,3,4,4,4-nonadeuteriobutanol (1.00 g) were dissolved in acetonitrile to make up 50.0 mL solution. Aliquots (5.0 mL) were added to Pyrex tubes which were purged with argon, sealed, and irradiated in a Rayonet photoreactor at 300 nm for 2 h at 20 °C. Samples of the unirradiated and irradiated reaction solutions were analyzed by GC. The unirradiated samples provided the ratio of isotopologic butanol and the irradiated samples the ratios of the isotopologic products. All experiments were performed in triplicate, and all samples were analyzed at least five times by GC. Control experiments showed that the product isotope ratio did not vary within the reaction time. To determine the isotope effect on the GC detection, both isotopologic products ($Ph(CH_2)_3OC_4H_9$ and $Ph(CH_2)_3OC_4D_9$) were synthesized independently. Phenylcyclopropane (0.30 g), 1-cyanonaphthalene (0.10 g), and *n*-butanol (1.00 g) were dissolved in acetonitrile to make up a 7 mL solution. This was irradiated for 21 h under argon (GC: 96% yield of $Ph(CH_2)_3OC_4H_9$). The product was isolated by preparative TLC (90:10 hexane:ethyl acetate) to give 0.189 g (39%) of $Ph(CH_2)_3OC_4H_9$. ^{1}H NMR ($CDCl_3$): δ 7.28−7.43 (m, 5 H), 3.51 (t, J = 6.0, 2H+2H), 2.80 (t, J = 8.0, 2 H), 1.98−2.03 (m, 2 H), 1.66−1.71 (m, 2 H), 1.49−1.54 (m, 2 H), 1.05 (t, J = 8.0, 3 H). ^{13}C NMR ($CDCl_3$): δ 142.55, 128.74, 126.18, 71.14, 70.33, 32.88, 32.42, 31.86, 19.92, 14.43. Analogously, an independent experiment with HOC_4D_9 gave $Ph(CH_2)_3OC_4D_9$ (19%). ^{1}H NMR ($CDCl_3$): δ 7.28−7.43 (m, 5 H), 3.48 (t, J = 6.0, 2 H), 2.76 (t, J = 8.0, 2 H), 1.92−2.01 (m, 2 H).

The isotope effects on the response factors (signal H/signal D) were subsequently determined to be 1.0124 ± 0.0024 (butanols) and 1.0135 ± 0.0024 (products). Since their ratio equals 1 within experimental error, no additional correction factor was applied. On the basis of this, no correction factor was applied in the case of **15** also.

Computational Methods. Semiempirical calculations (ROHF) were performed with MOPAC93[34] using the AM1 and PM3 parameters implemented therein. Transition states were located (with keyword **TS**) using the highest point of a reaction coordinate calculations (variation of C−O with 0.1 Å, from 3.0 to 1.6 Å) to obtain a reasonable starting geometry for the transition state optimization. B3LYP calculations were performed with Gaussian 94, using the 6-31G* basis set implemented therein.[35]

Acknowledgment. Research support was provided by the National Science Foundation (CHE-9312460) and by the donors of the Petroleum Research Foundation, administered by the American Chemical Society. T.R.S is the recipient of an Elon Huntington Hooker Graduate Fellowship. H.Z. is grateful to the Netherlands Organization for Scientific Research (NWO) for a postdoctoral Talent-stipendium.

Supporting Information Available: Gaussian 94 archive files are available for the B3LYP/6-31G* optimized minima (2 pages). See current masthead page for ordering and Internet access instructions.

JA963112S