# Photoinduced Electron-Transfer Substitution Reactions via Unusual Charge-Transfer Intermediates

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The photoinduced substitution reactions of halogenated alkanes (1-haloadamantanes, 1-haloronorbornanes, menthyl chloride) with a homologous series of amines or alcohols (methylamine, 2-methyl-2-aminopropane, methanol, or 2-methyl-2-propanol) to form the corresponding alkane-substituted amines or ethers and HCl were investigated. The geometry of the bridgehead carbons made $S_N2$ reactions impossible. Nonpolar reaction conditions were employed which made classical and nonclassical carbocation $S_N1$ reaction pathways unlikely. The reaction rates were measured. Trapping experiments indicated that free radical reactions were uninvolved in the substitution product formation. A novel, photoinduced electron-transfer reaction mechanism involving a charge-transfer intermediate is proposed to explain the observed production of secondary amines and ethers. The excitation wavelength dependence (action spectrum) was measured and found to be comparable to the ultraviolet absorption spectra of the charge-transfer complexes. The stereochemical implications of the reaction mechanism were investigated. The formation of the methyl ether of (1*R*,2*S*,5*R*)-menthol was the only organic reaction product observed in the photoreaction between (1*R*,2*S*,5*R*)-menthyl chloride and methanol.

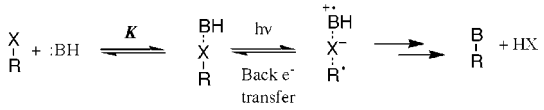
## Introduction

In the course of investigating the photoreactivity of chemically modified diamond surfaces, we observed an unusual mode of reactivity between halogenated diamond and Lewis bases, such as amines or thiols,[1] and more recently alcohols. The halogen was replaced by an amine, alcohol, or thiol, apparently without involving photoinduced bond homolysis.[2] To facilitate studying the details of the reaction mechanism, we performed a series of investigations using 1-chloroadamantane as a molecular analogue of the chlorinated diamond-111 surface. Additional studies using other halogenated alkanes were performed to probe the general utility of the mechanism proposed below.

In this work, we will show that the transformation of the alkyl halide into alkylamines or ethers occurs by the multistep process shown in Scheme 1. In this mechanism, an equilibrium donor−acceptor (charge-transfer) complex intermediate is formed, where the lone pair of the Lewis base (B) overlaps with the carbon−halogen (R−X) $\sigma^*$ orbital. This charge-transfer complex is characterized by a new absorption band in the ultraviolet (e.g., 155−160 nm for amine donors, ca. 145 nm for alcohol donors). Irradiation within a narrow range of wavelengths at the charge-transfer band induces electron transfer, which is apparently followed by rearrangement and formation of the alkyl-substituted base and a hydrogen halide. Free radicals are not involved in the substitution reaction pathway.

This reaction scheme should exhibit certain specific properties. First, the reaction as shown should exhibit second-order kinetics (first order in each of the donor and the acceptor) if photolysis is rate limiting. The process is likely to result from single-photon excitation. Second, free radical inhibitors will likely have no effect on the rate of the substitution reaction, since the proposed zwitterionic diradical intermediate should remain associated within a solvent cage. Third, a new, charge-transfer band should be observed in the ultraviolet−visible spectrum of the reaction solution, and the action spectrum of the photoreaction should correspond with the charge-transfer band. Finally, substitution should be stereospecific, occurring with retention, even for non-bridgehead systems, again since the diradical intermediate likely remains associated.

**Scheme 1. Photoinduced Electron-Transfer Substitution Reactions between an Alkyl Halide and a Lewis Base via a Charge-Transfer Intermediate**




Despite extensive research on bridgehead amines and ethers,[3] very little work has focused on the photochemical reactions of amines and alcohols at bridgehead halogenated carbons. The bulk of photochemical studies of such systems was performed in the early 1970s. The photoreaction between 1-bromoadamantane and methanol to produce 1-methoxyadamantane has been previously observed.[4] Ether formation was attributed to a free-radical substitution, even though detailed spectroscopic and mechanistic studies of the systems were apparently not

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(3) Rossi, R. A.; Pierini, A. B.; Palacios, S. M. *Adv. Free Radical Chem.* **1990**, *1*, 193.
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completed. In another earlier work,[5] electron-transfer chemistry was described for the photoreaction between alcohols and 1-bromo and 1-iodonorbornanes. In that work the reactivity was attributed to bond homolysis followed by electron-transfer; however, wavelength dependence studies were not completed, nor was the analogous photochemistry of alkyl chlorides investigated. The reaction of 1-bromoadamantane in liquid ammonia to yield 1-adamantaneamine has also been reported.[6] That was a side reaction observed during an investigation of the photocatalyzed $S_{RN}1$ reaction of thiolates with the 1-bromoadamantane; the liquid ammonia was the solvent, selected for its electron solvation properties, and the mechanism for formation of the 1-adamantylamine was not addressed.

A variety of reactions of halogenated bridgehead carbons, most notably 1-iodoadamantane and 1-bromoadamantane, with molecules containing group 15 and 16 heteroatoms have been documented.[7] Organic derivatives of phosphorus, arsenic, and antimony as well as selenide and telluride compounds have been shown to undergo $S_{RN}1$ radical substitution reactions with 1-haloadamantanes.[8] The reaction mechanisms were elucidated using free radical inhibitors and observing the effect such compounds had on the rates of the reactions and the product distributions. Radical inhibitors were found to retard the rate of formation of group 15 and 16 substitution products for third-row and higher elements.

It might be presumed from these trends that the formation of bridgehead ethers and amines could also proceed by the $S_{RN}1$ or another radical mechanism. We found that this was not the case. Instead, the rich and potentially useful and controllable class of photoinduced substitution reactions described in Scheme 1 was involved.

## Experimental Section

*tert*-Butylamine (Aldrich, 98%), *tert*-butyl alcohol (Fisher, 99%), methanol (Aldrich, HPLC grade), methylamine (Aldrich, 2.0 M in THF solution), 1-chloroadamantane (Aldrich 98%), cyclohexane (Aldrich, spectrophotometric grade), and pentane (Aldrich, HPLC grade) were obtained and used without further purification, except for *tert*-butylamine, which was fractionally distilled at atmospheric pressure prior to use. Other compounds were prepared as described.

Nuclear magnetic resonance spectra were obtained using either a Bruker 200 MHz or a JEOL Eclipse 400 MHz instrument. Infrared spectra were obtained using a Nicolet DX-5 with sample prepared as pressed KBR pellets. Gas-chromatography/mass spectra were obtained using a HP 5890 GC/MS. Analytical gas chromatography was performed on a Varian 3700 gas chromatograph fitted with a methyl silica capillary column and flame ionization detector.

**1-Adamantyl Methyl Ether.** A 5 g amount of 1-bromoadamantane was dissolved in 10 mL of 10:1 methanol−pentane and the solution placed into a 20 mL glass cylindrical reaction vessel capped on both ends with quartz plates. The solution was irradiated by a 1000 W Hg/Xe arc lamp for 96 h, which resulted in a dark yellow solution. The unfiltered lamp output was defocused to fill the endcap area of the reaction vessel, which was approximately 1 m from the lamp. The temperature of the solution was occasionally measured and did not rise above 30 °C. The solution was then transferred to a 50 mL round-bottom flask and reduced in volume by rotary evaporation to give a wet solid. The reaction products were isolated by preparatory gas chromatography using a Varian 2700 fitted with a 1/4 in. packed methyl silica column and a thermal conductivity detector. Separation was effected by the isothermal heating of the column to 170 °C with a flow rate of 6 mL/min of He. The 1-adamantyl methyl ether was collected as a flaky white powder in a U-tube cooled in liquid nitrogen. Spectroscopic analysis was consistent with literature values.[9] $^1$H NMR (400 MHz, $CDCl_3$) [$\delta$ (ppm)]: 1.25 (3H, s), 1.67 (6H, s), 2.13 (6H, s), 3.23 (3H, s). $^{13}$C NMR (400 MHz, $CDCl_3$) [$\delta$ (ppm)]: 31.2, 36.9, 40.7, 48.5, quaternary carbon not observed. IR (KBr): 2912 (s), 2846, 1674 (s), 1389, 1257 (w), 1098, 1025 (w), 806 (w), 661 (w) cm$^{-1}$.

**1-Adamantyl *tert*-Butyl Ether.** A 5.8 g amount of 1-bromoadamantane was dissolved in 10 mL of neat *tert*-butyl alcohol in the 20 mL quartz-capped reaction vessel described above. The solution was irradiated by a 1000 W Hg/Xe arc lamp for 144 h, resulting in a dark yellow solution. Product isolation was effected by preparatory gas chromatography as for the 1-adamantyl methyl ether. The isolated 1-adamantyl *tert*-butyl ether was collected as solid white needles in a liquid-nitrogen-cooled U-tube. Spectroscopic analysis was consistent with literature values.[9] $^1$H NMR (400 MHz, $CDCl_3$) [$\delta$ (ppm)]: 1.2 (3H, s), 1.5 (6H, m), 1.62 (9H, s), 2.1 (6H, s). $^{13}$C NMR (400 MHz, $CDCl_3$) [$\delta$ (ppm)]: 29.5 (3C, s), 31.5 (3C, s), 35.5 (3C, s), 45.7 (3C, s), 68.5 (1C, s), second quaternary carbon not observed. IR (KBr): 2929 (s), 2844 (s), 1729, 1635 (w), 1453, 1379 (w), 1271 (w), 744, 693 cm$^{-1}$.

***N*,*N*-Di-1-adamantyl-*tert*-butylamine.** A 5 g amount of 1-bromoadamantane was dissolved in 10 mL of neat *tert*-butylamine. The solution was irradiated for 96 h by a 1000 W Hg/Xe lamp in the 20 mL quartz-capped cylindrical reactor described above. A white solid precipitated during irradiation. The precipitate was filtered out and retained for further identification. The supernatant was reduced in volume by rotary evaporation to yield a wet solid. This solid was redissolved in 5 mL of pentane and the *N*,*N*-di-1-adamantyl-*tert*-butylamine reaction product isolated as a white powder by preparatory gas chromatography as for the 1-adamantyl methyl ether. $^1$H NMR (200 MHz, $CDCl_3$) [$\delta$ (ppm)]: 1.20 (9H, s), 1.60 (6H, s), 1.75 (6H, d, $J$ = 4 Hz), 2.00 (3H, s), 2.3 (1H, broad). $^{13}$C NMR (200 MHz, $CDCl_3$) [$\delta$ (ppm)]: 23.32, 26.33, 30.09, 40.3, quaternary carbons not observed. IR (KBr): 3410 (br), 2915, 2849, 1453, 1260, 1088, 1021, 799 cm$^{-1}$.

The filtered precipitate was dissolved in methanol, treated with base, and determined by gas chromatographic analysis to be a mixture composed primarily of the *tert*-butylamine starting material and a small amount of the *N*,*N*-di-1-adamantyl-*tert*-butylamine. Thus, the precipitates were identified as the hydrogen bromide salts of the amine starting material and the amine product.

***N*,*N*-Di-1-adamantylmethylamine.** A 5 g amount of 1-bromoadamantane was dissolved in ca. 10 mL of a 2.0 M solution of methylamine in tetrahydrofuran. This solution was irradiated for 96 h by a 1000 W Hg/Xe lamp in the 20 mL quartz-capped cylindrical reactor described above. A white solid precipitated during irradiation. The precipitate was filtered out and retained for further identification. The supernatant was reduced in volume by rotary evaporation to yield a wet solid. This solid was redissolved in 5 mL of pentane and the *N*,*N*-di-1-adamantylmethylamine product isolated as a white powder by preparatory gas chromatography as for the *N*,*N*-di-1-adamantyl-*tert*-butylamine above. $^1$H NMR (200 MHz, $CDCl_3$) [$\delta$ (ppm)]: 1.50 (3H, s), 1.61 (6H, s), 1.64 (6H, s), 2.13 (3H, s), amine hydrogen not observed. $^{13}$C NMR (200 MHz, $CDCl_3$) [$\delta$ (ppm)]: 25.8, 28.3, 32.0, 43.1, quaternary carbon not observed. IR (KBr): 3403 (br), 2915, 2849, 1653, 1453, 1260, 1088, 1021, 799 cm$^{-1}$.

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**Table 1. Donors, Acceptors, and Observed Substitution Products for the Photoinduced Substitution Reactions**

| donor | acceptor | obsd substitution product |
|---|---|---|
| methylamine | Ad-Cl, Ad-Br | *N*,*N*-di-1-adamantylmethylamine |
| *tert*-butylamine | Ad-Cl, Ad-Br | *N*,*N*-di-1-adamantyl-*tert*-butylamine |
| methanol | Ad-Cl, Ad-Br | 1-adamantyl methyl ether |
| *tert*-butanol | Ad-Cl, Ad-Br | 1-adamantyl *tert*-butyl ether |
| methylamine | Nor-Cl | *N*,*N*-di-1-norbornylmethylamine |
| methanol | Nor-Cl | 1-norbornyl methyl ether |
| methanol | (1*R*,2*S*,5*R*)-menthyl chloride | (1*R*,2*S*,5*R*)-menthyl methyl ether |

**Table 2. Charge-Transfer Complex Absorption Maxima, Kinetics Molar Ratios, Overall Quantum Yields, and Observed Rate Constants for the Photoinduced Substitution Reactions between Bridgehead Alkyl Chlorides and Lewis Bases**

| donor | acceptor | charge-transfer $\lambda_{max}$ (nm) | kinet molar ratios (donor:acceptor) | overall quantum yield ($\times 10^7$) | substitution $10^6 k_{obs}$ ($s^{-1}$) |
|---|---|---|---|---|---|
| $MeNH_2$ | Ad-Cl | 248 ± 2 | 2:1, 1:1, 1:2 | 2.1 ± 0.1 | 1.034 ± 0.098 |
| $(CH_3)_3CNH_2$ | Ad-Cl | 258 ± 2 | 10:1, 5:1, 2:1, 1:1, 1:2 | 4.4 ± 0.2 | 0.715 ± 0.078 |
| MeOH | Ad-Cl | 231 ± 2 | 15:1, 10:1, 3:1, 2:1, 1:1, 1:2 | 1.4 ± 0.2 | 0.153 ± 0.032 |
| $(CH_3)_3COH$ | Ad-Cl | 235 ± 2 | 10:1, 2:1, 1:1, 1:2 | 0.92 ± 0.08 | 0.071 ± 0.048 |
| $MeNH_2$ | Nor-Cl | 240 ± 5 | 2:1, 1:1 | 0.058 ± 0.002 | 1.42 ± 0.15 |
| MeOH | Nor-Cl | 230 ± 5 | 2:1, 1:1 | 0.015 ± 0.003 | 0.58 ± 0.18 |

The filtered precipitate was dissolved in methanol, treated with base, and determined by gas chromatographic analysis to be a mixture composed primarily of the methylamine starting material and a small amount of the *N*,*N*-di-1-adamantylmethylamine. Thus, the precipitates were identified as the hydrogen bromide salts of the methylamine starting material and the *N*,*N*-di-1-adamantylmethylamine product.

**$S_N2$ Synthesis of (1*R*,2*S*,5*R*)-Menthyl Methyl Ether.** A 5 g amount of (1*R*,2*S*,5*R*)-(−)-menthol (Aldrich, 99%) was added to 50 mL of 1 M potassium *tert*-butyl alkoxide in THF (Aldrich) in 250 mL three neck round-bottom flask equipped with a drying tube and liquid addition funnel charged with 7 mL of iodomethane (Aldrich, 99%). The flask was kept at positive pressure by slow $N_2$(g) flush. The entire reaction flask was wrapped in foil to exclude light. The iodomethane was added dropwise over the course of 20 min. The reaction was allowed to stir for 48 h, yielding a thick white suspension. The reaction solution was quenched by addition of 75 mL cold water and transferred to a separatory funnel. The reaction mixture was extracted with 2 × 50 mL portions of pentane. The pentane extract was dried with magnesium sulfate and filtered, and the solvent was removed by rotary evaporation. Purification of the product was effected by column chromatography with silica gel as the stationary phase and a 10:1 (by volume) solution of pentane and dichloromethane as the mobile phase. The target (1*R*,2*S*,5*R*)-menthyl methyl ether was isolated in 60% yield and 95% purity as determined by gas chromatography. $^1$H NMR (400 MHz, $CDCl_3$) [$\delta$ (ppm)]: 3.31 (3H, s), 2.90 (1H, td, $J$ = 10.5 Hz, 4.2 Hz), 2.16 (2H, m), 1.63 (2H, m), 1.33 (1H, m), 1.18 (1H, m), 0.97 (1H, td, $J$ = 12.6 Hz, $J$ = 3.5 Hz), 0.90 (3H, d, $J$ = 13.6 Hz), 0.88 (3H, d, 14.2 Hz), 0.81 (2H, m), 0.76 (3H, d, $J$ = 7.0 Hz).

**Photochemical Synthesis of (1*R*,2*S*,5*R*)-Menthyl Methyl Ether.** A 5 g amount of menthyl chloride [[1*S*-(1$\alpha$,2$\beta$,4$\beta$)]-2-chloro-4-methyl-1-(methylethyl)cyclohexane] (Aldrich 98%) was dissolved in 15 mL of a 10:1 (by volume) methanol−pentane solution in the 20 mL quartz-capped reaction vessel described previously. The solution was irradiated by a 1000 W Hg/Xe arc lamp for 170 h, after which the solution was a deep yellow, and it had attained a menthol-like odor not present in any of starting compounds. Volatiles were removed by rotary evaporation yielding a dark yellow viscous liquid. The reaction product was isolated as a white solid after separation by column chromatography (silica/pentane) and identified by $^1$H NMR as (1*R*,2*S*,5*R*)-menthyl methyl ether, identical to the compound prepared by $S_N2$ synthesis above.

**1-Chloronorbornane.** 1-Chlorobicyclo[2.2.1]heptane (1-chloronorbornane) was synthesized by a literature method[10] in 16% yield and isolated in 98% purity as determined by gas chromatography.

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## Methods

**Reaction Order Determination.** The reaction order of each of the reactants (donor, acceptor, and photon flux) was determined by the initial rates method. Reaction rates were measured with the molar ratios shown in Table 2. Concentrations of the acceptor species typically ranged from 0.5 to 1 mol $L^{-1}$. Reactions of all donors with both 1-chloroadamantane and 1-chloronorbornane were run under broad-band irradiation conditions from a 150 W Xe arc lamp. Concentrations of products were determined by gas chromatography, using an internal standard of *n*-nonane (added in an approximately 1:10 standard-to-sample ratio).

For light flux intensity determinations either a comb filter or neutral density filters (Oriel) were used to decrease the intensity of light incident on the reaction solution. A 1:1 donor−acceptor molar ratio was used for photon flux dependence measurements.

**Radical Inhibition.** Two free radical inhibitors were used to test their effect on rates of product formation. Either of 1,4-benzoquinone (Aldrich, 98%) or 2,2,6,6-tretramethyl-1-piperidinyloxy free radical (TEMPO) (Aldrich, 98%) was added to pentane solutions of a donor (*tert*-butylamine, methylamine, *tert*-butanol, or methanol) and acceptor (1-chloroadamantane or 1-chloronorbornane) having donor:acceptor:inhibitor ratios of ∼10:1:1. The typical acceptor/inhibitor concentrations were $10^{-4}$ M in pentane. Reactions were carried out under monochromatized irradiation from the 1000 W Hg/Xe lamp set to the maximum of the donor−acceptor charge-transfer band. Irradiation was stopped after 148 h, and the concentrations of products were determined by gas chromatography with a nonane internal standard. Rates of the reactions with the inhibitor inhibited reactions were compared to those of reaction solutions of similar reactant concentrations but lacking free radical inhibitors.

**Oxygen Exclusion.** Reactions of *tert*-butyl alcohol, *tert*-butylamine, and methanol with 1-chloroadamantane were carried out in the presence and absence of oxygen. Pentane solutions were prepared at 1 M in 1-chloroadamantane and 5 M in the other reactant. An aliquot of each solution was degassed by three freeze−pump−thaw cycles. In parallel experiments the degassed and as-prepared solutions were irradiated in quartz cuvettes under broad-band illumination from a 150 W Xe arc lamp, maintaining careful control of the lamp power settings and sample position to ensure equivalent photon dose. The concentrations of products were determined by gas chromatography with a nonane internal standard.

**Quantum Yield Determinations.** The intensity of the 1000 W Hg/Xe lamp was determined by ferrioxalate actinometry as follows. Potassium ferrioxalate was prepared by the aqueous metathesis reaction of ferric sulfate (Spectrum 98%) and potassium oxalate (Mallinckrodt 95%), resulting in a dark green solution, from which were precipitated dark green

crystals of $K_3[Fe^{III}(C_2O_4)_3]$ upon cooling. All solution preparation was performed in a room illuminated only by a sodium lamp. For the actinometric measurements 0.001 M aqueous $K_3[Fe^{III}(C_2O_4)_3]$ solutions were prepared.

The light from a 1000 W Hg/Xe arc lamp was monochromatized to a 10 nm band-pass with a 0.125 m grating monochromator blazed at 250 nm. The lamp intensity was then measured by ferrioxalate actinometry at 10 nm intervals from 200 to 300 nm. Actinometric measurements were carried out in 1 cm matched spectrophotometric grade quartz cuvettes (McCarthy Scientific Co.), using a Hewlett-Packard 8451A diode array spectrophotometer in the range 200−400 nm.

The ferrioxalate solutions were exposed to the monochromatized light from the arc lamp for 2, 5, and 10 min intervals. After exposure to the light source the amount of photoreduced $Fe^{2+}$ was measured spectroscopically after chelation by 1,10-phenathrolene in a sodium acetate buffer. All measured absorbances were corrected to the unexposed ferrioxalate solution absorbance. $Fe^{2+}$ analysis was accomplished by comparison to a series of standardized $Fe^{2+}$ solutions. The lamp intensity was determined by equation 1, where $I_i$ is the intensity of the incident radiation, $n_{Fe^{2+}}$ is the number of moles of $Fe^{2+}$ that are produced, $A$ is the absorbance at the wavelength for which the intensity is being determined, $t$ is the time of irradiation, and $\Phi_{Fe^{2+}}$ is the quantum yield of the actinometer at the wavelength of interest.

$$I_i = \frac{n_{Fe^{2+}}}{(1 - 10^{A})t\Phi_{Fe^{2+}}} \quad (1)$$

The measured lamp intensity was then used to calculate the overall quantum yields of the each of the reactions of the methanol, methylamine, *tert*-butyl alcohol, and *tert*-butylamine donors with 1-chloroadamantane. The overall quantum yield was determined (at the wavelength that gave the largest reaction rate constant) according to eq 2, where $\Phi_x$ is the quantum yield to be determined for product $x$ and $n_x$ is the number of moles of product $x$ produced.

$$\Phi_x = \frac{n_x}{(1 - 10^{A})tI_i} \quad (2)$$

**Rate Constant Determination.** The absolute rate constants were determined for the photoreactions of 1-chloroadamantane with methanol, *tert*-butyl alcohol, methylamine, and *tert*-butylamine under monochromatized (10 nm band-pass) irradiation from the 1000 W Xe/Hg arc lamp at the wavelength where the electron-transfer substitution product is the dominant photoproduct. Reaction solutions were typically 1 M in the 1-chloroadamantane and 5 M in the amine or alcohol with pentane as the solvent, with the exception of methylamine which was prepared as 1 M in 1-chloroadamantane and 2 M methylamine solution in THF. The rates of the reactions of methanol and methylamine with 1-chloronorbornane were similarly measured. Aliquots of 0.5 mL were removed periodically (generally at 4−8 h intervals), and the concentrations of reaction products were determined by gas chromatography using an *n*-nonane internal standard. The reaction rates were determined by measuring the amount of secondary amine or ether product formed (see Table 1), as well as the amount of three products produced by free-radical side reactions: adamantane, adamantyl dimer, and an unidentified adamantyl chloride rearrangement compound. The side products that were monitored for reactions involving 1-chloronorbornane were norbornane and the norbornyl dimer.

**Reaction Action Spectra.** The action spectra for the reactions between the methanol, methylamine, *tert*-butylamine, and *tert*-butyl alcohol donors with the 1-chloroadamantane acceptor were synthesized by determining the rates of reactions as functions of the exciting wavelength. The reaction for each set of reagents was carried out at 10 nm intervals from 200 to 300 nm, using the same wavelengths and monochromator band-pass (10 nm) for which the actinometric lamp intensities were measured.

**Spectroscopic Identification of Charge-Transfer Bands.** Ultraviolet spectra of the reaction solutions were obtained in the range 200−300 nm using a Cary 14 spectrophotometer, interfaced by an OLIS operating system, for the 1-chloroadamantane acceptor with each of the *tert*-butylamine, methylamine, *tert*-butyl alcohol, and methanol donors. The charge-transfer bands were identified by comparing the spectrum of each of a solution of the individual reactants (1-chloroadamantane and the respective amine or alcohol) with the spectrum of the solution containing both reagents. The solutions were typically 0.5 M in 1-chloroadamantane and 1−2 M in amine or 10 M in alcohol. Pentane was the solvent for the *tert*-butylamine, *tert*-butyl alcohol, and methanol donors. Cyclohexane was the solvent used for the methylamine donor, due to the limited solubility of methylamine in pentane.

## Results

**Photoreaction Products.** The reactions that were the focus of this investigation were the photoinduced substitution reactions of bridgehead alkyl halides (1-haloadamantanes (Ad-X), 1-chloronorbornanes (Nor-X), and (1*R*,2*S*,5*R*)-menthyl chloride) with members of a homologous series of amines or alcohols (methylamine, *tert*-butylamine, methanol, or *tert*-butyl alcohol). The primary products of each reaction, as summarized in Table 1, resulted from substitution at the halogenated carbon by an amine or alcohol to produce the corresponding secondary amine or ether.

Additional products were also detected when irradiating at relatively short wavelengths. These were most significant when broad-band irradiation conditions were used. Substitution products were not observed at wavelengths significantly longer than the charge-transfer absorption or in the dark.

For reactions involving 1-chloroadamantane and 1-bromoadamantane, the radical side products were determined by gas chromatography/mass spectrometry to consist primarily of adamantane and lesser quantities of an adamantyl dimer and a halogenated adamantyl rearrangement product which we did not isolate or further characterize. For reactions involving 1-chloronorbornane, the radical side products were determined by GC/MS to consist primarily of norbornane and lesser quantities of a norbornyl dimer and a large number of norbornane-derived rearrangement products. Again, these were neither isolated nor extensively identified. As will be shown below, the formation of these products was the result of free-radical reactions, excited by short wavelength radiation, which caused carbon−halogen bond homolysis and subsequent radical reactions. These reactions and products were *not* observed at significant levels when the system was irradiated within a narrow range of photon energies corresponding to the charge-transfer absorbance of the proposed intermediate complex. Many mechanistic studies of analogous radical reactivity have been carried out and extensively reviewed.[11] With the exception of the inhibition experiments and spectral activity determinations described below, we did not perform a more detailed analysis of those radical reactions, products, or mechanisms in this work.

**Spectroscopic Measurements.** Ultraviolet absorption spectra were obtained for each of the donors sepa-

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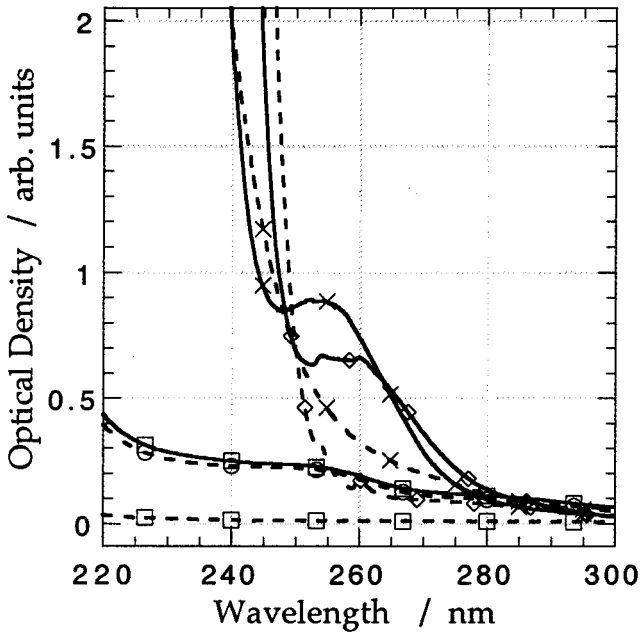


**Figure 1.** Comparative ultraviolet absorbance spectra for hydrocarbon solvent solutions of the Lewis base donors (dashed lines), the 1-chloroadamantane acceptor, and the donor−acceptor combinations (solid lines) (○, AdCl; □, methanol; □, methanol + AdCl; ◇, $NH_2t$-Bu; ◇, $NH_2t$-Bu + AdCl; ×, $MeNH_2$; ×, $MeNH_2$ + AdCl). The mixtures are equimolar in the donor and acceptor species. The feature red shifted from each amine donor n → $\sigma^*$ cutoff is the charge-transfer complex absorbance. (The charge-transfer complex absorption for the methanol donors is extremely weak.)

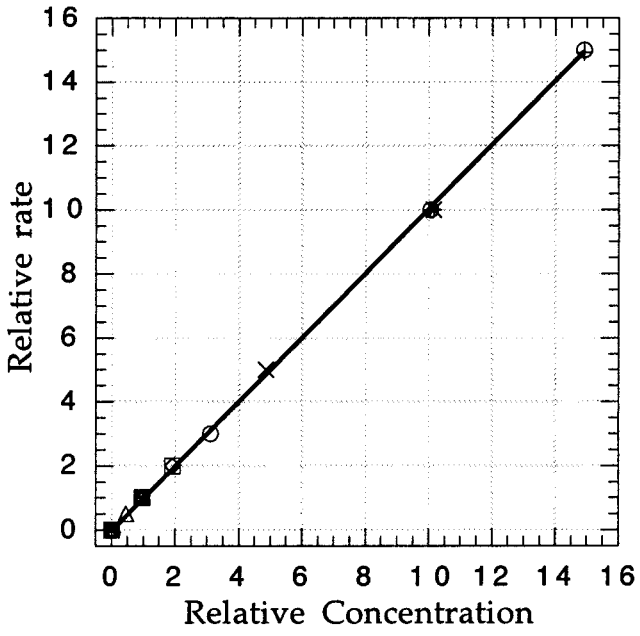


**Figure 2.** Relative photoreaction rates as a function of relative initial concentrations of the donor, the acceptor, and the photon flux for various combinations of Lewis base donor and bridgehead alkyl halide acceptor. The points indicate the species which was varied (○, methanol; □, AdCl; ◇, NorCl; ×, $NH_2t$-Bu; +, $t$-BuOH; Δ, photon flux). The diagonal line has a slope of one; it is not a fit to any of the data.

rately and in combination with the 1-chloroadamantane acceptor. Figure 1. shows the spectral comparisons for the methylamine and *tert*-butylamine donors. The $\lambda_{max}$ for the charge-transfer complexes are collected in Table 2. In all of the cases observed the energy required for electron promotion from n → $\sigma^*$ in the complex was smaller than from n → $\sigma^*$ in the unbound donor.

Well-defined charge transfer bands were identified for the amine donors. The charge-transfer bands for the alcohols were weaker and not always as well resolved. Careful solution preparation, spectroscopic analyses, and occasionally spectral deconvolution were required to distinguish the charge-transfer features for the alcohols. A complete examination of the charge-transfer complex spectroscopy and thermodynamics is detailed elsewhere.[12]

**Rate Law.** To determine the experimental rate law, the relative rates of the reactions were monitored as functions of the relative initial concentrations of the reactants and photon flux. Figure 2 displays the data obtained from the initial-rates experiments for the reactions of various combinations of methanol or *tert*-butyl alcohol with 1-chloroadamantane or 1-chloronorbornane. These data show that the reaction was first order in both reactants and second-order overall, regardless of the donor or acceptor used. Unsurprisingly, the data also indicate that the photoexcitation is a single-photon process. Thus the empirical rate law was found to be consistent with eq 3, where $k_{obs}$ is the observed rate constant for a given donor/acceptor pair, $I_a$ is the incident photon flux, and [D] and [A] are the donor and acceptor concentrations, respectively.

$$d[\text{product}]/dt = k_{obs} I_a [D][A] \quad (3)$$

**Radical Inhibition.** To determine if the electron-transfer substitution reactions that were being observed involved any free radical intermediates, the reactions were carried out in the presence of free radical inhibitors: TEMPO and quinone.[13] Due to the high molar absorptivity of both of these free radical inhibitors in the UV region, it was necessary to keep the concentrations of both the radical inhibitors below $10^{-3}$ M. At these low concentrations, the effect of their presence fell short of complete quenching of the radical pathways.

The reactions that were examined were 1-chloroadamantane with methanol *tert*-butylamine, methylamine, or *tert*-butyl alcohol using the TEMPO inhibitor and 1-chloronorbornane with methanol or methylamine using the quinone inhibitor. The observed rate constants for the photoinduced substitution reactions induced by monochromatized irradiation at the charge-transfer complex absorption are collected in Figure 3. Neither of the radical inhibitors had a statistically significant effect on the observed rate constants of the substitution reactions, as compared to uninhibited controls.

Free radical reactions are also generally inhibited by the presence of (ground-state) triplet oxygen in the reaction solution. Oxygen tends to form peroxy radicals by addition to free radicals in the system. Alkyl radicals are readily trapped by this reaction; thus, the rate of abstraction of hydrogen from the hydrocarbon solvent to form the corresponding alkane, as well as any other radical processes, should be retarded. Oxygen is also small, and thus it may be sterically better able to access

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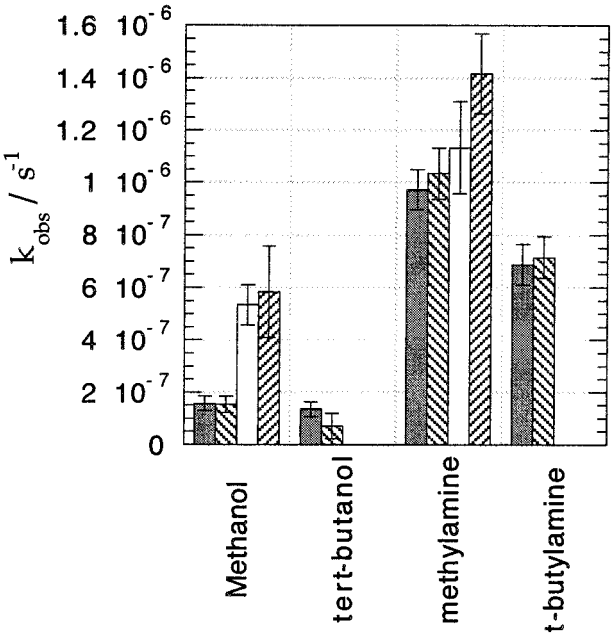


**Figure 3.** Comparison of the observed reaction rate constants for the photoreactions of various combinations of Lewis base donors (abcissa) and bridgehead alkyl halide acceptors with and without radical inhibitors (■, AdCl + TEMPO; ◺, AdCl; □, NorCl + quinone; ◪, NorCl). Each system was irradiated at the maximum absorbance of the charge-transfer complex with a band-pass of 10 nm. The error bars are the sample standard deviation for at least three replicate measurements.

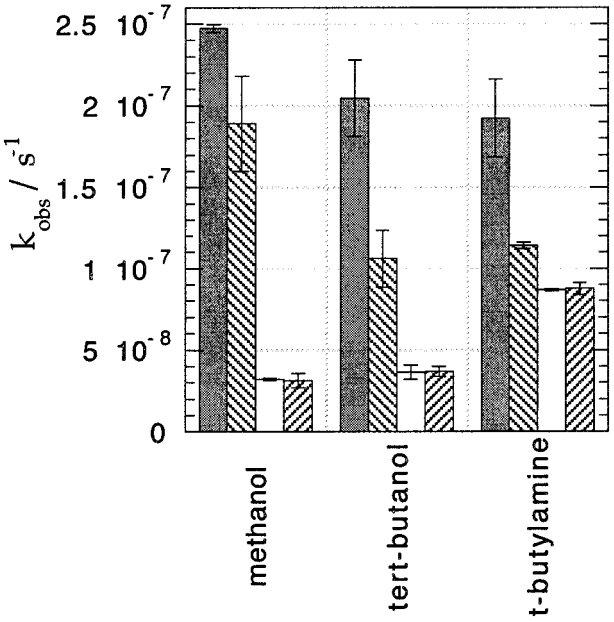


**Figure 4.** Comparison of the observed reaction rate constants for the substitution and radical photoreaction products from the reaction of various Lewis base donors (abcissa) and the 1-chloroadamantane acceptor in the presence of $O_2$ and after degassing by three freeze−pump−thaw cycles (FPT) [■, adamantane (FPT); ◺, adamantane ($O_2$); □, substitution (FPT); ◪, substitution ($O_2$)]. Formation of admantane (Ad-H) was used as a diagnostic product for the free radical reactions. Each system was irradiated under broad-band conditions. The error bars are the sample standard deviation for at least three replicate measurements.

a greater portion of the photoexcited complex than the relatively bulky TEMPO or quinone molecules.

Oxygen was removed from our system by a series of freeze−pump−thaw degassing cycles. The observed rate constants for products involving a free-radical intermediate (monitored by adamantane formation) and photoinduced substitution were determined for the reactions of 1-chloroadamantane with methanol, *tert*-butyl alcohol, and *tert*-butylamine irradiated under broad-band conditions. The observed rate constants of these reactions are collected in Figure 4. Oxygen exclusion experiments were not carried out for the methylamine donor; this gas-phase amine was uncontrollably expelled by the degassing procedures used to remove $O_2$.

The data show that by excluding oxygen from the reaction system the observed rate constants for the free-radical reactions (using adamantane formation as a diagnostic) were greater than when oxygen was present in the system. The data also show that the presence or absence of oxygen from the reaction system had no statistically significant effect on the observed rate constant for the photoinduced substitution reaction.

**Quantum Yield Determination.** Quantum yields were measured for the reactions of methanol, *tert*-butyl alcohol, methylamine, or *tert*-butylamine with 1-chloroadamantane, as well as the reactions of methanol or methylamine with 1-chloronorbornane. The lamp intensity was determined using ferrioxalate actinometry. The overall quantum yield was calculated at the wavelength where the observed rate constant for substitution product formation of each system was its maximum. Table 2 lists the overall quantum yields of substitution product formation. (We currently have no data related to the primary quantum yield for the photoexcitation step.)

**Action Spectra.** The rates of all of the observed reactions were found to be dependent on the excitation wavelength. Figure 5 shows a plot of relative product formation rates as functions of the irradiation wavelength for the reaction of 1-chloroadamantane with *tert*-butylamine or methanol. The relative formation rates of Figure 5 are normalized for photon flux and computed from eq 4, where $d[product]_{rel}/dt$ is the relative formation rate for the product of interest, $d[product]_{abs}/dt$ is the absolute formation rate for the product of interest, $I_{300}$ is the intensity of radiation at 300 nm (chosen as a standard where the formation rate for all products is zero), and $I_\lambda$ is the radiation intensity at the wavelength that is being utilized for the reaction respectively in photons.

$$d[product]_{rel}/dt = d[product]_{abs}/dt\left(\frac{I_{300}}{I_\lambda}\right) \qquad (4)$$

The substitution reaction rate for the amine was a maximum around 260 nm, coincident with the maximum absorbance of the charge-transfer complex intermediate. Quantitatively and qualitatively similar results were obtained for the substitution reaction between methylamine and 1-chloroadamantane. The substitution reaction rate was a maximum for the methanol donor with irradiation around 230−240 nm, again coincident with the maximum absorbance of the charge-transfer complex intermediate. Quantitatively and qualitatively similar results were obtained for the reaction of *tert*-butyl alcohol and 1-chloroadamantane. None of the reaction systems investigated produced substitution product with irradiation at wavelengths 200−220 nm or longer than 280 nm.

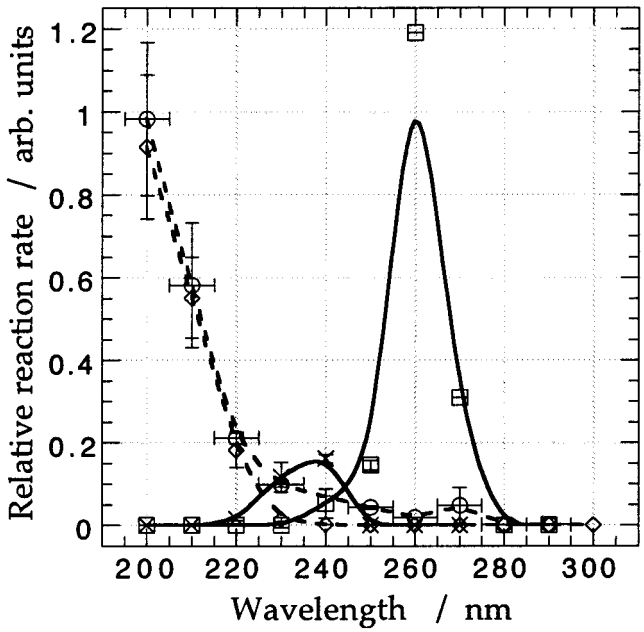


**Figure 5.** Action spectra for the photoreactions between *tert*-butylamine or methanol and 1-chloroadamantane. The relative formation rates for the photoproducts (○, adamantane (in amine system); □, *N*,*N*-di-1-adamantyl-*tert*-butylamine; ◇, adamantane (÷8, in alcohol system); ×, adamantyl methyl ether) are plotted as a function of excitation wavelength. Formation of admantane was used as a diagnostic for free radical reactions and is included for comparison. Each system was irradiated with monochromatized light from a Hg/Xe lamp. The formation rates are corrected for lamp flux at each wavelength. The *x*-axis error bars indicate the monochromator band-pass. The *y*-axis error bars are the sample standard deviation for at least three replicate measurements. The lines were added to guide the eye.

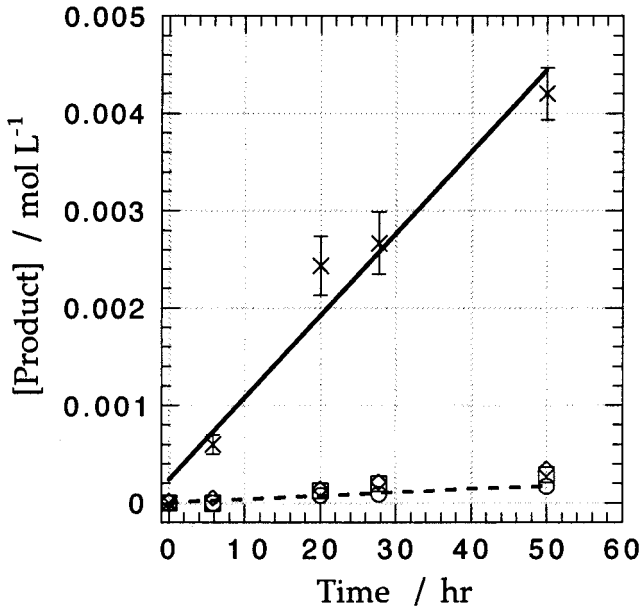


**Figure 6.** Evolution of photoproduct concentrations (○, adamantane; □, adamantane dimer; ◇, rearrangement product; ×, *N*,*N*-di-1-adamantyl-*tert*-butylamine) with time for the reaction of 1-chloroadamantane and *tert*-butylamine while irradiating at 260 nm, the wavelength that maximized the substitution pathway. The error bars are the sample standard deviation for at least three replicate measurements. The representative lines are linear fits to the amine and adamantane concentration data.

Irradiation at shorter wavelengths (below ~230 nm) primarily induced free-radical reactions, presumably initiated by carbon−halogen bond homolysis, and generated their associated products such as adamantane. As the irradiating wavelengths approached the absorbance of the charge-transfer complex intermediate, the rates of formation of the free-radical side products decreased sharply, while the rates of formation of the substitution products increased. The production of both the substitution and free-radical products ceased at longer wavelengths.

In the systems with alcohol donors, the free-radical products are generated more rapidly than with the amine donors under short wavelength irradiation. This was probably due to the lower molar absorptivity of the alcohols at the shorter wavelength as compared to the amines which have an n → $\sigma^*$ cutoff around 245 nm. This means that, for the alcohol systems, there are more photons available from the source flux to excite carbon−halogen bond homolysis; they are not being absorbed by any other competing chromophores.

**Rate Constant Determination.** The reaction rate constants were evaluated at the wavelengths for which the substitution product formation rates were maximized (see Table 2 and Figure 5). The absolute reaction rate constant was determined by measuring the velocity of the reaction and then normalizing by the overall quantum yield, the intensity of the exciting radiation, and the concentrations of the reactants. The intensity of the incident radiation was determined by ferrioxalate actinometry.[14] The overall quantum yields were measured as described above. The reaction velocities were determined by analysis of the product evolution for each reaction. A plot of concentration versus time for the products of the photoreaction of *tert*-butylamine with 1-chloroadamantane is seen in Figure 6, including the substitution product (*N*,*N*-di-1-adamantyl-*tert*-butylamine) and the trace free-radical products. The rate constants were calculated using eq 3. Table 2 contains the observed rate constants for the reactions of methanol, *tert*-butyl alcohol, methylamine, or *tert*-butylamine with 1-chloroadamantane, as well as for the reactions of methanol or methylamine with 1-chloronorbornane.

**Stereospecific Photochemical Substitution.** The formation of the charge-transfer complex intermediate depends on the overlap between the nonbonding lone pair of the Lewis base and the empty $\sigma^*$ orbital of the alkyl halide. (A computational study of this class of complex is underway in our laboratory.) The base is associated with the alkyl halide via the halogen; it is this *complex* that contains the photosubstitution chromophore. Upon absorption of a photon, the zwitterionic diradical intermediate is created. Substituted aliphatic radicals do not tend to planarize or rapidly invert, especially in cyclic systems. The configuration of the atoms about the stereocenter should remain unchanged; hence substitution can occur without the racemization common to $S_N1$ chemistry.

To test this prediction, we irradiated a mixture of (1*R*,2*S*,5*R*)-menthyl chloride and methanol. The only observed substitution product was (1*R*,2*S*,5*R*)-menthyl methyl ether, shown in Scheme 2. The stereochemistry

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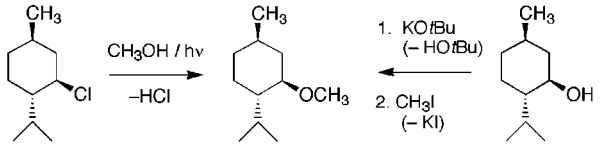
**Scheme 2. Comparison of Photoreaction and Standard Synthetic Reactions To Generate (1*R*,2*S*,5*R*)-Menthyl Methyl Ether**




at the substituted carbon was verified by $^1$H NMR spectral comparison with the (1*R*,2*S*,5*R*)-menthyl methyl ether synthesized from (1*R*,2*S*,5*R*)-(−)-menthol and methyl iodide, also shown in Scheme 2.

## Discussion

The observed substitution reactions all required light for them to produce the product amine or ether. Thermal substitution was mechanistically precluded (vide infra), and it was *not* observed in any of the systems examined. The polycyclic nature of the bridgehead alkyl halides eliminated the backside attack required for an $S_N2$ reaction. Nonclassical carbocation formation has been observed in the adamantyl systems,[15] which might suggest that the reactions we observed could have proceeded by an $S_N1$ reaction mechanism. However, this was unlikely in the low dielectric solvents (e.g., pentane) used for the reaction medium. Such an environment will not support the charge separation that is required to generate a halide anion and a 1-adamantyl carbocation. No thermal substitution was observed; thus, there was not any appreciable generation of such a nonclassical carbocation.

The first step of the photochemical mechanism proposed in Scheme 1 was the formation of the equilibrium charge transfer complex, creating the chromophore for the substitution reaction. Only after the complex is formed can photon-induced electron transfer occur. The observed rate constant for the substitution reaction as given in the rate law of eq 3 is a combination of the following: (1) the equilibrium formation of the charge-transfer complex, described by the equilibrium constant *K*, second-order overall (first order in each of the donor and the acceptor); (2) the overall quantum yield for the rate-limiting photon-induced electron transfer; (3) the rate constant for collapse of the proposed zwitterionic diradical intermediate, $k_{coll}$. If we assume a steady-state approximation for the charge-transfer intermediate, a more detailed description of the rate law of eq 3 for photoinduced substitution can be produced, as in eq 5, where $k_{BET}$.is the rate constant for back electron transfer, as shown in Scheme 1.

$$v = K \frac{\phi_e}{k_{BET}} k_{coll}[D][A] \qquad (5)$$

The transfer of the electron into the carbon−halogen $\sigma^*$ orbital is similar to dissociative electron attachment processes that have been observed[16] and computationally modeled.[17] Dissociation in alkyl halide anions is an activationless process and is associated with the C−Cl stretching mode. The collapse of our proposed diradical intermediate into the product is likely also a fast event, similar to a C−Cl−N bending mode, so $k_{coll}$ should be on the order of $10^9$ $s^{-1}$ or greater. Preliminary low-temperature electron-spin resonance spectroscopy experiments in our laboratory suggest that this photoinduced diradical is indeed formed upon irradiation of the charge-transfer complex. An evaluation of the formation and destruction energetics and kinetics of this charge-separated species is underway.

In a system with multiple donors present, specific substitution products could, in principle, be selectively generated by selectively exciting the appropriate charge-transfer complex. For example, on the basis of the charge-transfer absorption maxima collected in Table 2, an alkyl chloride could be induced to react with an amine if irradiated at about 255 nm, while the same alkyl chloride could be induced to react with an alcohol when irradiated at about 235 nm. The dependence on acceptor is likely to be less significant; it is doubtful that the reaction could discriminate between chlorine and bromine substituted centers, for example.

There is great atom economy in this photosubstitution process. Consider the two routes to the target menthyl methyl ether in Scheme 1. The photoreaction required no additional solvent, just an excess of the methanol reactant; its only byproduct was 1 equiv of HCl(g). The "standard" synthesis required two solvent systems and isolation of the intermediate alkoxide and produced 2 equiv of byproducts. The photoreaction does have the disadvantage of small reaction rate constants and low overall quantum yields. However, these issues could be overcome by using high-fluence sources.

## Conclusion

The data that have been presented are consistent with the involvement of a charge-transfer complex intermediate in the photosubstitution by Lewis bases for the halogen in an alkyl halide. This mechanism dominated when a mixture of the alkyl halide and the Lewis base was irradiated at the wavelength of a charge-transfer band absorption maximum. These conditions minimized products associated with free-radical reactions. Furthermore, free-radical inhibitors were not found to have a significant effect on the rate of substitution product formation. This suggested that free radical intermediates were not involved in the electron-transfer substitution reaction pathway. Instead, the proposed diradical intermediate is bound within a complex and is less available to the inhibitors, even those as small as $O_2$.

This photoinduced substitution reaction shows promise as a clean, direct, and even stereospecific synthetic method. The time and materials saved in reduction of steps and simplified purification may give this reaction scheme merit as one alternative to more conventional methods of synthesis.

**Acknowledgment.** This work was made possible by support from the National Science Foundation (Grant CHE-9712263) and by an award from the Research Corporation.

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