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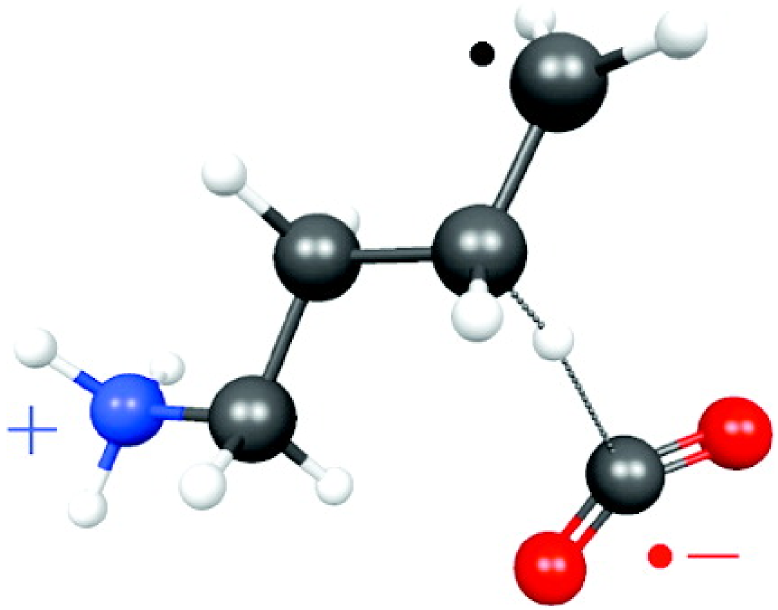

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A Computational Study of Remote C−H Activation by Amine Radical Cations: Implications for the Photochemical Reduction of Carbon Dioxide

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Abstract: A computational study, using density functional theory calibrated against higher-level methods, has been undertaken to evaluate tertiary amines whose radical cations might lose hydrogen atoms from positions other than the α carbons. The purpose was to find photochemically activated reducing agents for carbon dioxide that could be regenerated in a separate photochemical reaction. The calculations have revealed two reactions that might be suitable for this purpose. In one, the nitrogen of the radical cation makes a bond to a remote carbon with simultaneous displacement of a hydrogen atom. In the other, a remote hydrogen atom is transferred to the nitrogen, thereby creating a distonic radical cation that can lose a hydrogen atom β to the radical site. The latter reaction is found to be particularly favorable since it apparently involves a surface crossing that allows the amine radical cation and CO_2 radical anion to transform smoothly to a ground-state formate ion and an alkene. A number of structural motifs are investigated for the amines. The lower ionization potential of aromatic amines, compared to their aliphatic analogues, is desirable in that it could permit the use of longer wavelength light to drive the reaction. However, a thermochemical cycle shows that the reduction in ionization potential must be matched by an increase in proton affinity of the amine if the intramolecular hydrogen transfer is to be exothermic. Most aromatic amines do not satisfy this criterion and, hence, would have to rely on the displacement reaction for hydrogen-atom release if they were to be used as renewable reagents for CO_2 reduction. Examples of specific aromatic and aliphatic tertiary amines that should be suitable for the purpose are presented, and their relative merits and weaknesses are discussed.

Introduction

The photochemical reduction of atmospheric carbon dioxide might be environmentally beneficial, if it could be accomplished with solar radiation. For example, the first stable reduction product of CO_2, formic acid, can be used efficiently in direct-oxidation fuel cells.[1] Hence, the cycle of CO_2 removal by photochemical reduction and then return to the atmosphere by oxidation in a fuel cell would, in effect, provide a carbon-neutral means for storing solar energy in a transportable form.

In fact, the photochemical reduction of CO_2 is already known.[2−11] However, almost all of the laboratory procedures that permit this reaction use a sacrificial reductant, usually a tertiary amine. Obviously, no environmental or economic benefit can be expected if a mole of some reagent has to be irreversibly oxidized for every mole of CO_2 reduced.

One of the few exceptions to this conclusion occurs when the reducing agent is water, as it is in photosynthesis. Unfortunately, the exploitation of photosynthesis for addressing the world's energy and climate issues carries its own set of problems. Specifically, the need for arable land to grow crops such as corn for biofuels sets up an inevitable competition between energy and food production.[12] In addition, the true economic and environmental benefits of using plants to provide fuel are, at best, difficult to evaluate.[13−16]

Some of the drawbacks of biofuels could potentially be eliminated if an artificial photosynthetic system could be developed, since it would presumably be able to operate in environments hostile to plant life, provided there was plentiful sunlight. A great deal of research has been devoted to understanding the biological photosynthetic systems and to

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mimicking them in the laboratory.[17−23] The real challenge facing this approach is that the process of evolution has crafted an extremely complex apparatus, in which the protein components seem to be actively involved in the photochemistry.[24] Consequently design of less complex *in vitro* analogues has proven to be difficult, and to date, none has shown an efficiency or longevity to match that found in the biological photosystems.

The present work seeks to evaluate an alternative approach, building on the known chemistry using sacrificial redox reagents but exploring the possibility of making those reagents renewable. The overall concept can be illustrated with the following three photochemical reactions, any or all of which might involve a photocatalyst, although none is shown explicitly:

$$CO_2 + XH_2 \rightarrow HCO_2H + X \qquad (1)$$

$$H_2O + Y \rightarrow {}^{1}/_{2}O_2 + YH_2 \qquad (2)$$

$$X + YH_2 \rightarrow XH_2 + Y \qquad (3)$$

Reactions 1 and 2 represent the known chemistry.[25−30] The idea is to link them by one or more additional reactions, such that the sum of the individual steps gives the net transformation 4:

$$CO_2 + H_2O \rightarrow HCO_2H + {}^{1}/_{2}O_2 \qquad (4)$$

If successful, such a strategy would permit photosynthesis-like chemistry without the need for sophisticated molecular engineering. In particular, the separation of the difficult reduction and oxidation steps in reactions 1 and 2 means that these transformations could be carried out under mutually incompatible conditions, if that should prove advantageous. For example, the CO_2 reduction could be conducted in an anhydrous medium, an obvious impossibility if the water oxidation had to be accomplished at the same time.

The popularity of amines as the sacrificial reagents in reaction 1 arises from the fact that this reaction commonly involves single-electron transfer to an electronically excited photocatalyst (PC*),[4,31,32] as shown in reactions 5−8, and amines are among the best electron donors of common organic molecules.

$$PC + h\nu \rightarrow PC^* \qquad (5)$$

$$PC^* + XH_2 \rightarrow PC^{\bullet-} + XH_2^{\bullet+} \qquad (6)$$

$$CO_2 + PC^{\bullet-} \rightarrow CO_2^{\bullet-} + PC \qquad (7)$$

$$CO_2^{\bullet-} + XH_2^{\bullet+} \rightarrow\rightarrow HCO_2H + X \qquad (8)$$

When XH_2 is a tertiary amine (with the hydrogens therefore being on a hydrocarbon side chain), the formation of the radical cation is relatively facile. Furthermore, the removal of a nonbonding electron from the amine nitrogen greatly weakens any α C−H bonds,[33] facilitating the formal hydrogen atom and proton transfers that must occur to complete the reduction of CO_2. These transfers, summarized in reaction 8, have recently been explored computationally for the case of triethylamine as the reducing agent.[34]

The principal problem with using tertiary amines for this purpose is that their radical cations usually decompose to complex mixtures of products, from which a clean regeneration of the amine would be difficult. The complexity of the decomposition arises, in part, because loss of an α hydrogen atom from the radical cation generates an electrophilic iminium ion, whose subsequent deprotonation generates a nucleophilic enamine. These electrophilic and nucleophilic intermediates can undergo a variety of bimolecular reactions with each other. In addition, the starting amine has relatively weak α C−H bonds (BDE typically 90−95 kcal/mol), and abstraction of these hydrogens by the amine radical cation is generally exothermic.[35] The resulting radicals can then contribute to the reaction complexity.

The question that we sought to resolve with the present calculations was whether it might be possible to design tertiary amines whose oxidative decompositions would avoid iminium ions, enamines, and α-amino radicals and might therefore give clean products that would be amenable to re-reduction in a subsequent photochemical reaction. The renewable character of any such amines could make some investment of effort in their synthesis worthwhile.

Elucidation of Reaction Types and Evaluation of Computational Models

The removal of an electron from a tertiary amine weakens the α C−H bonds by about 60 kcal/mol.[33] This phenomenon can be ascribed to the formation of a C−N π bond, partially compensating for the loss of the C−H bond upon homolysis, as shown in reaction 9.

$$R_2N^{\bullet+}{-}CH_2R' \rightarrow R_2N^{+}{=}CHR' + H^{\bullet} \qquad (9)$$

But that analysis raises interesting questions. Since C−N σ bonds will, in general, be stronger than C−N π bonds, should it not be possible to activate a remote C−H bond to homolysis by ring formation to an amine radical cation? Alternatively, could a distonic radical cation formed by intramolecular hydrogen transfer (and recently detected experimentally in the case of *n*-butylamine radical cation[36]) act as a reducing agent

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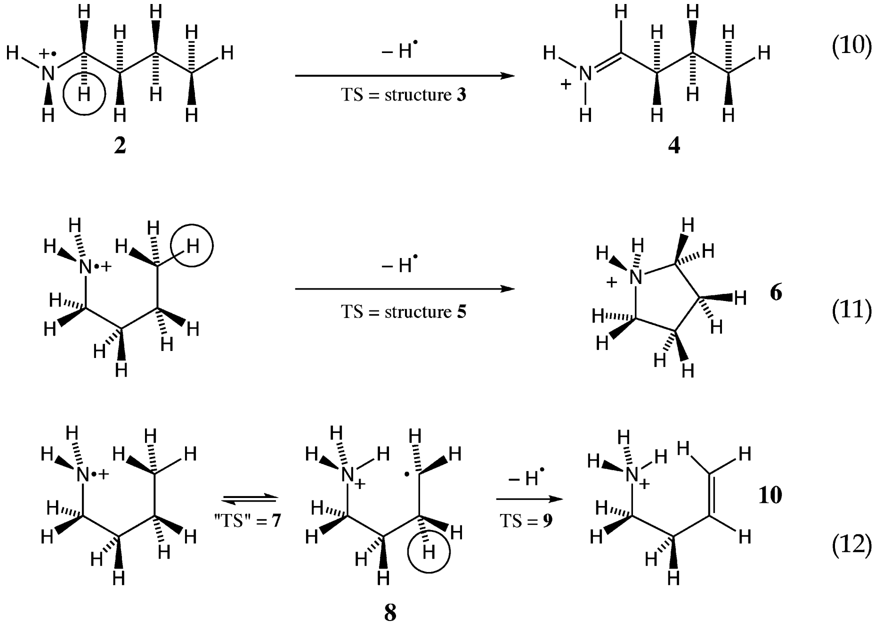
Scheme 1. Three Reactions Leading to H-Atom Loss from *n*-Butylamine Radical Cation[a]



[a] In each case the hydrogen being lost is circled.

Table 1. Calibration of DFT and MP2 Calculations for the Reactions of *n*-Butylamine Radical Cation Shown in Scheme 1 and Figure 1[a]

species	DFT[b]	MP2[c] (⟨$\mathbf{S}^2$⟩)	CC-1[d]	CC-2[e]	DFT-corr[f]
3	26.5	19.6 (0.8140)	23.7	23.9	20.5
4 + H•	26.5	13.8 ([0])	20.6	20.4	20.5
5	37.9	29.0 (0.8057)	34.2	34.0	31.9
6 + H•	20.5	1.7 ([0])	10.8	10.6	14.5
7	1.6	2.4 (0.7790)	−3.0[g]	−2.8[h]	−4.4
8	0.3	−7.7 (0.7634)	−5.0	−4.5	−5.7
9	38.6	33.9 (0.9551)	33.3	33.7	32.6
10 + H•	39.4	23.6 ([0])	30.9	30.6	33.4

[a] Energies of all species are 298 K enthalpies in kcal/mol with respect to the *n*-butylamine radical cation (**2**) as the defined zero. [b](U)B3LYP/6-31+G(d,p). [c](U)MP2/aug-cc-pVDZ; values in parentheses are expectation values of the $\mathbf{S}^2$ operator (excluding H• when it is listed in column 1). [d](U)CCSD(T)/cc-pVTZ//(U)CCSD/cc-pVDZ with UB3LYP/6-31+G(d,p) zero-point and thermal corrections. [e](U)CCSD(T)/cc-pVTZ//(U)CCSD/cc-pVDZ with (U)MP2/aug-cc-pVDZ zero-point and thermal corrections. [f]DFT results empirically corrected by raising the energy of the *n*-butylamine radical cation by 6 kcal/mol (see text). [g]Result based on UCCSD(T)/cc-pVTZ//UB3LYP/6-31+G(d,p) calculation for structure **7**. [h]Result based on UCCSD(T)/cc-pVTZ//UMP2/aug-cc-pVDZ calculation for structure **7**.

for CO_2? If either of these reactions proved to be possible, it may be feasible to prepare amines whose oxidation intermediates and products would be less susceptible to side reactions than those formed by loss of an α hydrogen.

The questions were addressed by carrying out a variety of calculations on reactions of an *n*-butylamine radical cation. Although the amines of principal interest for CO_2 reduction are tertiary, the selection of this smaller primary amine for the prototype calculations made it possible to use coupled-cluster methods as the benchmark against which lower level models, to be used with larger molecules, could be compared. Calibration was expected to be particularly important for the reactions of interest in the present work, because radical ions present real challenges to most of the popular electronic-structure methods. For the present purposes, those challenges take several different forms:

(1) Common density functional theory (DFT) methods suffer from a self-interaction error that can become particularly serious in radical ions.[37]

(2) Unrestricted second-order Møller−Plesset theory (UMP2), which does not suffer from the self-interaction error, does frequently suffer from bad spin contamination.[38]

(3) Several of the reactions of interest involve ionic intermediates and only become energetically accessible in polar solvents. Some sort of solvent model consequently has to be included in the calculations for reactions of this type.

(4) The reactions of interest are photochemically initiated, and so some steps necessarily involve crossings between excited and ground potential energy surfaces.

Three reactions leading to loss of a hydrogen atom from the *n*-butylamine radical cation were considered (Scheme 1). The first was the normal loss of an α hydrogen, with concomitant generation of an iminium ion, reaction 10. The second was displacement of a hydrogen atom from the methyl group, affording the pyrrolidinium ion, reaction 11. The third was intramolecular hydrogen-atom transfer from the methyl to the nitrogen, leading to a distonic radical ion,[36] which could subsequently lose a hydrogen atom to give the 3-butenylammonium ion, reaction 12.

Several computational models were used to evaluate the energetics of these reactions. The highest level, used as a benchmark for the others, was (U)CCSD(T)/cc-pVTZ//(U)-CCSD/cc-pVDZ, with zero-point and thermal corrections calculated at either the DFT or MP2 levels specified next. Despite its potential shortcomings,[37] one of the few credible electronic-structure models deemed to be computationally feasible for some of the large molecules discussed later was the hybrid DFT method (U)B3LYP/6-31+G(d,p), and so it was compared to the benchmark for the prototype reactions. In earlier work on

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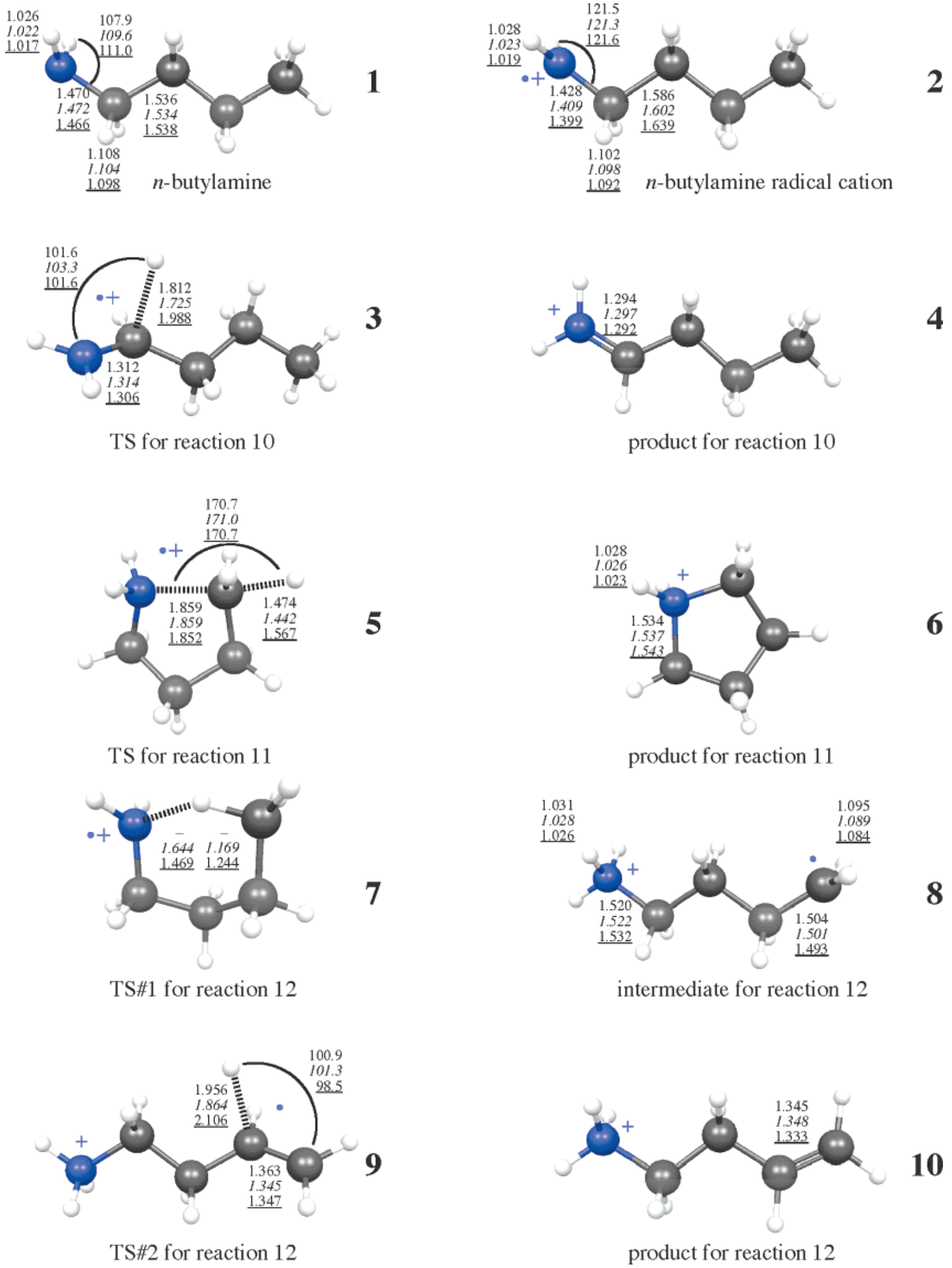


Figure 1. Selected geometrical parameters for stationary points in reactions 10−12. Distances are in angstroms with respect to all other species, and angles, in degrees. Plain text values are from (U)CCSD/cc-pVDZ, italic values are from (U)MP2/aug-cc-pVDZ, and underlined values are from (U)B3LYP/6-31+G(d,p) calculations. Transition structure **7** could not be found at the UCCSD/cc-pVDZ level (see text).

reduction of CO_2 by triethylamine, (U)MP2/aug-cc-pVDZ had been found to be satisfactory,[34] and so it too was compared to the coupled-cluster model. The results are summarized in Table 1.

Initial inspection of the results summarized in the first two data columns of Table 1 seemed to confirm the concerns about the DFT and MP2 models under evaluation. They differed in their estimates of the enthalpies of some of the stationary points by as much as 19 kcal/mol. However, comparison of the results with the coupled-cluster (CC) benchmarks revealed that the errors were apparently largely systematic. For example, the DFT results were all higher than the CC values by about the same amount, suggesting that there could be a significant error in the calculation on the reference zero, i.e., the *n*-butylamine radical cation. Further calculation seemed to confirm that conclusion, since the (U)B3LYP/6-31+G(d,p) value for the adiabatic ionization potential (IP) of *n*-butylamine was 6.0 kcal/mol below the experimental value. Raising the energy of the *n*-butylamine radical cation by 6.0 kcal/mol produced the corrected DFT values in the rightmost column of Table 1. These exhibited rms differences from the CC-1 and CC-2 references of 2.2 and 2.4 kcal/mol, respectively.

It is likely that the origin of the problem in the DFT calculation on the *n*-butylamine radical cation is the well-known self-interaction error, which leads to an abnormal favoring of states with delocalized charge and spin over localized ones.[37] Consistent with this interpretation, we note that the minimum-energy geometry for the radical cation in the DFT calculation has a seemingly larger contribution from C−C hyperconjugation than that optimized at the UCCSD level. The C−N and Cα−Cβ distances are, respectively, 1.399 and 1.639 Å at the UB3LYP level but 1.428 and 1.586 Å at the UCCSD level (Figure 1).

In order to assess the likely transferability of this information to the tertiary and aromatic amines considered later, UB3LYP/6-31+G(d,p) calculations of the adiabatic ionization potentials for trimethylamine, ethyldimethylamine, *tert*-butyldimethylamine, triethylamine, and *N*,*N*-dimethylaniline were also carried out. The results were found to be respectively 5.3, 5.7, 4.6, 7.6, and 1.6 kcal/mol below the experimental values. The consistent underestimate of the energy of the radical cations but the decrease in the magnitude of the discrepancy for the conjugated example all point to the self-interaction error as the likely source of the problem. Together, the calibration calculations suggested that the UB3LYP/6-31+G(d,p) calculations on the reactions of the aromatic amine radical cations described later should be reasonably reliable without correction but that calculations on the aliphatic amines would be improved if the energies of the amine radical cations were raised by about 6 kcal/mol.

The MP2 calculations on the reactions of the *n*-butylamine radical cation also showed systematic discrepancies, but with a less obvious origin. The adiabatic IP for *n*-butylamine was found to be within the error of the experimental value. The transition states for each of the reactions 10−12 were found to have energies within ±3 kcal/mol of the CC values, but for reasons that could not be determined, the products of H-atom expulsion were found to be too stable by ~8 kcal/mol. In addition, when MP2 calculations were carried out on some of the aromatic amine radical cations considered later in this paper, extreme spin contamination ($\langle \mathbf{S}^2 \rangle \approx 1.3$) was encountered. Given these problems, and given the substantially greater computational effort required for MP2 over DFT calculations (especially for vibrational frequencies), the decision was made to use the DFT model for the subsequent calculations in this study.

The calculations revealed that, as the simple thermochemical analysis had suggested, C−H homolysis with concomitant C−N σ bond formation (reaction 11) should be thermodynamically more favorable than simple α C−H scission. However, it was found to be kinetically less favorable, by about 10 kcal/mol in $\Delta H^{\ddagger}$. The third mechanism for H-atom loss (reaction 12) was found to be similarly kinetically disadvantaged and also to be thermodynamically less favorable than either of the other two.

No transition state for the intramolecular hydrogen-atom transfer could be found at the UCCSD/cc-pVDZ level. Two pieces of evidence suggest the reason is that, at the CC level and probably in reality,[36] the reaction is activationless. UCCSD(T)/cc-pVTZ calculations at the geometries of either the DFT or MP2 transition structures afforded negative activation enthalpies for the reaction (Table 1). The same result came from the empirical correction of the DFT calculations described above. Of course, even if the conclusion was correct, the transfer would only be activationless from a conformation of the butylamine radical cation capable of bringing the ends of the molecular chain together. There would be conformational barriers to be surmounted in reaching such a structure from the minimum-energy geometry of the amine radical cation. That conclusion, in turn, obviously suggests exploration of conformationally restricted amines that could be held in geometries appropriate for the intramolecular H transfer. Examples of such amines are discussed below.

The assessment of relative favorabilities for the three mechanisms of gas-phase unimolecular H-atom expulsion could not be assumed to mirror relative favorabilities for H-atom transfer to $CO_2^{\bullet-}$ in a polar solvent, as would presumably occur in the desired CO_2 reduction process. In particular, the conversion of photochemically generated radical ion pairs into closed-shell products requires a surface crossing, presumably a conical intersection, to be negotiated at some stage. In earlier work on reduction of CO_2 by triethylamine, we showed that the direct transfer of an α hydrogen atom from the amine radical cation to the carbon of CO_2 is apparently not accompanied by the necessary surface crossing and that reduction of CO_2 probably has to start along a coordinate for *proton* transfer to *oxygen*.[34] During this encounter, the closed-shell surface is always lower in energy than the open-shell one, and so a back electron transfer can potentially regenerate neutral CO_2 and the starting amine, leading, obviously, to a lower quantum yield for the reduction of CO_2 (although the earlier calculations have suggested that the thermodynamics of this process place it well into the Marcus inverted region[34]). The question of interest for the new reactions considered here was whether a more efficient reduction could be anticipated.

In the earlier work on CO_2 reduction by triethylamine, the issue of a surface crossing during hydrogen transfer was addressed by comparing closed-shell restricted DFT or MP2 results to broken-symmetry unrestricted solutions, with the two being expected to be roughly degenerate at a surface crossing. The acetonitrile solvent was simulated by a polarizable-continuum model, the details of which were described in the earlier paper.[34] Use of these approximate models was necessitated by the lack of readily available methods for carrying out conical-intersection searches with simultaneous solvent simulation. Similar issues were faced in the present work, and so a similar approach was employed.

Unfortunately, despite repeated attempts, no transition structure could be located for direct cyclization of *n*-butylamine and simultaneous transfer of a hydrogen to CO_2 in acetonitrile. Thus the question of surface crossings along this coordinate could not be directly addressed. However, since the closed-shell state is certainly far below the lowest open-shell state for both reactants (CO_2 and *n*-butylamine) and products (pyrrolidinium ion, **6**, and formate ion), it seems improbable that there would be a crossing between these surfaces at any intermediate point in the reaction. Hence, by analogy with the α hydrogen transfer, we hypothesize that the reaction starting from the amine radical cation and CO_2 radical anion would have to progress part way along a path for proton transfer to oxygen before encountering a surface crossing. At this crossing there would presumably be

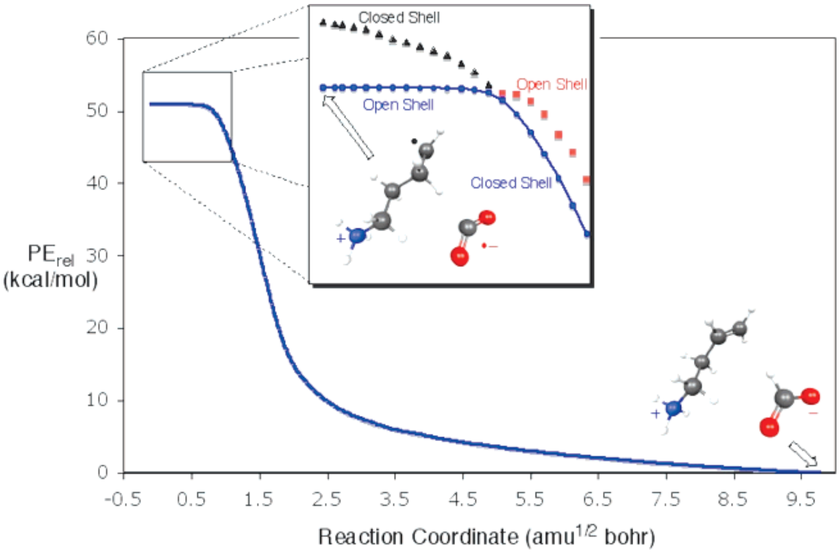


Figure 2. UB3LYP/6-31+G(d,p) intrinsic reaction coordinate for hydrogen transfer from distonic radical ion **8** to $CO_2^{\bullet-}$. Calculations used a PCM simulation of CH_3CN solvent. The closed-shell points to the left of the intersection came from RB3LYP calculations. The open-shell points to the right of the intersection came from empirical corrections to calculations on the triplet state (see text).

pathways for productive CO_2 reduction and unproductive back electron transfer. Consequently there is no reason to believe that this reaction would be more (or less) efficient than the transfer of an α hydrogen for effecting CO_2 reduction.

It was anticipated that the situation might be quite different for the hydrogen-atom transfer from distonic radical ion **8** to $CO_2^{\bullet-}$. We expected that, at the equilibrium geometries of **8** and $CO_2^{\bullet-}$, the open-shell state should be lower in energy than a closed-shell state, corresponding to CO_2 plus a zwitterion. For the products, **10** plus formate ion, there was little doubt that the ground electronic state would be closed shell. If these expectations were verified, then a crossing between open- and closed-shell potential energy surfaces would have to occur somewhere along the hydrogen-transfer coordinate.

A transition structure for the hydrogen transfer was located at the UB3LYP/6-31+G(d,p) level, using a polarizable-continuum simulation of acetonitrile solvent. It was found to have $\langle \mathbf{S}^2 \rangle = 0.7556$, indicating an open-shell ground state. An intrinsic reaction coordinate (IRC) calculation revealed that it was the transition structure for direct hydrogen transfer between the distonic radical ion **8** and $CO_2^{\bullet-}$ and, of principal interest, that it did cross over to a closed-shell ground state during the transfer. On the reactant side, the IRC led to a local minimum corresponding to a radical ion pair that was very similar in both structure and energy to the hydrogen-abstraction transition structure. In fact, when zero-point energy corrections were included, there was no barrier to the reaction.

In order to map out the rough shape of the crossing energy profiles, single-point RB3LYP calculations were carried out for each of the points along the IRC with open-shell ground states. In addition, the energy of the lowest triplet state was calculated at points of the IRC near the crossing. The energy gap between open-shell singlet and triplet states was well described (±0.5 kcal/mol) by a simple quadratic function of the reaction coordinate parameter. By assuming that this function would continue to be valid after the closed-shell configuration had become the ground state, it became possible to estimate the energy of the open-shell singlet state from calculations on the triplet. The resulting curve crossing is shown in Figure 2.

In summary, the following conclusions could be drawn from the calibration calculations.

(1) (U)B3LYP/6-31+G(d,p), in some cases augmented by an empirical correction, was judged to be an adequate theoretical model for describing the larger amine radical ions to be discussed later in the paper. (U)MP2/aug-cc-pVDZ, although shown to be superior to DFT in earlier work,[34] was here found to suffer from some systematic energy errors and unacceptable spin contamination for certain species.

(2) The remote C−H activation reactions forming the principal focus of the present work were calculated to be kinetically disadvantaged by ~10 kcal/mol in $\Delta H^{\ddagger}$ with respect to simple α C−H homolysis of the amine radical cation. However, this comparison was made for the unimolecular H-atom extrusion reactions in the gas-phase rather than for the solution-phase H-atom transfers to $CO_2^{\bullet-}$. In addition, the ring-forming reaction, 11, was found to be thermodynamically more favorable than α C−H homolysis.

(3) It was concluded that hydrogen displacement reaction 11 would probably have no kinetic advantage over transfer of an α hydrogen to $CO_2^{\bullet-}$, although that issue could not be addressed directly because the transition state for the reaction could not be located in the calculations.

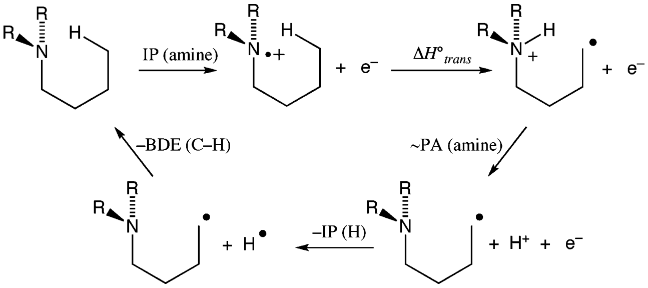
(4) The reaction sequence 12, involving intramolecular hydrogen transfer, although calculated to be the least favorable of the unimolecular gas-phase fragmentations, was found to provide potentially the most favorable route to solution-phase CO_2 reduction. The basis for this conclusion was the discovery of an apparent surface crossing along the reaction coordinate for direct hydrogen transfer from distonic radical ion **8** to the carbon of $CO_2^{\bullet-}$.

With these fundamental issues established for the theoretical models and reactions under consideration, attention was turned to larger amines that could be evaluated as candidates for experimental studies on photochemical CO_2 reduction.

Evaluation of Aromatic Amines for CO_2 Reduction

The purpose of the calculations described in this paper was to evaluate ways to avoid the complications in amine oxidation

Scheme 2. Thermodynamic Cycle for Evaluating the Enthalpy of Intramolecular Hydrogen-Atom Transfer ($\Delta H°_{trans}$) in an Amine Radical Cation



that can follow the loss of an α hydrogen. The most obvious way to accomplish that would be to design amines that either had no α hydrogens or possibly had them at locations that would disfavor their loss (such as at the bridgehead sites of small bicyclic systems). For purely aliphatic amines this is not easy to achieve. Two of the side chain α sites could be used up in bridgehead positions if one adopted the bicyclic strategy, but the third side chain would still have to be a *tert*-butyl group or something similar. The synthesis of such amines is not straightforward, and their potential for fragmentation upon oxidation might be a cause for concern.

These issues would obviously be easily addressed if one chose to use aromatic amines rather than aliphatic ones. That solution could offer the added benefit that aromatic amines tend to have lower ionization potentials than aliphatic ones. A lower IP for the amine would potentially mean that longer wavelength light could be used for the photochemical CO_2 reduction. At present, most schemes for achieving this reaction rely on UV light, whereas the maximum in sea-level solar irradiance occurs well into the visible.[39] However, in the case of the mechanism relying on intramolecular hydrogen transfer (reaction 12 being the prototype) a lower IP for the amine could also have undesirable consequences. The problem is illustrated by the thermodynamic cycle[40] shown in Scheme 2.

In reactions such as 12, the energy of the incident photon is available to produce the amine radical cation and $CO_2^{\bullet-}$. It is not available to promote the hydrogen-atom transfer from carbon to nitrogen if that should turn out to be either endothermic or to have a large activation barrier. Hence, in order to be fast enough to compete with back electron transfer, one needs the hydrogen transfer to be exothermic or thermoneutral and to have little or no barrier. The cycle in Scheme 2 seeks to evaluate the factors influencing the thermodynamics of the reaction. Starting from the amine, the first step defines the ionization potential. The second step is the reaction of interest. The third step defines the proton affinity (PA) of the distonic radical ion, which is taken to be approximately the same as the PA of the starting amine. The fourth step is simply the negative of the IP of a hydrogen atom (13.6 eV), and the final step is the negative of the C−H bond dissociation enthalpy (BDE) of the starting amine, which is assumed to have a constant value equal to the terminal C−H BDE of propane (101 kcal/mol).[41] With these assumptions, one can estimate $\Delta H°_{trans}$ by eq 13, for which all variables are in units of kcal/mol:

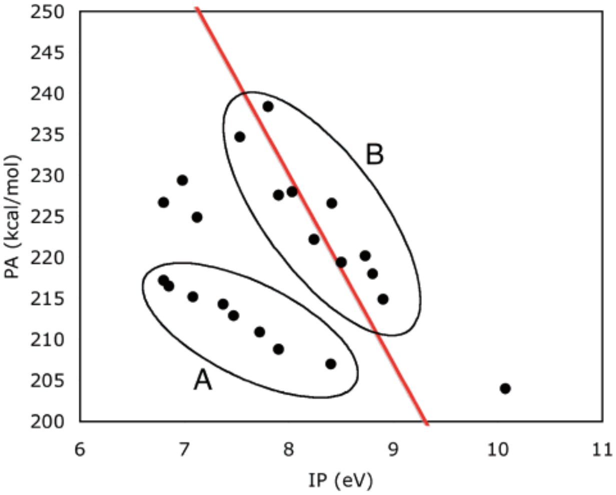


Figure 3. Plot of proton affinity (PA) vs ionization potential (IP) for several amines. Identities of the amines and data used to construct the plot are available in the Supporting Information. The amines in group A are ring-substituted anilines. Group B contains aliphatic amines. The isolated point at the lower right is ammonia. The other three points are *N*,*N*-dialkylanilines. The red line marks the predicted boundary of thermoneutrality for intramolecular hydrogen transfer from carbon to nitrogen in the amine radical cation.

$$\Delta H°_{trans} = 414.6 - \mathrm{IP(amine)} - \mathrm{PA(amine)} \qquad (13)$$

This equation shows that reducing the IP of the amine will increase the enthalpy for the hydrogen transfer unless it is accompanied by a compensating increase in proton affinity of the amine. Within structurally related groups of amines, there does tend to be an inverse correlation between IP and PA, but between structural classes there is not. Figure 3 shows a plot of PA vs IP for a number of amines. It also shows a red line corresponding to thermoneutrality for the hydrogen-atom transfer. Points to the right of the line are predicted to have exothermic transfers from carbon to nitrogen, whereas those to the left are predicted to have endothermic transfers.

Confidence in the reliability of eq 13 was bolstered by results for *n*-butylamine where the predicted value of $\Delta H°_{trans} = -6.9$ kcal/mol, using experimental IP and PA values, could be compared with the directly calculated values of −4.5 to −5.0 kcal/mol from the coupled cluster results in Table 1, and for *o*-ethylaniline which gave a predicted $\Delta H°_{trans}$ of +28.0 kcal/mol from eq 13 and a calculated value of +25.7 kcal/mol at the CBS-QB3 level.

Figure 3 reveals that there is little hope of making the hydrogen transfer thermoneutral or exothermic for any amine based on a simple aniline motif. *N*,*N*-Dialkylanilines do somewhat better but still need an almost 30 kcal/mol higher proton affinity to approach the red line. However, it should be emphasized that this conclusion applies only to CO_2 reductions based on mechanisms like reaction 12. If maximizing the wavelength of the light used to drive the reaction turns out to be more important than improving the quantum yield for the reaction, use of aromatic amines in schemes exemplified by reaction 11 may turn out to be worth investigating. In addition, since the goal is to design a renewable amine for CO_2 reduction, a greater synthetic investment may be warranted than would

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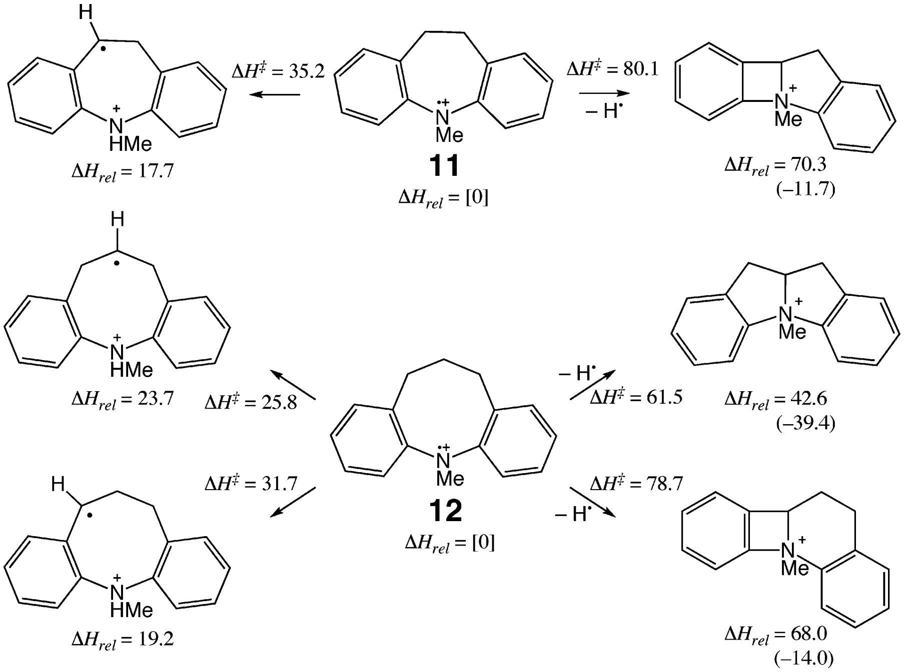
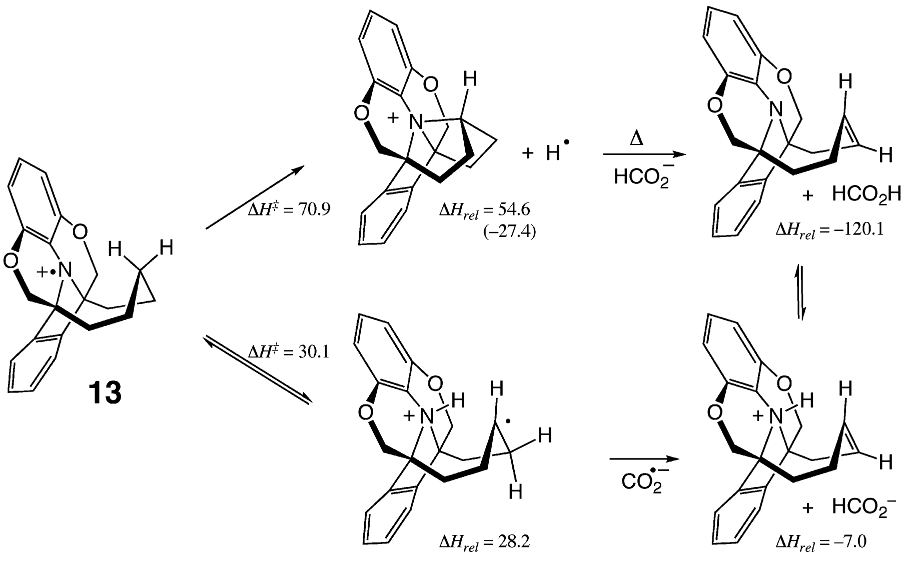
(39) Pap, J. M.; Frohlich, C. *J. Atmos. Sol.-Terr. Phys.* **1999**, *61*, 15−24.
(40) A similar analysis has previously been applied to hydrogen transfers in imine radical cations and the ammonia radical cation: (a) Qin, X.-Z.; Williams, F. *J. Am. Chem. Soc.* **1987**, *109*, 595−597. (b) Williams, F. *J. Am. Chem. Soc.* **1962**, *84*, 2895−2898.
(41) Blanksby, S. J.; Ellison, G. B. *Acc. Chem. Res.* **2003**, *36*, 255−263.

Scheme 3. (U)B3LYP/6-31+G(d,p) Enthalpy Changes for Remote C−H Activation by Two Singly Bridged Diarylamines[a]



[a] All numbers are in kcal/mol. Numbers in parentheses under the right-hand structures correspond to the enthalpy changes for formation of the indicated ion plus formate ion from the starting radical cation + $CO_2^{\bullet-}$.

Scheme 4. Reactions and Thermochemistry of a Polycyclic Monoarylamine Radical Cation



be the case if the amine was a sacrificial reducing agent. With additional synthetic effort it is possible to construct aromatic amines with structural features that do promote the carbon-to-nitrogen hydrogen transfer in the radical cation. An example is included in the list of amines whose suitability for CO_2 reduction is evaluated below.

Singly Bridged Diarylamines

In an effort to verify some of the general conclusions described above, and also as a preliminary exploration of any additional parameters of the problem, calculations (here and from now on taken to be at the (U)B3LYP/6-31+G(d,p) level, in the gas phase) were conducted on the analogues of reactions 11 and 12 for amine radical cations **11** and **12** (Scheme 3). The α hydrogens of the *N*-methyl groups in these species might make them unsuitable in reality, but for the present purposes that was not a concern.

The adiabatic IPs of the amines leading to **11** and **12** were calculated to be 6.84 and 6.67 eV, respectively. The earlier calibration calculations suggest that these ought to be close to the true values. Consistent with the low IPs and the expectations from eq 13, the intramolecular hydrogen-atom transfers were all found to be endothermic. Not surprisingly, the abstractions of benzylic hydrogens were calculated to be thermodynamically more favorable, although not by as much as one might have expected. The new information from these calculations was that hydrogen transfer through a six-membered ring transition structure should be kinetically favored. This is consistent with the conclusions from experiments on hydrogen transfers in aliphatic amine radical cations[36] and from a computational study on hydrogen-atom transfers in hydrocarbon radicals.[42]

The hydrogen-atom displacement reactions were all found to be very endothermic, with corresponding high activation energies, when computed as unimolecular dissociations. However, the direct bimolecular hydrogen transfers to $CO_2^{\bullet-}$ were all exothermic. Transition structures for the bimolecular reactions were not located because these would need to be optimized with simultaneous solvent simulation, and those calculations would be prohibitively time-consuming.

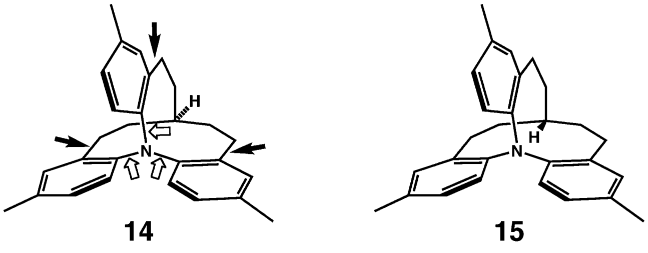
In summary, the amines leading to radical ions **11** and **12** would be expected to have the virtue of low IPs but would be unsuitable for CO_2 reduction by reactions of type 12. Analogues lacking α hydrogens may be suitable for CO_2 reduction by reactions of type 11, especially when the displacement avoids the formation of a strained ring.

A Polycyclic Monoarylamine

Building on the idea of remote activation of the 5 position in an azacyclooctane derivative, which was identified as favorable in the calculations on radical cation **12**, an effort was made to design an amine that would have a very low IP but whose radical cation might still be capable of carrying out useful C−H activation of this kind. The one eventually selected for evaluation is shown in Scheme 4. The adiabatic IP of the amine leading to radical cation **13** was calculated to be only 6.54 eV. The calibration studies suggest that the true value might be about 0.1 eV higher. Given that triethylamine (IP 7.53 eV) can be oxidized to its radical cation and CO_2 reduced to its radical anion using photocatalysts and light at 308 nm,[4] the present calculations predict that the radical cation **13** should be easily formed from its amine with photocatalysts absorbing in the visible. The question, of course, is whether **13** is capable of transferring a hydrogen to $CO_2^{\bullet-}$ by an energetically accessible mechanism.

Given the predicted low IP for the amine leading to **13**, it was not surprising that the intramolecular hydrogen-atom transfer was found to be endothermic, although, since the amine also has a quite high proton affinity (230 kcal/mol), the effect of the IP is somewhat mitigated. Nonetheless, the predicted barrier of 30 kcal/mol means that, as expected, this mechanism would almost certainly not provide a viable route for CO_2 reduction.

The displacement route appears even more unfavorable if one looks only at the unimolecular hydrogen-atom extrusion. It was calculated to be endothermic by about 55 kcal/mol and to face a barrier of 71 kcal/mol. However, the direct hydrogen transfer to $CO_2^{\bullet-}$ was found to be exothermic by 27 kcal/mol. Undoubtedly the enthalpic barrier for the bimolecular reaction would be lower than that for the unimolecular one, but by how much is hard to assess since the gas-phase calculation converges on the wrong electronic state (corresponding to hydrogen transfer from the neutral amine to CO_2), and the calculation with simultaneous solvent simulation was too computationally intensive to attempt.



14

H_{rel} = [0]

15

H_{rel} = 4.0 kcal/mol

Figure 4. Stereoisomers of a bridged triarylamine potentially suitable for CO_2 reduction. Plausible synthetic routes might make the bonds indicated by the solid arrows or by the open arrows.

The polycyclic ammonium ion generated by the displacement reaction can be exothermically opened to an alkene in a Hofmann elimination, with a formate ion acting as base. Again, calculation of the barrier for this reaction would require geometry optimization and frequency calculations with concurrent solvent simulation, and so was not attempted. Photochemical transfer-hydrogenation of the alkene, which is known for cyclooctene,[43] would regenerate the original amine. It is perhaps worth reiterating that the design of amines whose oxidation products have this recyclable quality constituted the motivation for this whole study.

Stereoisomeric C_3 Triarylamines

The hydrogen-transfer and hydrogen-displacement reactions separate nicely in the two stereoisomers of a C_3 triarylamine, shown in Figure 4.

It will be apparent by inspection that the radical cation of amine **14** should be capable of effecting the hydrogen-displacement reaction at the bridgehead site but that there is no plausible hydrogen-transfer pathway. By contrast, the radical cation of amine **15** looks predisposed to hydrogen transfer but has no obvious hydrogen-displacement reaction. The two isomers were calculated to be quite close in heat of formation by the DFT model (and even closer at the MP2 level, which found only 0.4 kcal/mol difference), and so it seems probable that syntheses relying on formation of the set of bonds indicated by the solid arrows in Figure 4, or the set indicated by the open arrows, would be likely to afford a mixture of the two amines. The enthalpy changes of the reactions expected for the corresponding radical cations are summarized in Scheme 5.

Interestingly, amines **14** and **15** were calculated to have very different adiabatic IPs. The IP for amine **14** was found to be 6.25 eV, whereas that for **15** was 7.63 eV. Consistent with eq 13 and the relatively high IP for amine **15**, the equilibrium geometry for its radical cation was found to have a bridged structure, in which the hydrogen inside the cage was shared between the nitrogen and bridgehead carbon, although more tightly bound to the former (Figure 5). Loss of a hydrogen atom from that structure apparently involves no transition state; i.e., the addition back of the hydrogen to the alkene is calculated to be activationless.

The final oxidation product of either **14** or **15** is a bridgehead alkene, but the rings are large enough that this seems to cause little strain in the molecule, as evidenced by the fact that the overall enthalpy change for amine$^{\bullet+}$ + $CO_2^{\bullet-}$ going to alkene + formic acid was found to be very similar for **13** (−120.1 kcal/mol) and **14** (−121.9 kcal/mol).

The alkene derived from **15** has some potentially interesting properties. The ammonium ion in this molecule would presum-

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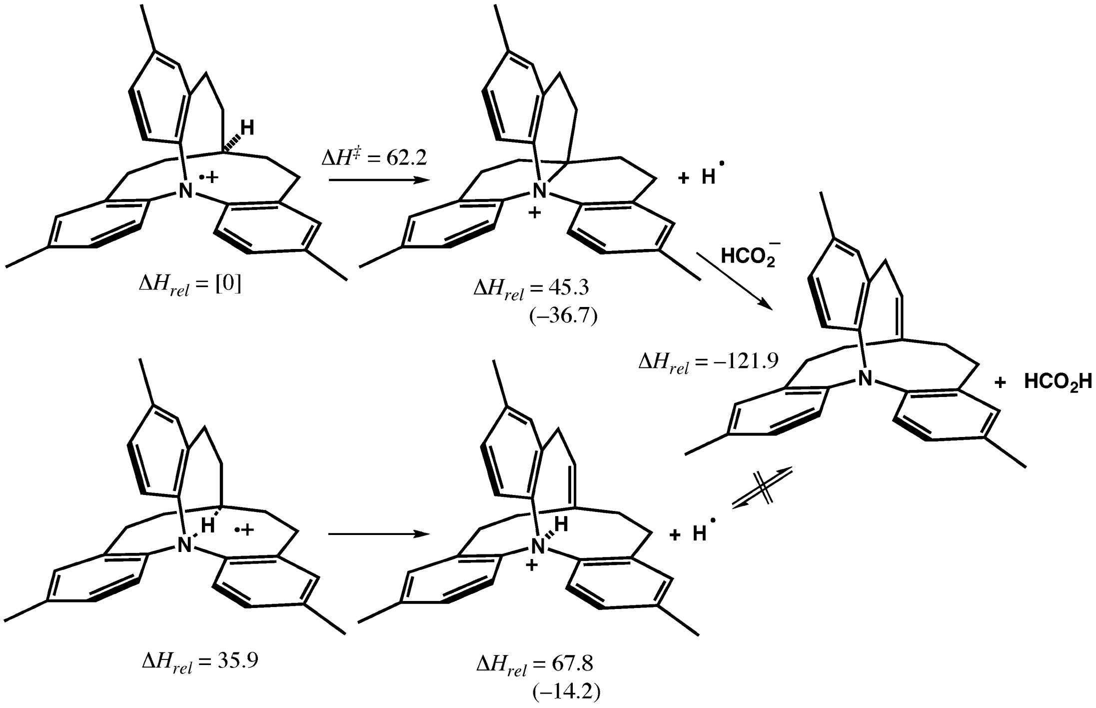
(42) Huang, X. L.; Dannenberg, J. J. *J. Org. Chem.* **1991**, *56*, 5421−5424.

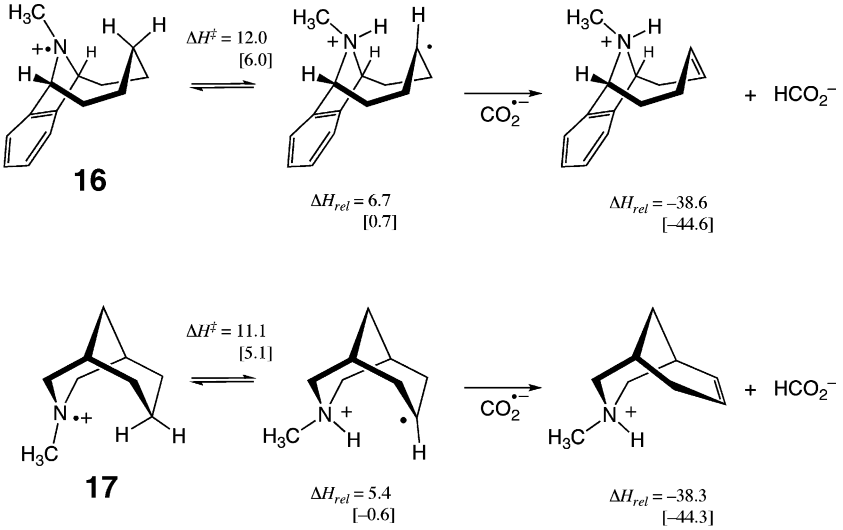
(43) Hanaoka, T.; Matsuzaki, T.; Sugi, Y. *J. Mol. Catal. A* **1999**, *149*, 161−167.

Scheme 5. Calculated Enthalpy Changes for the Key Reactions of the Radical Cations from Amines **14** and **15**[a]



[a] Numbers in parentheses correspond to enthalpy changes for direct hydrogen-atom transfer to $CO_2^{\bullet-}$.

Scheme 6. Calculated Thermochemistry for the H-Transfer Reactions of Radical Cations **16** and **17**[a]



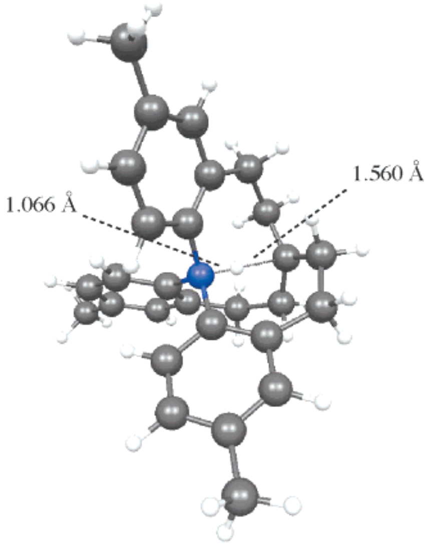
[a] Numbers in square brackets include the empirical correction deduced from the calibration studies.

ably be quite difficult to deprotonate in any intermolecular reaction, since the proton on nitrogen is buried within the molecular cage. However, intramolecular proton transfer should be very facile, because the ammonium proton is held only 1.8 Å away from the bridgehead carbon (Figure 5). This could make the alkene unusually susceptible to nucleophilic addition, although that question was not pursued in the present calculations. If the prediction should turn out to be correct, it might open up new hydride-addition routes for reduction of the alkene back to **15**.

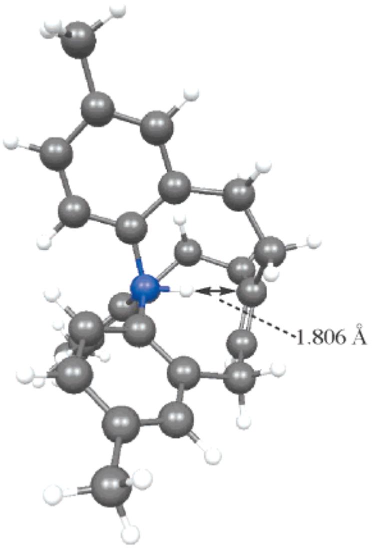
Policyclic Trialkylamines

Although the calculations on **15** suggested that it should be possible to find an aryl amine radical cation for which intramolecular hydrogen-atom transfer would be thermodynamically favorable, the molecular design that made this possible also raised the IP of the amine to a value more typical of aliphatic amines. Given that fact, it seemed worthwhile to explore an alternative strategy for effecting CO_2 reduction by reactions of type 12.

If a trialkylamine could be designed in which the intramolecular reaction would be both fast and exothermic, then α hydrogens might be tolerated, because the loss of those atoms by bimolecular transfer to $CO_2^{\bullet-}$ would presumably be slower than the unimolecular rearrangement. For the butylamine radical cation the calculations found that the only barrier to hydrogen transfer from the methyl group was conformational. Consequently, if one could find an amine radical cation whose lowest



Radical cation from **15**



Alkene from **15**

Figure 5. Key distances in the radical cation and alkene product derived from amine **15**.

energy conformation was already appropriate for the reaction, its intramolecular transfer should be very fast. Two candidate structures were explored. One, **16**, was a simplified structural analogue of **13**. The other was 3-methyl-3-azabicyclo[3.3.1]-nonane, **17**, for which the atoms of the transition structure for intramolecular hydrogen migration should adopt an adamantane-like geometry. The calculated thermochemistry for their hydrogen transfer is summarized in Scheme 6.

The IPs of the amines leading to **16** and **17** were found to be 6.95 and 7.18 eV, respectively. On the basis of the calibration studies described earlier, we would judge that the true values are probably about 0.25 eV higher. That correction should also be applied to the activation and reaction enthalpies of the radical ions, leading to the numbers in square brackets in Scheme 6.

One sees that for both **16** and **17** the hydrogen-transfer steps are predicted to be very nearly thermoneutral and to face only small barriers. Reactions of these radical cations with $CO_2^{\bullet-}$ could therefore be in the classic Curtin−Hammett situation where yields of products from the original radical cation or from the distonic radical ion would depend on the free energy barriers to the two hydrogen-transfer steps. As described in the section on the butylamine radical cation, we believe that the direct hydrogen transfer to the carbon of $CO_2^{\bullet-}$ involves a favorable surface crossing for the distonic radical ion but not for the amine radical cation, and so it seems plausible that the former would be faster, although that issue was not susceptible to direct computation with the available theoretical models.

Summary and Conclusions

The following principal conclusions could be drawn from the calculations described in this paper.

(1) Two remote C−H activation modes were identified for amine radical cations. One was a hydrogen-atom displacement reaction, involving formation of a new C−N σ bond and a ring. The other was an intramolecular hydrogen-atom transfer, involving a distonic radical ion as an intermediate. Both would be expected to lead eventually to oxidation products from which the original amine could be regenerated. The displacement reaction was found to be thermodynamically more favorable than α C−H cleavage, provided that the ring being formed was not too small. However, both new reactions were calculated to be kinetically less favorable than α C−H cleavage when all were treated as unimolecular fragmentations.

(2) Although a transition state for ring formation and direct hydrogen transfer to the carbon of $CO_2^{\bullet-}$ could not be located, it was concluded that there was probably no crossing of the S_0 and S_1 potential energy surfaces along the direct reaction coordinate for this process. By contrast, the hydrogen transfer from a model distonic radical cation to the carbon of $CO_2^{\bullet-}$ was found to be activationless and to involve an apparent surface crossing. This would seem to make the distonic intermediate a more efficient reducing agent than the original amine radical cation.

(3) Since the energy of the incident photon is available only for the preparation of the amine radical cation, any subsequent reactions of that intermediate must be thermally activated. Earlier work on the transfer of an α hydrogen to $CO_2^{\bullet-}$ suggested that this would be a reaction involving a small enthalpic barrier. It was judged to be likely that the new hydrogen displacement reaction studied in the present work would face a similar barrier if the extruded hydrogen atom was donated directly to $CO_2^{\bullet-}$, but that could not be determined directly because a transition state for the reaction could not be located. For the mechanism involving intramolecular hydrogen transfer to compete with these other two, its first step must be fast and thermodynamically favorable. A simple thermochemical cycle was used to show that the enthalpy change for the hydrogen transfer could be estimated from the IP and PA of the starting amine. Since these quantities are known experimentally for a large number of amines, the suitability of general classes of amine could be quickly assessed. That analysis indicated that simple aryl amines would generally be unsuitable because the formation of the distonic radical ion would be strongly endothermic.

(4) Although generally unsuitable for CO_2 reductions relying on the intramolecular hydrogen-transfer mechanism, aryl amines do have the virtue of low IPs, permitting the use of longer wavelength light for the reaction. Aryl amines that could utilize the hydrogen-displacement mechanism might therefore still be

useful renewable reducing agents if the wavelength of the light employed was judged to be more important than the quantum yield of the reaction.

(5) Some polycyclic trialkyl amines were designed for which the calculations suggested that the formation of the distonic radical cation should be fast and nearly thermoneutral. These compounds could be useful renewable reducing agents for the photochemical reduction of CO_2 under circumstances where the quantum yield of the reaction was judged to be more important than the wavelength of the light employed.

Work is under way to prepare the most promising amines identified in the present study.

Acknowledgment. Support of this work by the Leverhulme Trust is gratefully acknowledged. The Physical Organic Chemistry Centre at Cardiff University was created with a Science and Innovation Award from the Engineering and Physical Sciences Research Council and by a grant from the Strategic Research Infrastructure Fund (SRIF) of the Higher Education Funding Council for Wales (HEFCW), which are also gratefully acknowledged. The computations were carried out in part on the Helix cluster at Cardiff University, funded by SRIF (HEFCW).

Supporting Information Available: Coordinates and energies of all stationary points for the reactions described above, identities of amines and values of their IP and PA, used in preparing Figure 3, and full literature references for the computational packages and theoretical models used in this work. This material is available free of charge via the Internet at http://pubs.acs.org.

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