JOC*Note*
pubs.acs.org/joc

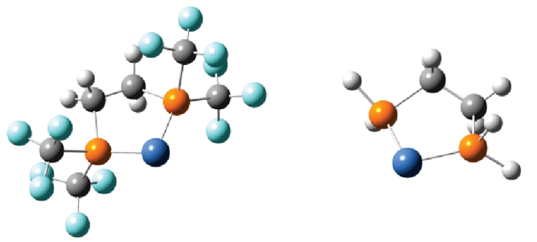
A Computational Study of Metal-Mediated Decomposition of Nitrene Transfer Reagents

Thomas R. Cundari* and Glenn R. Morello

Department of Chemistry for Advanced Scientific Computing and Modeling (CASCaM), University of North Texas, P.O. Box 305070, Denton, Texas 76203-5070

t@unt.edu

Received May 5, 2009



Metal-mediated decomposition to form nitrene complexes is investigated by using DFT for prototypical organic azides and iodonium imides used in organic synthesis. Each system exhibited exothermic pathways via formation of cyclic intermediates, which decompose to yield LNi=NX+Y (L = bis-phosphine, NX = nitrene, Y = N_2 or IPh). Also, the typical heterotransfer reagents used in organic synthesis show a greater tendency toward triplet nitrene complexes and hence the potential for metal-free reactivity than aliphatic and aromatic substituted versions.

Aziridines are important chemical intermediates, and are often synthesized via metal-catalyzed nitrene transfer to olefins.[1] The model catalyst, (dhpe)Ni (dhpe = 1,2-bis(dihydrophosphino)ethane), was shown via DFT to be thermodynamically and kinetically competent for activation and decomposition of aliphatic azides to yield N_2 and nitrene complexes, (dhpe)Ni=NR.[2] However, the transfer reagent is typically a heteroatom-substituted entity in most syntheses. For example, Martinez-Garcia et al. studied the effect of calyx[4]pyrrole on the CuCl-mediated reaction of chloramine-T ($TsNCl^-Na^+$) with styrene.[3] Compounds like [*N*-(*p*-tolylsulfonyl)imino]phenyliodinane (PhI=NTs) are also convenient for aziridination and amination of organic substrates in the presence of transition metal (TM) catalysts.[4]

Nitrene transfer has gained importance recently with the need for cost-effective, eco-friendly catalytic reactions to produce amines and aziridines from simple organic substrates.[5] These concerns have motivated the use of simple organic azides for which N_2 is a benign leaving group. Transition metals can bind to the different nitrogens of RN_3,[5] depending on both electronic and steric effects as discussed in an excellent review by Cenini et al.[5]

The majority of biologically important molecules such as natural products and pharmaceuticals contain nitrogen in their frameworks.[1] Designing effective catalysts has been explored by many groups.[1,6] For example, Li and He explored Ag catalysts (in the presence of an oxidant) to produce aziridines from olefins and amines by hydrocarbon C−H bond activation.[6] Perez and co-workers have reported Cu complexes that catalyze nitrene transfer reactions with PhI=NTs.[7−9] Warren's group, in collaboration with our own, studied copper−β-diketiminates for nitrene transfer[10,11] with organic azides used as nitrene transfer reagents in the experiments.[11] Dias et. al. synthesized stable Cu(I) and Ag(I) complexes of organic azides having highly flourinated scorpionate coligands to compare the bonding mode of organic azides to that of different metal centers.[12]

Nitrene complexes have long been proposed as key intermediates in metal-catalyzed nitrene transfer,[5] although their isolation for catalytically competent systems is usually difficult. Late (groups 9−12) transition metals, particularly the 3d metals, have seen recent success in terms of isolating stable nitrene complexes and inspecting their reactivity. Examples of nitrene complexes, which were until recently largely limited to metals from the early and middle portions of the d-block, have recently been augmented by those of the later transition metals.[8,9,13]

$$(\text{dhpe})\text{Ni}+\text{XN-Y}\rightarrow(\text{dhpe})\text{Ni}{=}\text{NX}+\text{Y} \tag{1}$$

where XN−Y = organic azide ($R''N_3$) and iodonium imide (RN=IR′).

---

(1) Watson, I. D. G.; Yu, L.; Yudin, A. K. *Acc. Chem. Res.* **2006**, *39*, 194.

(2) Cundari, T. R.; Pierpont, A. W.; Vaddadi, S. *J. Organomet. Chem.* **2007**, *692*, 4551.

(3) Mertinez-Garcia, H.; Morales, D.; Pérez, J.; Coady, D. J.; Bielawski, C. W.; Gross, D. E.; Cuesta, L.; Marquez, M.; Sessler, J. L. *Organometallics* **2007**, *26*, 6511.

(4) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Org. Chem.* **1991**, *56*, 6744.

(5) Cenini, S.; Gallo, E.; Caselli, A.; Ragaini, F.; Fantauzzi, S.; Piangiolino, C. *Coord. Chem. Rev.* **2006**, *250*, 1234.

(6) Li, Z.; He, C *Eur. J. Org. Chem.* **2006**, 4313.

(7) Perez, P. J.; Brookhart, M.; Templeton, J. L. *Organometallics* **1993**, *12*, 261.

(8) Fructos, M. R.; Trofimenko, S.; Mar Diaz-Requejo, M.; Perez, P. J. *J. Am. Chem. Soc.* **2006**, *128*, 11784.

(9) Mar Diaz-Requejo, M.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Perez, P. J. *J. Am. Chem. Soc.* **2003**, *125*, 12078.

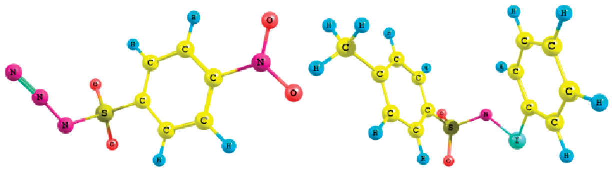
(10) (a) Amisial, L. D.; Dai, X.; Kinney, R. A.; Krishnaswamy, A.; Warren, T. H. *Inorg. Chem.* **2004**, *43*, 6537. (b) Badiei, Y. M.; Dinescu, A.; Dai, X.; Palomino, R. M.; Heinemann, F. W.; Cundari, T. R.; Warren, T. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 9961.

(11) (a) Kogut, E.; Weincko, H. L.; Zhang, L.; Cordeau, D. E.; Warren, T. H. *J. Am. Chem. Soc.* **2005**, *127*, 11248. (b) Badiei, Y. M.; Krishnaswamy, A.; Melzer, M. M.; Warren, T. H. *J. Am. Chem. Soc.* **2006**, *128*, 15056.

(12) Dias, H. V. R.; Polach, S. A.; Goh, S.; Archibong, E. F.; Marynick, D. S. *Inorg. Chem.* **2000**, *39*, 3894.

(13) Gullick, J.; Taylor, S.; Kerton, O.; McMorn, P.; King, F.; Hancock, F. E.; Bethell, D.; Bulman Page, P. C.; Graham, P.; Hutchings, G. J. J. *Catal. Lett.* **2001**, *75*, 151.

DOI: 10.1021/jo900941u Published on Web 06/17/2009



1 Ns **2** PhI=NTs

FIGURE 1. Compounds studied for Ni-mediated nitrene transfer.

Previous computations suggests that Ni–bis(phosphines) are viable catalysts for amination of C_{sp^3}–H bonds, particularly catalysts with electron-withdrawing perfluoroalkyl substituents on phosphorus.[14] In this Note we present a study of the decomposition of nitrene transfer compounds, Figure 1, utilizing synthetically relevant heteroatom-substituted groups, X in eq 1. On the basis of thermodynamic data obtained from DFT calculations, **1** and **2** show the most exothermic reactions with (dhpe)Ni among the organic azides and iodonium imides we investigated and will be the focus of this Note. Enthalpic and structural data for other $R''N_3$ and RN=IR′ species are similar and are available as Supporting Information.

Computational Methods

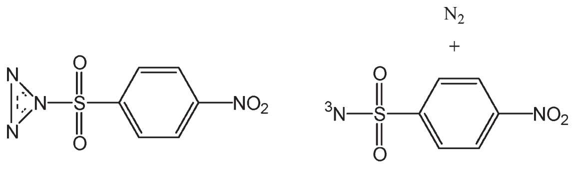
The Gaussian 03 package was used for all calculations.[15] The B3LYP functional was employed,[16,17] in conjunction with the effective core potentials and valence basis sets (CEP-121G) of Stephens et al.[18] The basis sets were augmented with a d-polarization function for main group elements.

Hybrid quantum/molecular mechanics calculations employed the ONIOM[19−21] methodology, using the Universal Force Field (UFF)[22] for molecular mechanics regions and the B3LYP/6-31G(d) level of theory for the quantum region.

Calculated Hessians confirm stationary points as minima or transition states (zero or one imaginary frequency, respectively). Thermochemistry is determined at 1 atm and 298.15 K.

4-Nitrobenzenesulfonyl Azide. The mechanism of azide decomposition has been discussed by Ison et al. for Re complexes,[23] who showed that TM-nitrene complexes form at ambient temperatures without thermal or photochemical activation, producing N_2 as the only byproduct. DFT and ab initio calculations by Hall et al.[24] evaluated the pathways for thermal decomposition of organic azides as well as nonthermal decomposition of nitrenes by the Re complexes of Ison et al.

"Metal-free" pathways for decomposition of **1** (4-nitrobenzenesulfonyl azide, Ns) prior to nickel binding involve azide cyclization (**1a**) and N_2 loss (**1b**), and are endothermic by +37.5 and +7.7 kcal/mol, respectively, Figure 2. In the latter, the nitrene is in its triplet ground state. The enthalpic cost to reach **1b** from **1**, when coupled with a favorable $T\Delta S$ term for fragmentation, may allow it to be accessible, and competitive with a metal-catalyzed cycle to form organic products.



1a **1b**

FIGURE 2. Geometric rearrangements for Ns (^{3}Ns denotes triplet ground state of lowest free energy).

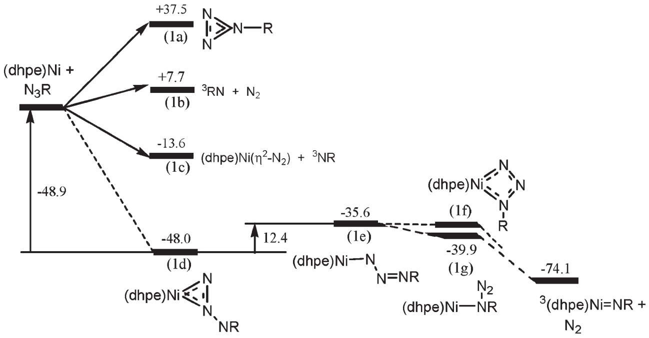


FIGURE 3. Calculated reaction diagram for the decomposition of the organic azide **1** (R = SO_2(*p*-nitrobenzene)). Quoted values are enthalpies (kcal/mol) and are determined at 298.15 K and 1 atm. (**1f** was not stable as a minimum or TS; hence, no enthalpy value was available.)

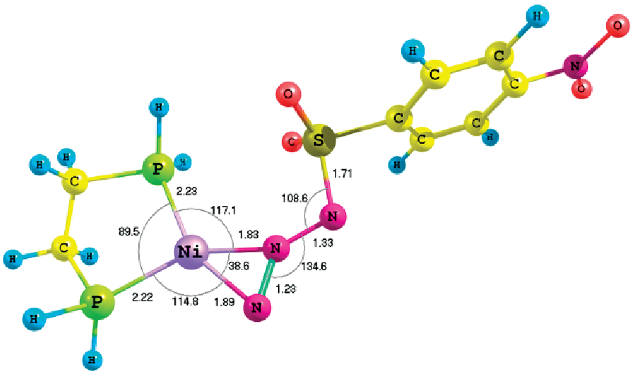


FIGURE 4. Calculated geometry of **1d**: (dhpe)Ni–(η^2-NN-**1**). Bond lengths in Å, angles in deg.

Favorable thermodynamics are calculated upon reacting (dhpe)Ni and **1**, Figure 3. The most stable structure entails η^2-*N*,*N* coordination of the terminal two nitrogens of azide **1** (Figure 4); ligation is exothermic by −48.0 kcal/mol. The stability of **1d**, Figure 4, is consistent with products determined in a recent study of the reaction of aryl azides with Ni^0 starting materials.[25] The calculated geometry of **1d** compares well to the X-ray structure of (dtbpe)Ni(η^2-N,N–N_3Ar),[25] dtbpe = 1,2-bis(di-*tert*-butylphosphino)ethane, Ar = mesitylazide; calcd: Ni–N = 1.89 (N_1), 1.83 (N_2) Å; N_1–N_2 = 1.23 Å; N_2–N_3 = 1.33 Å, exptl: Ni–N = 1.91 (N_1), 1.81 (N_2) Å; N_1–N_2 = 1.24 Å; N_2–N_3 bond length: 1.31 Å.[25]

After η^2-NN azide bonding to (dhpe)Ni, rearrangement to a linear isomer (**1e**) is calculated to be endothermic by +12.4 kcal/mol.

---

(14) Cundari, T. R.; Jiminez-Halla, J. O. C.; Morello, G. R.; Vaddadi, S. *J. Am. Chem. Soc.* **2008**, *130*, 13051–13058.

(15) Frisch, M. J. et al. *GAUSSIAN 03*, Revision C.02; Gaussian Inc., Wallingford, CT, 2004.

(16) Becke, A. D. *Phys. Rev.* **1998**, *A38*, 3098.

(17) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev.* **1998**, *B37*, 785.

(18) Stephens, W. J.; Basch, H.; Krauss, M. *J. Chem. Phys.* **1984**, *81*, 6026.

(19) Humbel, S.; Sieber, S.; Morokuma, K. *J. Chem. Phys.* **1996**, *105*, 1959.

(20) Svensson, M.; Humbel, S.; Froese, R.; Matsubara, T.; Sieber, S.; Morokuma, K. *J. Phys. Chem.* **1999**, *100*, 19357.

(21) Vreven, T.; Morokuma, K. *J. Chem. Phys.* **1999**, *111*, 8799.

(22) Rappe, A. K.; Casewit, C. J.; Colwell, K. S.; Goddard, W. A. III; Skiff, W. M. *J. Am. Chem. Soc.* **1992**, *114*, 10024.

(23) Ison, E. A.; Cessarich, J. E.; Travia, N. E.; Fanwick, P. E.; Abu-Omar, M. M. *J. Am. Chem. Soc.* **2007**, *129*, 1167.

(24) (a) Thomson, L. M.; Hall, M. B. *J. Phys. Chem.* **2000**, *104*, 6247. (b) Wu, H.; Hall, M. B. *J. Am. Chem. Soc.* **2008**, *130*, 16452.

(25) Waterman, R.; Hillhouse, G. L. *J. Am. Chem. Soc.* **2008**, *130*, 12628.

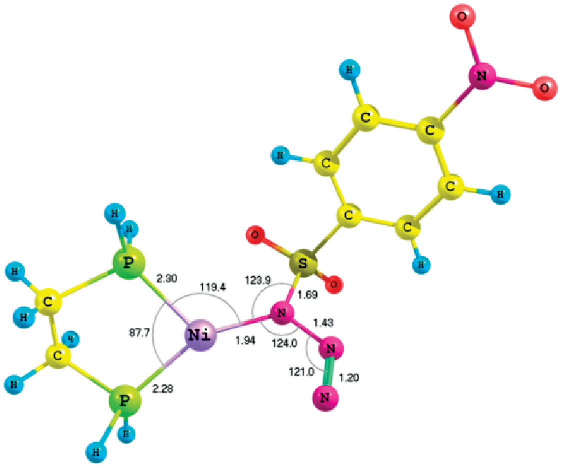


FIGURE 5. Geometry of local minima **1g**. The enthalpy is 4.3 kcal/mol lower than that of complex **1e**. Bond lengths in Å, angles in deg.

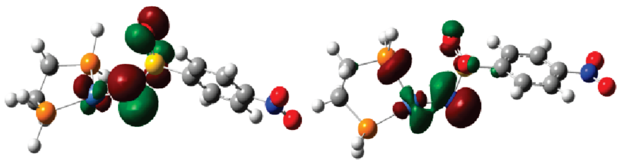


FIGURE 6. Molecular orbital representation of singly occupied Kohn–Sham orbitals in ^{3}(dhpe)Ni=N–SO$_2$(*p*-nitrobenzene).

This rearrangement provides an accessible pathway for cyclization, which eliminates N_2 and yields the triplet (dhpe)Ni=NX product in a very exothermic reaction. Calculations did produce a novel linkage isomer (**1g**, Figure 5), 4.3 kcal/mol lower in energy than **1e**, in which Ns coordinates to nickel via the internal nitrogen of the azide moiety. From this geometry, N_2 could be readily liberated in a manner similar to that proposed by Hall et al.[24] A transition state (TS) for N_2 elimination from (dhpe)Ni–Ns could not be found despite having isolated such TSs in previous studies of aliphatic azides,[2] presumably reflecting the great exothermicity of N_2 loss from Ns. Alternative pathways (singlets, triplets) yielded no favorable geometries. Transition state searches reverted to lower energy minima already found.

Elimination of N_2 from **1g** is exothermic by 34.1 kcal/mol, Figure 3. Interestingly, the (dhpe)Ni=NX complex that is formed from **1** is predicted to have a triplet ground state, 4.4 kcal/mol more stable (ΔH) than the singlet. This is in contrast with results for nitrenes with aryl and alkyl substituents, which predict a singlet as the most stable nitrene spin state.[2,14,26]

Figure 6 displays the two Kohn–Sham orbitals in which the unpaired electrons reside, one primarily on Ni and the other located on the nitrene nitrogen. Disruption of a NiN π-bond is indicated in this diradical nitrene. The Ni–N$_{\text{nitrene}}$ bond length elongates to 1.81 Å in ^{3}(dhpe)Ni–NX in comparison to the singlet bond length of 1.70 Å in ^{1}(dhpe)Ni=NX.

[*N*-(Tolylsulfonyl)imino]phenyliodinane. Compound **2**, [*N*-(tolylsulfonyl)imino]phenyliodinane (PhI=NTs), contains polyvalent iodine. One "isomer" is seen for metal-free reaction, Figure 7. Optimization of triplet PhI=NTs results in **2a**, in which PhI dissociates. This pathway is endothermic by only +0.7 kcal/mol ($\Delta G = -15.2$ kcal/mol). A triplet nitrene is thus calculated to be more energetically accessible from iminoiodinane **2** than azide **1**. Once PhI=NTs coordinates to the Ni catalyst, it can form several linkage isomers. The highest energy metal-bound isomer isolated is exothermic by −18.2 kcal/mol relative to uncoordinated reactants, and is a phenyl iodine complex of (dhpe)Ni, which makes ^{3}NTs the leaving group. Figure 8 shows the energy diagram for decomposition of PhI=NTs.

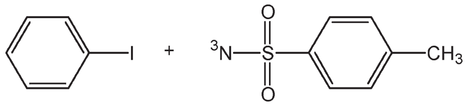


FIGURE 7. Triplet "isomer" of PhI=NTs (**2**).

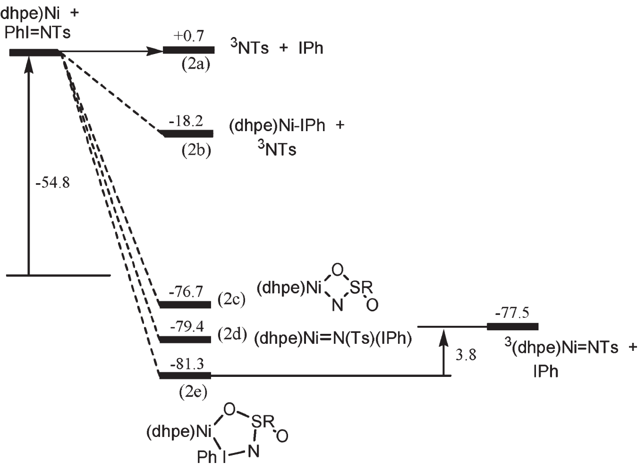


FIGURE 8. Calculated energy diagram for the decomposition of PhI=NTs (R = *p*-tolyl). Quoted values are enthalpies (in kcal/mol).

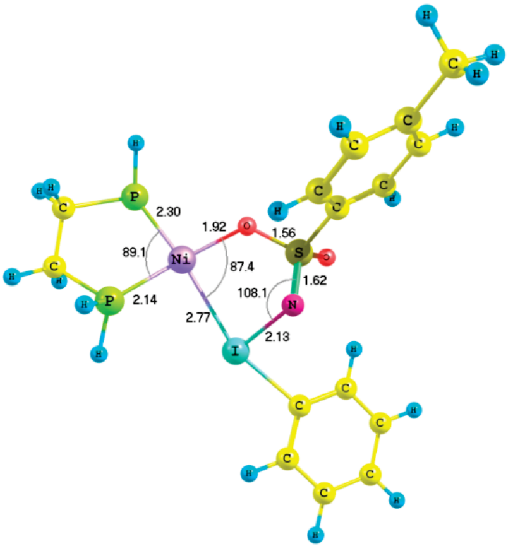


FIGURE 9. Lowest energy linkage isomer of (dhpe)Ni–PhI=NTs, **2e**. Bond lengths in Å, angles in deg.

Well below (dhpe)Ni–IPh+^{3}NTs is a manifold of conformations in which NTs is ligated to Ni with PhI dissociated. The lowest energy (dhpe)Ni(PhI=NTs) conformation (**2e**), 81.3 kcal/mol below separate reactants, contains a Ni–O–S–N–I ring, Figure 9. The elongation of the Ni–I bond (2.77 Å) suggests weak binding of iodine to nickel. Selected bond distances and their comparison with experimental models are given in the Supporting Information.

---

[26] Harrold, N. D.; Waterman, R.; Hillhouse, G. L. In *Abstracts of Papers*; 233rd National Meeting of the American Chemical Society, Chicago, IL, 2007; American Chemical Society: Chicago, IL, 2007.

Rearrangement of **2e**, with loss of PhI, to triplet nitrene (dhpe)Ni=NTs, Figure 8, is endothermic by only +3.8 kcal/mol. A triplet GS for (dhpe)Ni=NTs is in accord with the results discussed for the triplet nitrene formed by the reaction of (dhpe)Ni and 4-nitrobenzenesulfonyl azide (vide supra).

2,6-Diisopropylphenyl Azide. A third complex of interest substitutes CF_3 groups in place of the hydrogens attached to phosphorus, Figure 10. Previous work has shown (dfmpe)Ni(NAr) activates CD−H bonds through a thermodynamically favorable pathway (Ar = 2,6-diisopropylphenyl, dfmpe = bis(di(trifluoromethyl)phosphino)ethane).[14] Pathways to C−H bond functionalization are enhanced by introduction of perfluoroalkyl substituents to dhpe: with the dfmpe chelate engendering a stronger metal−amine bond and a weaker metal−amide bond.[14] ONIOM calculations were employed to study a synthetic route previously proposed from experiments.[25,26] The ONIOM methodology[19−21] was employed. The UFF force field[22] was used to treat the *ortho* isopropyl groups on Ar, while B3LYP/6-31G(d) was used to treat the rest of the system.

Compound **3** shows similarities to **1** in nitrene transfer thermodynamics. Coordination of ArN_3 to (dfmpe)Ni results in several exothermic processes, Figure 11. The formation of free nitrene and a dinitrogen complex, **3b**, is exothermic, −38.6 kcal/mol, and produces (dfmpe)Ni(η^2-N_2).

The most exothermic reaction for (dfmpe)Ni/ArN_3 interaction, −46.5 kcal/mol, results in η^2-coordination to Ni of the terminal nitrogens of azide, **3c**. This geometry is similar to that seen in the (dhpe)Ni model with Ns and reported by Waterman.[25] DFT calculated Ni−N = 1.84 (N_1), 1.86 (N_2) Å; N_1−N_2 = 1.24 Å; N_2−N_3 = 1.27 Å are all in very good agreement with experiment.[25]

Rearrangement of **3c** to linear **3d** costs only 6.1 kcal/mol. Unlike Ns, a four-member ring was isolated via the ONIOM calculations. To reach complex **3f**, **3d** must overcome an energy barrier of +8.5 kcal/mol. Elimination of N_2, resulting in (dfmpe)Ni=NAr, singlet, occurs exothermically by −43.2 kcal/mol and completes the catalytic cycle yielding our desired product and N_2 gas. As in (dhpe)Ni, an internal bound geometry was found, **3e**, that is competitive with the cyclization geometry, **3f**. No transition state pathway to obtain **3e** has been found. The (dfmpe)Ni=NAr singlet GS is more stable (Δ*H*) than the triplet by 2.1 kcal/mol. This follows the trend discussed for nitrenes with aryl substituents.[25,27]

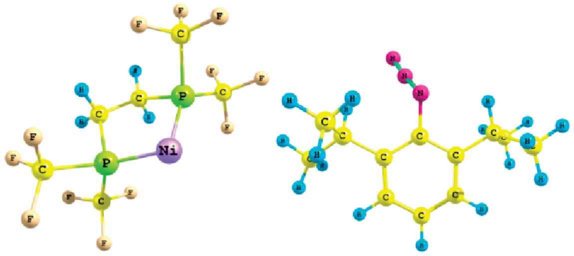


FIGURE 10. Nickel 1,2-*bis*(di(trifluorphosphino)ethane; (dfmpe)Ni, and 2,6-diisopropylphenyl-azide; ArN_3.

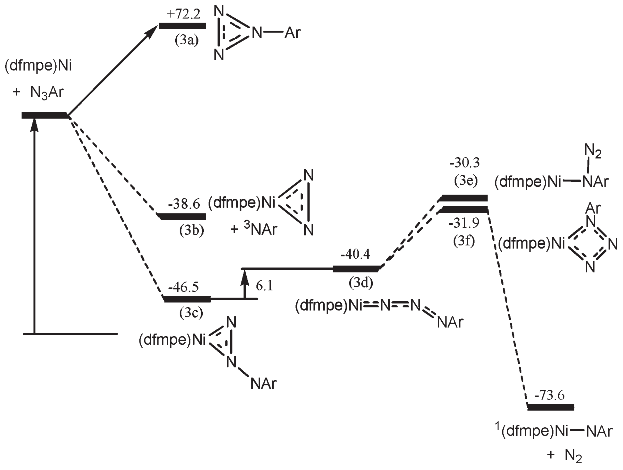


FIGURE 11. Calculated energy diagram for decomposition of 2,6-diisopropylphenyl azide. Quoted values are enthalpies (kcal/mol).

In summary, we have presented DFT calculated results on the decomposition of heterosubstituted azides and iodonium imides by Ni complexes. The general reaction mechanisms are similar for each system studied. While reaction with the nickel center yields LNi=NX (L = bis-phosphine) plus N_2 (phenyl iodide in the case of PhI=NTs), it appears as though cyclization may not always be the only pathway for decomposition. Using larger, more synthetically relevant heteroatom-substituted species for the nitrene source results in nitrene intermediates for which a triplet (diradical) nitrene intermediate is most stable, which differs from previous reports of singlet species being favored when the nitrene is substituted with aliphatic and aromatic groups.[2,14,27] Hence, modeling more synthetically "popular" heteroatom-substituted organic azides (and iodonium imides, see below in the Supporting Information) indicates a greater propensity toward triplet intermediates, which may have important implications for the selectivity of organic syntheses with use of such nitrene transfer reagents.

Acknowledgment. The authors acknowledge the NSF for their support of the UNT Chemistry computational facility (CRIF, CHE-0741936). This research is supported by a grant from the Offices of Basic Energy Sciences, U.S. Department of Energy (Grant No. DEFG02-03ER15387). G.R.M. acknowledges the UNT Toulouse Graduate School for a College of Arts and Sciences Graduate Research Fellowship.

Supporting Information Available: Cartesian coordinates of uncomplexed and complexed nickel structures discussed in detail as well as thermodynamic data of all species initially modeled. This material is available free of charge via the Internet at http://pubs.acs.org.

---

(27) Cundari, T. R.; Vaddadi, S. *THEOCHEM* **2006**, *801*, 47.