Metal-Free Alkane Transformation

DOI: 10.1002/anie.201207997

Carbon–Carbon Bond Activation in Saturated Hydrocarbons by Field-Assisted Nitrogen Fixation**

*Guangtao Li, Xin Li, Zheng Ouyang, and R. Graham Cooks**

Alkanes are the most abundant organic compounds in nature. They are readily combusted but chemically unreactive and their conversion to functionalized compounds[1,2] forms the basis for the chemical industry. Selective activation and functionalization of alkanes, however, is very difficult and it has been recognized as a "holy grail" of chemistry.[3] Organometallic catalyzed C–H bond activation was reported by Janowicz and Bergman[4] and the subject continues to be of high interest.[5–10] The activation of C–C bonds is even more challenging. The direct insertion of metal ions into C-C bonds in the gas phase is known[11] but noncyclic alkane activation has not yet been reported in solution, although insertion into strained cycloalkanes is known.[12,13] The direct insertion of a metal into C–C bonds of noncyclic alkanes has not yet been reported, although insertion into strained cycloalkanes is known.[11–13] Impressive mechanistic insights into metal-based catalytic functionalization of alkanes have been gained, including those based on gas-phase metal ion reactions.[9,14] However, practical challenges for the organometallic approach to hydrocarbon functionalization[7] include the expense and toxicity of organometallic catalysts, usually based on palladium and platinum, their air-sensitivity and low activity.[15] These facts make metal-free alkane transformations ("green chemistry") highly desirable.[16]

The fixation of atmospheric dinitrogen—another readily available but chemically inert compound—is critical to life and human activities.[17] This is achieved industrially by ammonia synthesis using the energy-intensive Haber–Bosch process. In nature, atmospheric nitrogen is converted into ammonia by bacteria which use nitrogenase enzymes, typically having FeMo-active sites. Biomimetic approaches to artificial nitrogenases have not yet been realized even after decades of intensive effort.[18,19]

Here, we report a strategy for the direct insertion of nitrogen into C–C bonds of saturated alkanes to form iminium salts without involving metal species. This reaction occurs on a very small scale but product is collected and characterized. Iminium salts are characterized by a C=N bond and are typically prepared by condensation of amines and carbonyl compounds.[20] They react readily with a number of electron-rich molecules and are widely used in organic synthesis.[21,22] Nitrogen atoms from dinitrogen gas were inserted into solid alkane molecules in a strong electric field. (Figure 1) The resulting iminium cations are chemically stable and could be soft-landed and collected on a suitable surface at atmospheric pressure. These experiments also offer a new strategy for mass spectrometric analysis of petroleum products.

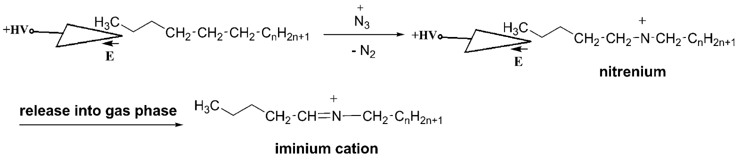

Figure 1. Insertion of atomic nitrogen ion into C–C bonds of large *n*-alkanes (*M*) on an electrically floated substrate, for example, paper, to give $[M+N]^+$ insertion products. Note the nitrenium ion intermediate and iminium ion product.

The experiment was performed by depositing n-$C_{60}H_{122}$ alkane as a thin film onto the tip of a triangular filter paper and applying a potential of about 5 kV to the paper in a heated nitrogen atmosphere (typically 150 °C). The cations leaving the paper were either 1) deposited on a surface and analyzed independently or 2) sucked into the vacuum system of a mass spectrometer for on-line analysis. The latter experiment gave mass spectra (Figure 2 a) dominated by just one type of ion: $[M+N]^+$ where M represents the alkane as verified by exact mass measurements. A minor product corresponded to the dimeric species $[2M+N-2H]^+$. Nitrogen incorporation was observed for the C_{31}, C_{35}, C_{40}, C_{41}, C_{46}, and C_{50} *n*-alkanes (see Table S1 in the Supporting Information) as well as for the heavy *n*-alkane standards Polywax 1000 (Figure 2 a) and Polywax 500 (Figure S11).

The main peak envelope in these spectra corresponds to the N-inserted alkanes. For example, the ion at nominal m/z 1558 corresponds to the N atom adduct with carbon number C_{110} (average chemical mass 1558.95; exact mass of the ^{12}C isotope 1557.74, measured mass 1557.7) while the isotopic distribution (Figure S6) agrees well with that calculated for $C_{110}H_{222}N$. The molecular weight distribution in Figure 2 b extends to at least m/z 1895, n-$C_{134}H_{270}$ saturated hydro-

---

[*] G. Li,[+] Dr. X. Li,[+] Prof. R. G. Cooks
Department of Chemistry, Purdue University
560 Oval Drive, West Lafayette, IN 47907 (USA)
E-mail: cooks@purdue.edu

Prof. Z. Ouyang
Weldon School of Biomedical Engineering, Purdue University
West Lafayette, IN 47907 (USA)

[+] These authors contributed equally to this work.

[**] We thank Dr. Jobin Cyriac for the Raman measurements. This work was supported by NSF under grant number CHE 08948650 and by the Separations and Analysis Program, Office of Basic Energy Sciences, US Department of Energy under grant number DE-FG02-06ER15807.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201207997.

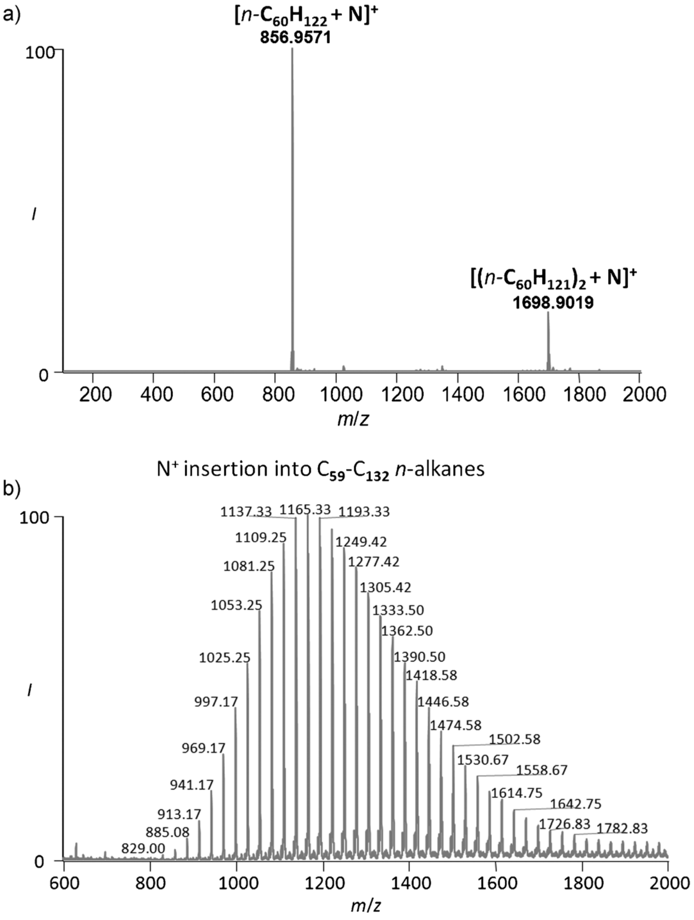

Figure 2. a) Mass spectrum of wax n-$C_{60}H_{122}$ in N_2 at 325 °C, 6 kV, using high-resolution mass spectrometer. b) Mass spectrum of alkane mixture Polywax 1000 in N_2 at 400 °C using ion trap mass spectrometer.

carbon, while the most abundant species, m/z 1165.33, corresponds to n-$C_{82}H_{166}$. These observations are consistent with the manufacturer's data (Figure S12).

The $[M+N]^+$ ion signal lasted several hours using 10 µg alkane with no appreciable loss of intensity, allowing the product to be deposited continuously on an inert surface such as a gold substrate. Figure 3 shows a chronogram displaying the total ion signal over a period of 81 minutes. The mass spectrum is dominated by the $[M+N]^+$ ion. This collection experiment did not involve a mass spectrometer although the collected product was characterized by MS and other means. Nanoelectrospray ionization of the collected sample produced ions, the MS/MS fragmentation patterns of which were identical to those recorded on-line for the ions $[M+N]^+$ and $[2M+N-2H]^+$ (Figure S2). This result confirms successful collection of the nitrogen-functionalized compounds. Raman analysis of the collected sample showed a distinctive absorption band around 1664 cm^{-1} (Figure 4), a characteristic Raman-active band of neutral imines.[23] The chemical stability of the nitrogen-incorporated species indicates that the nitrogen could not have been inserted into C–H bonds of alkanes, as these compounds are unstable and moisture-sensitive.[24]

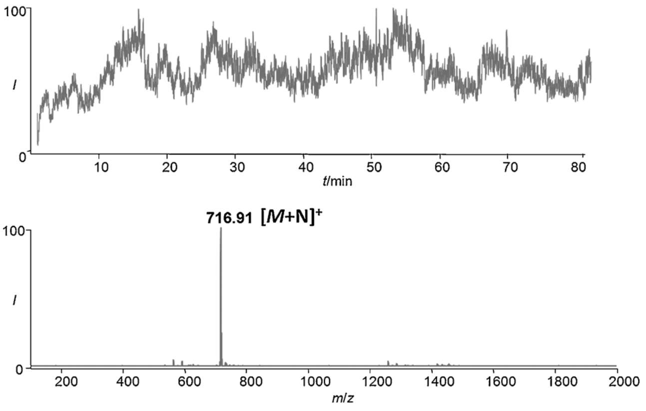

Figure 3. Total ion chronogram of ionized n-$C_{50}H_{122}$ and its reaction products recorded on-line. The dominant product is the N-atom insertion product m/z 716 $[M+N]^+$.

Multiple stage experiments (MS/MS and MS^3) provided further information on the chemical structure of the $[M+N]^+$ ions. Isolation and collisional dissociation of $[M+N]^+$ resulted in a series of alkene eliminations starting with ethylene as seen in the case of the wax n-$C_{60}H_{122}$ (Figure 5 a). Further fragmentation of any of the fragment ions generated by alkene loss from the $[M+N]^+$ precursor (i.e. formally lower homologs $[M+N]^+$) occurs by loss of size-specific alkyl amines to give alkenyl cations with a distinctive and narrow range of carbon numbers (Figure 5 b). These MS^3 data indicate that the primary fragmentation is directed by the (random) position of the nitrogen atom and that further fragmentation occurs by alkyl amine elimination (Figure S4, Scheme S1) as also occurs in aliphatic primary amines.[25,26]

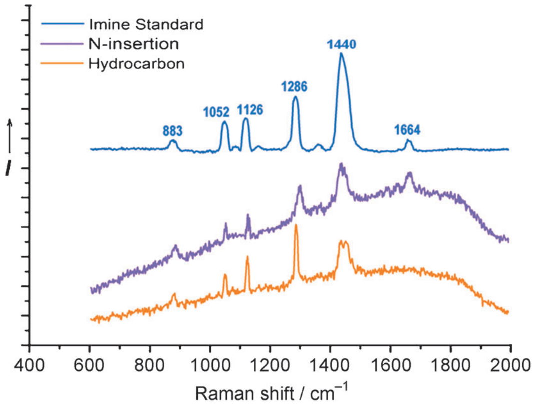

Figure 4. Raman spectra of an authentic imine, n-$C_{16}H_{33}N^+H{=}CH_3$, octadecane, and deposited reaction product $[M+N]^+$ of octadecane.

All these data suggest that the nitrogen-incorporated species are iminium ions formed by nitrogen insertion into C–C bonds of alkanes and that neutral imines are formed upon surface deposition. To test this, authentic imines $R^1CH=NR^2$ (where R^1 and R^2 are linear alkyl groups) were synthesized.[27] The protonated iminium ions displayed dominant peaks because of eliminations of the alkenes $[R^1$–H] and $[R^1$–

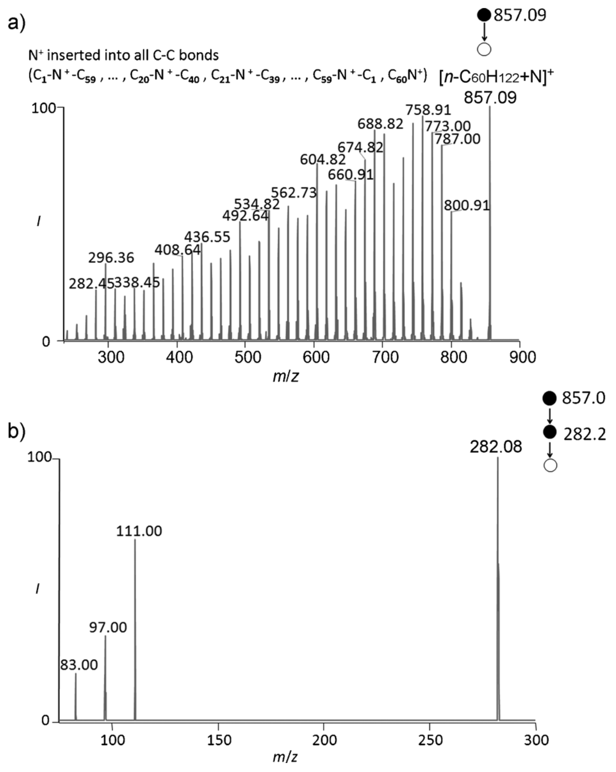

Figure 5. a) Continuous distribution of alkene elimination fragments observed on dissociation of the N-insertion product of n-$C_{60}H_{122}$.
b) Further fragmentation of a typical product ion, m/z 282.2, observed as the MS^3 spectrum.

CH_3] in their MS/MS spectra (Figure S4a). For example, the authentic iminium ion n-$C_{16}H_{33}N^+H{=}CH$(n-$C_{17}H_{35}$) m/z 492.6, fragmented to give $C_{16}H_{33}N^+H{=}CHCH_3$ and $C_{16}H_{33}N^+H{=}CH_2$. Tellingly, the further fragmentation of these ions as seen in their MS^3 spectra showed very similar patterns to the MS^3 spectra of the $[M{+}N]^+$ reaction products. For example, $C_{16}H_{33}N^+H{=}CH_2$ (Figure S4) showed only the three alkenyl ions, m/z 83, 97, and 111 yielded by the N-insertion product (Figure 5b). Based on this evidence, it is concluded that nitrogen is inserted nonspecifically into the C–C backbone of alkanes to form the continuous distribution of homologous iminium ions seen in Figure 5a. The experiment is selective in that one type of reaction (N atom insertion) is dominant, even though the position of insertion is not specific.

A tentative mechanism for nitrogen insertion is shown in Figure 1 (compare Figure S3). It is supported by the fact that 1) only low volatility alkanes undergo nitrogen insertion, 2) functionalized organic compounds were also examined under these reaction conditions (Supporting Information) and were found simply to undergo protonation and 3) the major ions generated during microdischarges in atmospheric pressure nitrogen are N_3^+ and $N_4^{+\bullet}$.[28] This leads to the proposal that the primary reaction with polarized alkanes involves azidium ion insertion with dinitrogen elimination (Figure S3). Further mechanistic study is necessary but the data offer a novel strategy for alkane functionalization by nitrogen insertion into C–C bonds in one step. The reaction is not restricted to paper substrates (Figures S7, S13) and it can be performed in air, rather than in pure nitrogen (Figure S8). The experiment is useful for the analysis of heavy hydrocarbons in complex mixtures (Figure S14); it also presents a novel strategy for chemical transformation of alkanes by nitrogen fixation, with the potential to be scaled up.

Experimental Section

The Polywax 500 and 1000 samples were purchased from Restek Corporation (Bellefonte, PA), all other chemicals were purchased from Sigma–Aldrich (St. Louis, MO). All chemicals were used as received. The gold substrates were silicon wafers coated with 10 nm of Cr and 200 nm of Au, purchased from International Wafer Service, Inc (Colfax, CA). Mass spectra and multiple stage mass spectra (MS/MS and MS^3) were recorded using a Thermo LTQ ion trap mass spectrometer (Thermo Scientific, San Jose, CA). A Thermo Scientific Exactive Orbitrap mass spectrometer for high-resolution mass measurements. Raman spectra were recorded using a HORIBA Jobin Yvon Raman spectrometer equipped with a CCD detector and a 632.8 nm He-Ne 35 mW excitation laser source (Melles Griot, USA).

Optimized conditions for alkane ionization from dry paper in a nitrogen atmosphere were used to produce the data shown. The experiment was done in a N_2 atmosphere in an isolated chamber normally used for atmospheric pressure chemical ionization, electrically heated to 150–400 °C, with a potential of 5–6 kV applied a paper substrate on the tip of which the sample had been deposited. Nitrogen gas had a minimum purity of 99.9% and it was passed at a rate of 5–15 $L\,min^{-1}$ during reaction. The default experimental conditions were used unless explicitly indicated otherwise.

For ion deposition, the paper substrate connected to a +5 kV high voltage was directed toward a grounded Au/Si wafer substrate (about 10 mm away), while a heated nitrogen stream was introduced at a gas flow rate of 10 $L\,min^{-1}$ to maintain the nitrogen atmosphere. Figure S1 illustrates the apparatus. The Au/Si wafer was cooled by liquid nitrogen to better retain the deposited species although ambient collection was also successful. After one hour of collection, the wafer was warmed up to room temperature for Raman measurements. Alternatively, the wafer was rinsed using hexane solvent and the rinse solution was analyzed by nanoESI.

Received: October 3, 2012
Published online: November 26, 2012

Keywords: C-C activation · hydrocarbons · mass spectrometry · nitrogen fixation · petroleum analysis

---

[1] R. G. Bergman, *Nature* **2007**, *446*, 391–393.
[2] A. E. Shilov, G. B. Shul'pin, *Chem. Rev.* **1997**, *97*, 2879–2932.
[3] B. A. Arndtsen, R. G. Bergman, T. A. Mobley, T. H. Peterson, *Acc. Chem. Res.* **1995**, *28*, 154–162.
[4] A. H. Janowicz, R. G. Bergman, *J. Am. Chem. Soc.* **1982**, *104*, 352–354.
[5] L. M. Lech, B. S. Freiser, J. R. Gord, *J. Am. Chem. Soc.* **1989**, *111*, 8588–8592.
[6] H. Schwarz, D. Schroder, *Pure Appl. Chem.* **2000**, *72*, 2319–2332.
[7] J. A. Labinger, J. E. Bercaw, *Nature* **2002**, *417*, 507–514.
[8] K. M. Waltz, J. F. Hartwig, *Science* **1997**, *277*, 211–213.
[9] N. Dietl, M. Schlangen, H. Schwarz, *Angew. Chem.* **2012**, *124*, 5638–5650; *Angew. Chem. Int. Ed.* **2012**, *51*, 5544–5555.
[10] D. A. Colby, A. S. Tsai, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2012**, *45*, 814–825.

[11] D. B. Jacobson, B. S. Freiser, *J. Am. Chem. Soc.* **1985**, *107*, 67–72; P. B. Armentrout, *Organometallics* **2007**, *26*, 5473–5485; P. B. Armentrout, *Organometallics* **2007**, *26*, 5486—5500; M. C. Holthausen, A. Fiedler, H. Schwarz, W. Koch, *Angew. Chem.* **1995**, *107*, 2430–2432; *Angew. Chem. Int. Ed.* **1995**, *34*, 2282–2285.
[12] C. F. H. Tipper, *J. Chem. Soc.* **1955**, 2045–2046.
[13] S. C. Bart, P. J. Chirik, *J. Am. Chem. Soc.* **2003**, *125*, 886–887.
[14] J. Roithova, D. Schroder, *Chem. Rev.* **2010**, *110*, 1170–1211.
[15] R. H. Crabtree, *J. Organomet. Chem.* **2004**, *689*, 4083–4091.
[16] E. N. Jacobsen, D. W. C. MacMillan, *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 20618–20619.
[17] D. E. Canfield, A. N. Glazer, P. G. Falkowski, *Science* **2010**, *330*, 192–196.
[18] J. Chatt, J. R. Dilworth, R. L. Richards, *Chem. Rev.* **1978**, *78*, 589–625.
[19] J. J. Scepaniak, C. S. Vogel, M. M. Khusniyarov, F. W. Heinemann, K. Meyer, J. M. Smith, *Science* **2011**, *331*, 1049–1052.
[20] A. F. Abdel-Magid, K. G. Carson, B. D. Harris, C. A. Maryanoff, R. D. Shah, *J. Org. Chem.* **1996**, *61*, 3849–3893.
[21] H. Bohme, H. G. Viehe, *Iminium Salts in Organic Chemistry*, Wiley, New York, **1976**.
[22] B. E. Maryanoff, H. C. Zhang, J. H. Cohen, I. J. Turchi, C. A. Maryanoff, *Chem. Rev.* **2004**, *104*, 1431–1628.
[23] J. J. Lopez-Garriga, G. T. Babcock, J. F. Harrison, *J. Am. Chem. Soc.* **1986**, *108*, 7241–7251.
[24] H. H. Strain, *J. Am. Chem. Soc.* **1930**, *52*, 820–823.
[25] M. L. Gross, *Int. J. Mass Spectrom.* **2000**, *200*, 611–624.
[26] N. J. Jensen, K. B. Tomer, M. L. Gross, *J. Am. Chem. Soc.* **1985**, *107*, 1863–1868.
[27] A. F. D. Alcantara, D. PiloVeloso, D. L. Nelson, *J. Braz. Chem. Soc.* **1996**, *7*, 225–232.
[28] I. Dzidic, D. I. Carroll, R. N. Stillwell, E. C. Horning, *Anal. Chem.* **1976**, *48*, 1763–1768.