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Exploring the Chemistry of *N,N′*-Diamidocarbenes with Organophosphorus Compounds

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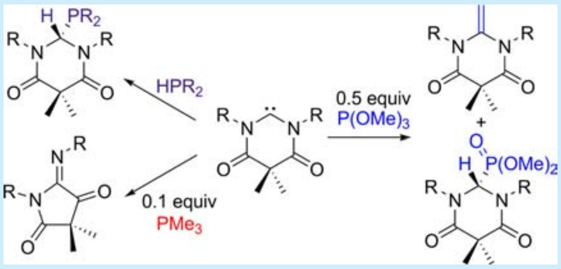
Supporting Information

ABSTRACT: A readily available *N,N′*-diamidocarbene (DAC) was found to insert into the P–H bonds of primary and secondary phosphines as well as a phosphonate ester. In contrast, tertiary phosphines catalyzed the ring contraction of the DAC to an iminopyrrolidinedione. Treating the DAC with trimethyl phosphite afforded the corresponding diamidophosphonate ester and olefinic products expected from an Arbuzov-type reaction.



The rapidly evolving view of stable carbenes[1] as functional mimics for transition metals has coincided with the rise of carbene–phosphorus chemistry. For example, recent studies have realized the stabilization of white phosphorus,[2] phosphanyl cations,[3] and phosphorus centered-radicals[4] using carbenes—chemistry that has historically required the use of transition metals (e.g., vanadium, tungsten, niobium, etc.) Additionally, analysis of the ^{13}C NMR chemical shifts displayed by carbene-derived phosphinidenes has been introduced as a new method for quantifying the π-accepting character of carbenes[5] and complements the frequently used Tolman electronic parameters.[6]

However, despite the critical roles of both P–H insertions in hydrophosphinylations[7] and phosphorus–metal ligation in catalysis,[8] there is only one report of P–H activation using isolable carbenes (i.e., **1**[9] or **2**[10] in Figure 1).[11,12] Similarly, P→C$_{carbene}$ interactions are extremely rare.[13,14] The realization and understanding of such chemistry is not only fundamentally attractive but practical as it should facilitate access to new classes of organophosphorus and other important phosphine containing compounds[7d] with high atom economy.

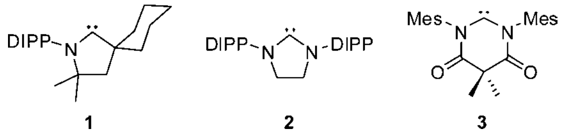
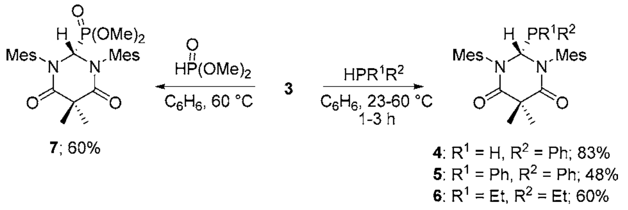


Figure 1. Structures of isolable carbenes **1** and **2** and an *N,N′*-diamidocarbene (**3**).

Building on our recent report[15] describing the N–H insertion chemistry of the readily available *N,N′*-diamidocarbene[16] (DAC) **3**, we reasoned that such carbenes may facilitate isolobal P–H insertions. Our hypothesis was inspired by a recent study[17] by Hudnall who revealed that **3** stabilizes P_4 through a mechanism that likely involves the attack of the carbene by an incipient anionic phosphorus center, an intriguing result which suggested to us that DACs may be capable of accepting electron density from nucleophilic phosphines. Herein, we show that a DAC inserts into the P–H bonds of primary and secondary phosphines as well as dimethyl phosphite. Additionally, the DAC underwent ring contraction in the presence of catalytic tertiary phosphines and afforded the products expected from an Arbuzov-type reaction involving trimethyl phosphite, potentially via ylidic intermediates.

Our efforts began by adding an equimolar quantity of phenylphosphine to a C_6H_6 solution of **3** ($[\mathbf{3}]_0 = 0.199$ M). After being stirred at 23 °C for 1 h, the aforementioned mixture was analyzed by ^{13}C NMR spectroscopy (C_6D_6) which revealed a doublet ($J = 11.6$ Hz) at 75.5 ppm that was attributed to a diamidomethine (cf., the carbene nucleus in **3** has been reported[16c] to resonate at 277.7 ppm). Combined with the ^{1}H and ^{31}P NMR signals observed at 6.17 and −60.4 ppm, respectively, the spectroscopic data supported the formation of the P–H insertion product **4**, which was subsequently isolated in 83% yield. As summarized in Scheme 1, alkyl- and arylphosphines as well as a phosphonate ester were successfully treated with **3** to afford the corresponding P–H insertion products **4**–**7** in up to 83% yield.[18] The structure of **5** was

Scheme 1. Treatment of 3 with Phosphines and Phosphites



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unambiguously determined via single-crystal X-ray diffraction (XRD) analysis which confirmed the expected sp^3-hybridized carbon center (e.g., the sum of N1−C1−N2, N1−C1−P1, and N2−C1−P1 angles = 333.34°), and a distance typical of a carbon−phosphorus single bond was measured (1.92 Å; Figure 2).[19] To the best of our knowledge, these are the first examples of isolable carbenes facilitating P−H insertions into alkyl phosphines or a phosphonate ester.

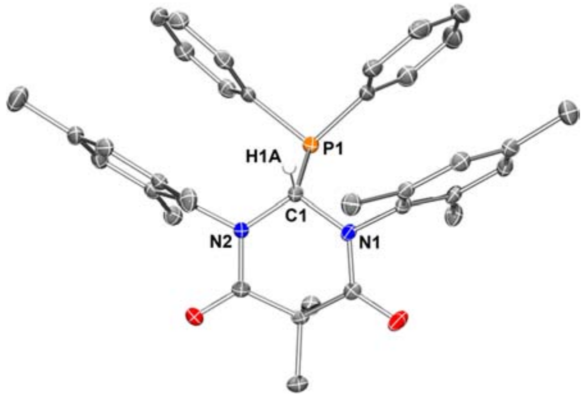


Figure 2. ORTEP diagram of **5** with thermal ellipsoids drawn at 50% probability with H-atoms except at the carbenoid carbon and a cocrystallizing solvent molecule omitted for clarity. Selected distances (Å) and angles (deg): C1−P1, 1.9176(16); C1−N1, 1.4739(19); C1−N2, 1.4690(19); P1−C1−N1, 110.26(10); P1−C1−N2, 111.96(10); N1−C1−N2, 111.12(12).

We hypothesized that if the aforementioned DAC-facilitated P−H activation processes proceeded via ylidic intermediates, as observed with **3** and various N−H insertion reactions,[15] stable ylides might be obtained upon the exposure of **3** to tertiary phosphines. To test, an equimolar quantity of trimethylphosphine (1.0 M in C_7H_8) was added to a C_6D_6 solution of **3** ($[\mathbf{3}]_0$ = 0.133 M), and then the resulting mixture was heated to 60 °C for 3 h, which resulted in the formation of a bright red solution. ^{1}H NMR spectroscopic analysis of the crude reaction mixture revealed that a new compound with lower symmetry than **3** had formed, as indicated by the presence of two sets of aryl protons in equal integration at 6.78 and 6.76 ppm. Surprisingly, the signals associated with trimethylphosphine at 0.81 and −61.9 ppm in the ^{1}H and ^{31}P NMR spectra, respectively, were unchanged, and new ^{31}P signals were not observed. Combined with the ^{13}C NMR signals assigned to keto (194.7 ppm) and amido (174.9 ppm) functional groups, the spectroscopic data were consistent with the formation of the iminopyrrolidinedione **8**. The product was subsequently isolated by silica gel chromatography in 88% yield, and the structure was unambiguously confirmed by XRD analysis (Figure 3).

To probe the generality of the aforementioned rearrangement, **3** was treated to tertiary phosphines containing relatively bulky substituents (e.g., ethyl, propyl, butyl, or phenyl). However, the formation of **8** was not observed even at elevated temperatures (e.g., 100 °C), likely due to steric inhibition. Although **8** was obtained after treating **3** with chlorodiethylphosphine, larger chlorodialkyl- (e.g., isopropyl or *tert*-butyl) or chlorodiarylphosphines were not observed to facilitate the aforementioned rearrangement. Quantitative conversion to **8** was observed in the presence of catalytic quantities (10 mol %) of trimethyl- or chlorodiethylphosphine. Collectively, the aforementioned results suggested to us that the isomerization was initiated by nucleophilic attack of the phosphine on the carbene nucleus which generated a transient phosphonium ylide. Subsequent intramolecular addition of the carbanion into the carbonyl group of an amide would form a strained, bicyclic, and zwitterionic intermediate that expelled trimethylphosphine and yielded **8** upon collapse (Scheme 2).

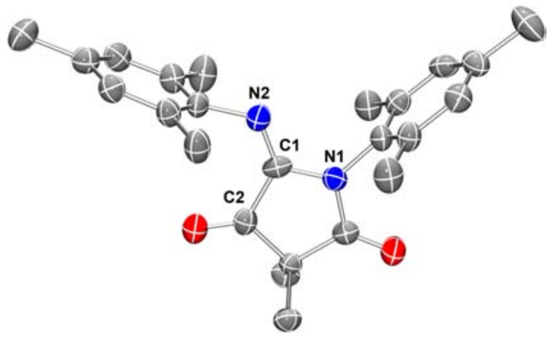
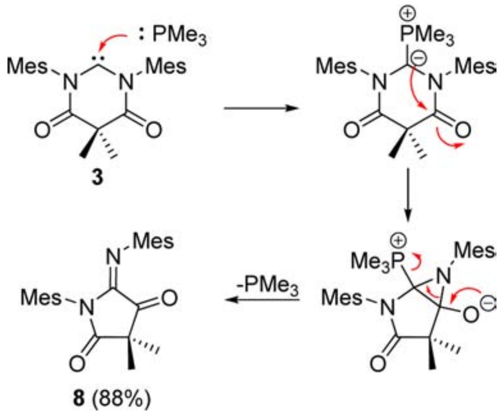


Figure 3. ORTEP diagram of **8** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity. Selected distances (Å) and angles (deg): C1−N1, 1.385(5); C1−N2, 1.277(5); N1−C1−N2, 122.6(3); N1−C1−C2, 106.4(3); C2−C1−N2, 131.0(2).

Scheme 2. Proposed PMe$_3$-Catalyzed Rearrangement of 3



Having examined tertiary phosphines, we next focused on the reaction of **3** with an electron-deficient phosphite (as compared to the analogous phosphine) to deconvolute the role of electronics. In an initial experiment, equimolar quantities of **3** ($[\mathbf{3}]_0$ = 0.27 M) and trimethyl phosphite were dissolved in C_6D_6 and heated to 60 °C, which resulted in the formation of a colorless precipitate after 12 h. Analysis of the crude reaction mixture by ^{1}H and ^{31}P NMR spectroscopy revealed the presence of residual phosphite as well as the formation of a new product. Considering that the spectroscopic data recorded for the precipitate were identical to those of **7** and taking mass balance into account, the new product was predicted to be the exocyclic olefin **9**. To increase the yield of this material, the aforementioned reaction was repeated using 2 equiv of **3** with respect to the trimethyl phosphite. Collection of the resultant precipitate followed by washing with pentane afforded pure **7** (76% isolated yield), whereas purification of the filtrate residue by silica gel column chromatography yielded **9** (53%), as determined by NMR spectroscopy and XRD analysis (Figure 4).[20,21]

As summarized in Scheme 3, the formation of **7** and **9** may have proceeded through an Arbuzov- or a direct methylation-

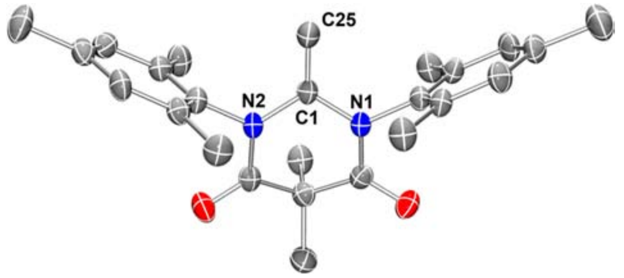


Figure 4. ORTEP diagram of **9** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity. Selected distances (Å) and angles (deg): (a) C1−N1, 1.420(5); C1−N2, 1.420(5); C1−C25, 1.331(6); N1−C1−N2 = 114.9(3); N1−C1−C25 = 122.1(3); N2−C1−C25 = 122.8(3).

type pathway. In the former, **3**, acting as an electrophile, would undergo attack from trimethyl phosphite to form the corresponding ylide. Subsequent demethylation by a second equivalent of **3** followed by proton transfer between the resultant resonance-stabilized ion pair would then afford the observed products. Alternatively, the direct methylation of nucleophilic **3** by trimethyl phosphite followed by proton transfer would afford **8** and dimethyl phosphite, which was previously shown to undergo P−H insertion with **3** (see Scheme 1). As the ylide intermediate of the Arbuzov-type pathway may be expected to undergo intramolecular rearrangement and lead to the formation of **8**, which was not observed, the direct methylation pathway may be preferred.[22]

In summary, DAC-facilitated insertions were extended to encompass compounds containing a variety of P−H bonds, including the first insertions of an isolable carbene into dialkylphosphines and a phosphonate ester. The rearrangement of **3** to the iminopyrrolidinone **8** catalyzed by trimethylphosphine or chlorodimethylphosphine also supported the ability of the DACs to develop negative charge at the carbenoid center and to form ylidic intermediates. Furthermore, the reaction of **3** with trimethyl phosphite afforded the products expected from an Arbuzov-type reaction, although a distinct mechanism that involves the direct methylation of the DAC may be operative. More broadly, the results extend the abilities of stable carbenes to mimic transformations typically expected from transition metals and afford access to novel organophosphorus derivatives. Moreover, the reactions presented herein effectively broaden phosphorus-carbene chemistry and are envisioned to facilitate the synthesis of new phosphine-containing compounds and ligands.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details, crystallographic data, and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For excellent reviews on stable carbenes, see: (a) Vignolle, J.; Cattoën, X.; Bourissou, D. *Chem. Rev.* **2009**, *109*, 3333. (b) Dröge, T.; Glorius, F. *Angew. Chem., Int. Ed.* **2010**, *49*, 6940. (c) Melaimi, M.; Soleilhavoup, M.; Bertrand, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 8810. (d) Martin, D.; Soleilhavoup, M.; Bertrand, G. *Chem. Sci.* **2011**, *2*, 389.

(2) (a) Masuda, J. D.; Schoeller, W. W.; Donnadieu, B.; Bertrand, G. *J. Am. Chem. Soc.* **2007**, *129*, 14180. (b) Back, O.; Kuchenbeiser, G.; Donnadieu, B.; Bertrand, G. *Angew. Chem. Int.* **2009**, *48*, 5530. (c) Holshumacher, D.; Bannenberg, T.; Ibrom, K.; Daniliuc, C. G.; Jones, P. G.; Tamm, M. *Dalton Trans.* **2010**, *39*, 10590. (d) Martin, C. D.; Weinstein, C. M.; Moore, C. E.; Rheingold, A. L.; Bertrand, G. *Chem. Commun.* **2013**, *49*, 4486.

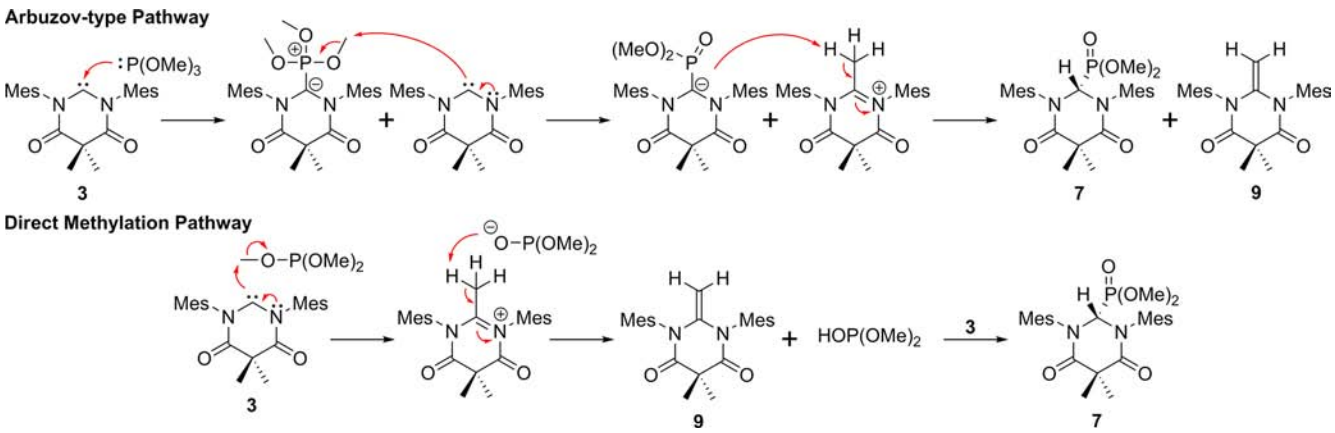
(3) Back, O.; Donnadieu, B.; Parameswaran, P.; Frenking, G.; Bertrand, G. *Nat. Chem.* **2010**, *2*, 369.

(4) Back, O.; Donnadieu, B.; von Hopffgarten, M.; Klein, S.; Tonner, R.; Frenking, G.; Bertrand, G. *Chem. Sci.* **2011**, *2*, 858.

(5) Back, O.; Henry-Ellinger, M.; Martin, C. D.; Martin, D.; Bertrand, G. *Angew. Chem., Int. Ed.* **2013**, *52*, 2939. (b) Rodrigues, R. R.; Dorsey, C. L.; Arceneaux, C. A.; Hudnall, T. W. *Chem. Commun.* **2013**, *50*, 162.

(6) (a) Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313−348. (b) Chianese, A. R.; Li, X.; Janzen, M. C.; Faller, J. W.; Crabtree, R. H. *Organometallics* **2003**, *22*, 1663. (c) Kelly, R. A., III; Clavier, H.; Giudice, S.; Scott, N. M.; Stevens, E. D.; Bordnder, J.; Samardjiev, I.; Hoff, C. D.; Cavallo, L.; Nolan, S. P. *Organometallics* **2008**, *27*, 202.

Scheme 3. Possible Mechanistic Pathways Leading to the Formation of 7 and 9



(7) (a) Coudray, L.; Montchamp, J.-L. *Eur. J. Org. Chem.* **2008**, 3601. (b) Greenberg, S.; Stephan, D. W. *Chem. Soc. Rev.* **2008**, *37*, 1482. (c) Glueck, D. S. *Top. Organomet. Chem.* **2010**, *31*, 65. (d) Ortial, S.; Fisher, H. C.; Montchamp, J.-L. *J. Org. Chem.* **2013**, *78*, 6599.

(8) (a) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176. (b) Nolan, S. P.; Clavier, H. *Chem. Soc. Rev.* **2010**, *39*, 3305.

(9) (a) Lavallo, V.; Mafhouz, J.; Canac, Y.; Donnadieu, B.; Schoeller, W. W.; Bertrand, G. *J. Am. Chem. Soc.* **2004**, *126*, 8670. (b) Lavallo, V.; Canac, Y.; Präsang, C.; Donnadieu, B.; Bertrand, G. *Angew. Chem., Int. Ed.* **2005**, *44*, 5705.

(10) Frey, G. D.; Lavallo, V.; Donnadieu, B.; Schoeller, W. W.; Bertrand, G. *Science* **2007**, *316*, 439.

(11) Frey, G. D.; Masuda, J. D.; Donnadieu, B.; Bertrand, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 9444.

(12) Formal carbene insertions into P−H bonds have also been reported via treatment of enetetraamines with phosphites. See: Hocker, J.; Merten, R. *Justus Liebigs Ann. Chem.* **1978**, 16. Küçükbay, H.; Çetinkaya, E.; Çetinkaya, B.; Lappert, M. F. *Synth. Commun.* **1997**, *27*, 4059.

(13) (a) Buron, C.; Gornitzka, H.; Romanenko, V.; Bertrand, G. *Science* **2000**, *288*, 834. (b) Goumri-Magnet, S.; Polishchuk, O.; Gornitzka, H.; Marsden, C. J.; Baceiredo, A.; Bertrand, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 3727.

(14) In contrast, $C_{carbene}$→P adducts are relatively well-known. See: (a) Arduengo, A. J., III; Krafczyk, R.; Marshall, W. J.; Schmutzler, R. *J. Am. Chem. Soc.* **1997**, *119*, 3381. (b) Burford, N.; Cameron, S.; LeBlanc, D. J.; Phillips, A. D. *J. Am. Chem. Soc.* **2000**, *122*, 5413. (c) Böttcher, T.; Shyshkov, O.; Bremer, M.; Bassil, B. S.; Röschenthaler, G.-V. *Organometallics* **2012**, *31*, 1278. (d) Tian, C.; Nie, W.; Borzov, M. V.; Su, P. *Organometallics* **2012**, *31*, 1751. (e) Gaillard, S.; Renaud, J.-L. *Dalton Trans.* **2013**, *42*, 7255.

(15) Moerdyk, J. P.; Blake, G. A.; Chase, D. T.; Bielawski, C. W. *J. Am. Chem. Soc.* **2013**, *135*, 18798.

(16) (a) Hudnall, T. W.; Bielawski, C. W. *J. Am. Chem. Soc.* **2009**, *131*, 16039. (b) César, V.; Lugan, N.; Lavigne, G. *Eur. J. Inorg. Chem.* **2010**, 361. (c) Hudnall, T. W.; Moerdyk, J. P.; Bielawski, C. W. *Chem. Commun.* **2010**, *46*, 4288. (d) Hobbs, M. G.; Forster, T. D.; Borau-Garcia, J.; Knapp, C. J.; Tuononen, H. M.; Roesler, R. *New. J. Chem.* **2010**, *34*, 1295. (e) Braun, M.; Frank, W.; Reiss, G. J.; Ganter, C. *Organometallics* **2010**, *29*, 4418. (f) Hudnall, T. W.; Tennyson, A. G.; Bielawski, C. W. *Organometallics* **2010**, *29*, 4569.

(17) Dorsey, C. L.; Squires, B. M.; Hudnall, T. W. *Angew. Chem., Int. Ed.* **2013**, *52*, 4462.

(18) Although dialkyl phosphites are known to exist in two tautomeric forms, the tetravalent isomer is favored; see: Pietro, W. J.; Hehre, W. J. *J. Am. Chem. Soc.* **1982**, *104*, 3594. O−H insertion arising from the insertion of **3** into the hydroxyl group of the trivalent tautomer was not observed by NMR spectroscopy

(19) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, S1.

(20) (a) Knappeke, C. E. I.; Arudengo, A. J., III; Jiao, H.; Neudörfl, J.-M.; Jacobi von Wangelin, A. *Synthesis* **2011**, *23*, 3784.

(21) Treating **3** with triethyl phosphite or 4-methyl-2,6,7-trioxa-1-phospha[2.2.2]octane (prepared as described in Cole, J. R.; Dellinger, M. E.; Johnson, T. J.; Reinecke, B. A.; Pike, R. D.; Pennington, W. T.; Krawiec, M.; Rheingold, A. L. *J. Chem. Crystallogr.* **2003**, *33*, 341) at 60−100 °C for several days resulted in decomposition; see: Moerdyk, J. P.; Bielawski, C. W. *Chem.—Eur. J.* **2013**, *19*, 14773.

(22) Trimethyl phosphite has been previously reported as a methylating agent; see: Meek, J. S.; Fowler, J. S. *J. Org. Chem.* **1968**, *33*, 3422.