JOC*Article*

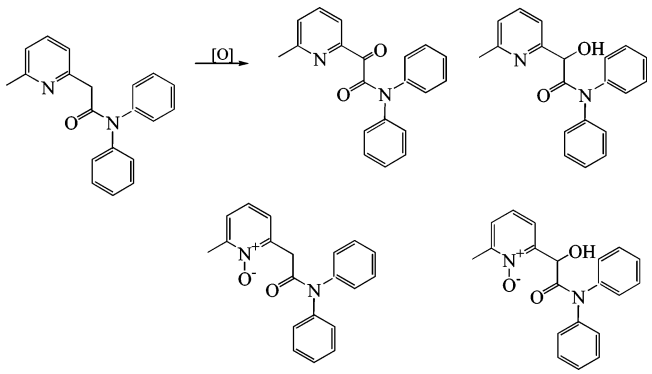
Oxidation Reactivity Channels for 2-(Pyridin-2-yl)-*N*,*N*-diphenylacetamides

Sylvie Pailloux,[†] Iris Binyamin,[†] Lorraine M. Deck,[†] Brian M. Rapko,[‡] Benjamin P. Hay,[§] Eileen N. Duesler,[†] and Robert T. Paine*,[†]

Department of Chemistry, University of New Mexico, Albuquerque, New Mexico 87131, Pacific Northwest National Laboratory, P.O. Box 999, Richland, Washington 99352, and Oak Ridge National Laboratory, P.O. Box 2008, Oak Ridge, Tennessee 37831

rtpaine@unm.edu

Received July 10, 2007



Synthetic routes to 2-(pyridin-2-yl)-*N*,*N*-diphenylacetamide and 2-(6-methylpyridin-2-yl)-*N*,*N*-diphenylacetamide are described along with results from the chemical oxidation of these compounds with peracetic acid, *m*-chloroperbenzoic acid, and OXONE. In each case, oxidations generate four products in varying amounts depending on the oxidant and reaction conditions. Each product has been characterized by spectroscopic methods and the molecular structures of several of the new compounds have been confirmed by X-ray crystallography.

Introduction

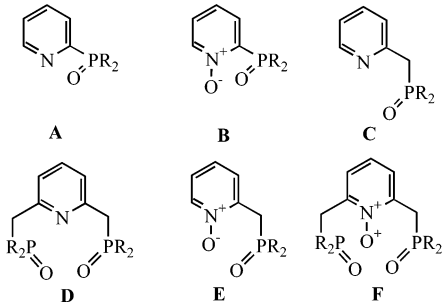
There is much interest in the design and synthesis of organic ligands suitable for selective recognition and separation of f-block metal ions from aqueous solutions via solvent extraction.[1−4] These ligands often contain two or more neutral oxygen donor groups such as phosphine oxides or amides. As examples, carbamoylmethylphosphonates (CMP), $(RO)_2P(O)CH_2C(O)NR_2$,[5] carbamoylmethylphosphine oxides (CMPO), $R_2P(O)CH_2C(O)NR_2$,[6−9] and alkyl malonamides, $[RR'NC(O)]_2CR''H$,[10−17] have been actively examined and each displays potentially useful characteristics. In our group, we have considered the utility of

* To whom correspondence should be addressed. Phone: (505) 277-1661.
[†] University of New Mexico.
[‡] Pacific Northwest National Laboratory.
[§] Oak Ridge National Laboratory.

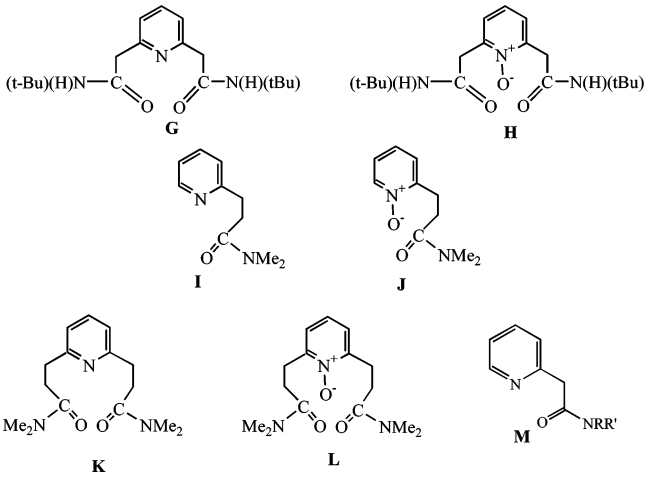
(1) Draganic, I. G.; Draganic, Z. D.; Adloff, J. P. *Radiation and Radioactivity on Earth and Beyond*; CRC Press: Boca Raton, FL, 1990.
(2) Nash, K. L.; Madic, C.; Mathur, J. N.; Lacquemont, J. In *The Chemistry of the Actinide and Transactinide Elements*; Morss, L. R., Edelstein, N. M., Fuger, J., Eds.; Springer: Dordreckt, The Netherlands, 2006; Vol. 4, Chapter 24, pp 2622−2798.
(3) Mathur, J. N.; Murali, M. S.; Nash, K. L. *Solvent Extr. Ion Exch.* **2001**, *19*, 357−390.
(4) Nash, K. L. *Solvent Extr. Ion Exch.* **1993**, *11*, 729−768.
(5) Horwitz, E. P.; Martin, K. A.; Diamond, H.; Kaplan, H. *Solvent Extr. Ion Exch.* **1986**, *4*, 449.
(6) Horwitz, E. P.; Martin, K. A.; Diamond, H.; Vandegrift, G. F.; Schultz, W. W. *Solvent Extr. Ion Exch.* **1985**, *3*, 75.
(7) Ozawa, M.; Koma, Y.; Nomura, K.; Tanaka, Y. *J. Alloys Compd.* **1988**, *271−273*, 538.
(8) Mathur, J. N.; Murali, M. S.; Natarajan, P. R.; Badhelka, L. P.; Bannerji, A.; Ramanujam, A.; Dhami, P. S.; Gopalakrishnan, V.; Dhumwad, R. K.; Rao, M. K. *Waste Manage* (*Amsterdam, Neth.*) **1993**, *13*, 317.
(9) Myasoedov, B. F.; Chmutova, M. K.; Smirnov, I. V.; Shadrin, A. U. In *Global '93*: *Future Nuclear Systems*: *Emerging Fuel Cycles and Waste Disposal Options*; American Nuclear Society: La Grange Park, IL, 1993.
(10) Cuillerdier, C.; Musikas, C.; Hoel, P.; Nigond, L.; Vitart, X. *Sep. Sci. Technol.* **1991**, *26*, 1229.
(11) Tan, X. F.; Wang, Y. S.; Tan, T. Z.; Zhou, G. F.; Bao, B. R. *J. Radioanal. Nucl. Chem.* **1999**, *242*, 123.
(12) McNamara, B. K.; Lumetta, G. J.; Rapko, B. M. *Solvent Extr. Ion Exch.* **1999**, *17*, 1403.
(13) Lumetta, G. J.; McNamara, B. K.; Rapko, B. M.; Hutchinson, J. M. *Inorg. Chem.* **1993**, *32*, 2164.

10.1021/jo701408y CCC: $37.00
Published on Web 11/01/2007

pyridine and pyridine *N*-oxide as platforms for the assembly of selective ligands, and structures of the general types **A**−**F** have been developed.[18−31] Ligands **E** and **F** form particularly stable complexes, and derivatives, carrying lipophilic substituents such as 2-ethylhexyl, provide impressive separations performance for lanthanides (Ln^{+3}) and Am^{+3} from strongly acidic HNO_3 (>1 M) solutions.[31]



Despite these successes, there remain fundamental and practical interests in further expansion of available extractant molecules, especially those that might provide a slightly softer donor environment and more selective separations, e.g., Am/Cm partitioning. Representative target ligands include acetamido and propionamido functionalized pyridine and pyridine *N*-oxide platforms. In that regard, we have recently reported the syntheses and coordination chemistry for examples of **G**−**L**.[32,33] These results have stimulated efforts to prepare the *N*,*N*-diorganyl acetamide analogues of **C**−**F**. Herein we report the syntheses and oxidation chemistry of the "one-armed" derivatives **M**.



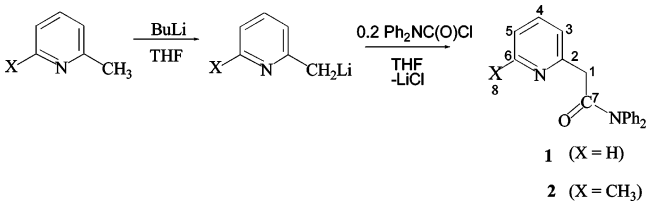
Results and Discussion

Limited attention has been given to the development of efficient syntheses for 2-(pyridin-2-yl) acetamides **M** and, as far as we are aware, no reports of the corresponding *N*-oxide derivatives have appeared. Reich and Levine[34] described the synthesis of **M** (R = R′ = Me, Et, *n*-Bu and R = Me, R′ = Ph) in low to modest yields from the combination of picolylithium and the corresponding diorganyl carbamoyl chlorides. Murray,[35] as part of broad patent claims, included a description of the synthesis of *N*,*N*-dimethyl-(2-pyridyl) acetamide by using an aggressive (autoclave, 90 °C, 96 h) amination of ethyl 2-pyridylacetate with excess Me_2NH/MeOH; however, formation of other derivatives relevant to our study is not indicated. More recently, in a general study of heteroaromatic nucleophilic substitutions by various carbanions via an $S_{RN}1$ mechanism, Wolfe and co-workers[36] outlined the interaction of the potassium enolate of *N*,*N*-dimethylacetamide with 2-bromopyridine under photolytic conditions which produced **M** (R = R′ = Me) in 74% yield along with 5% of the double substitution product. Moloney and co-workers[37] also reported a Reformatsky reagent approach (dibenzylbromoacetamide/Zn) on 2-bromopyridine with microwave radiation assistance. This reaction gave **M** (R = R′ = Bn) in 73% yield. The only route reported for a wide variety of *N*,*N*-dialkyl derivatives has been summarized in a patent describing syntheses of 4*H*-quinolizin-4-one compounds.[38] The approach employed peptide coupling methods with 2-pyridylacetic acid hydrochloride and symmetric and asymmetric dialkylamines.

In the studies summarized above, no mention was made regarding the applicability of these methods for the formation of **M** (R = R′ = Ph) or the outcome of chemical oxidation as a route to the corresponding *N*-oxides. Although we are potentially interested in the *N*,*N*-dialkyl derivatives for lipophillic solvent extraction schemes, we initially focused on obtaining **M** (R = R′ = Ph) (hereafter labeled as compound **1**) and its *N*-oxide derivative since aryl derivatized ligands typically provide better opportunities to obtain well-defined, crystalline

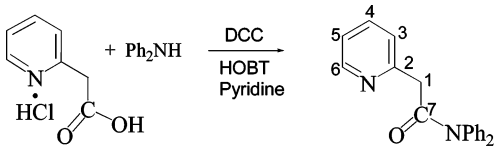
(14) Spjuth, L.; Liljenzin, J. O.; Hudson, M. J.; Drew, M. G. B.; Iveson, P. B.; Madic, C. *Solvent Extr. Ion Exch.* **2000**, *18*, 1.
(15) Facchini, A.; Amato, L.; Modolo, G.; Nannicini, R.; Madic, C.; Baron, P. *Sep. Sci. Technol.* **2000**, *35*, 1055.
(16) Courson, O.; Lebrun, M.; Malmbeck, R.; Pagliosa, G.; Romer, K.; Satmark, B.; Glatz, J. P. *Radiochim. Acta* **2000**, *88*, 857.
(17) Lumetta, G. J.; Rapko, B. M.; Garza, P. A.; Hay, B. P.; Gilbertson, R. D.; Weakley, T. J. R.; Hutchinson, J. E. *J. Am. Chem. Soc.* **2002**, *124*, 5644.
(18) McCabe, D. J.; Russell, A. A.; Karthikeyan, S.; Paine, R. T.; Ryan, R. R.; Smith, B. F. *Inorg. Chem.* **1987**, *26*, 1230.
(19) Conary, G. C.; Russell, A. A.; Paine, R. T.; Hall, J. H.; Ryan, R. R. *Inorg. Chem.* **1988**, *27*, 3242.
(20) Blaha, S. L.; McCabe, D. J.; Paine, R. T.; Thomas, K. W. *Radiochim. Acta* **1989**, *46*, 123.
(21) Rapko, B. M.; Duesler, E. N.; Smith, P. H.; Paine, R. T.; Ryan, R. R. *Inorg. Chem.* **1993**, *32*, 2164.
(22) Englehardt, U.; Rapko, B. M.; Duesler, E. N.; Frutos, D.; Paine, R. T. *Polyhedron* **1995**, *14*, 2361.
(23) Bond, E. M.; Duesler, E. N.; Paine, R. T.; Nöth, H. *Polyhedron* **2000**, *19*, 2135.
(24) Gan, X. M.; Parveen, S.; Smith, W. L.; Duesler, E. N.; Paine, R. T. *Inorg. Chem.* **2000**, *39*, 4591.
(25) Bond, E. M.; Duesler, E. N.; Paine, R. T.; Neu, M. P.; Matonic, J. H.; Scott, B. L. *Inorg. Chem.* **2000**, *39*, 4152.
(26) Gan, X.; Duesler, E. N.; Paine, R. T. *Inorg. Chem.* **2001**, *40*, 4420.
(27) Gan, X.; Paine, R. T.; Duesler, E. N.; Nöth, H. *J. Chem. Soc., Dalton Trans.* **2003**, 153.
(28) Bond, E. M.; Englehardt, U.; Deere, T. P.; Rapko, B. M.; Paine, R. T.; FitzPatrick, J. R. *Solvent Extr. Ion Exch.* **1997**, *15*, 381.
(29) Bond, E. M.; Englehardt, U.; Deere, T. P.; Rapko, B. M.; Paine, R. T.; FitzPatrick, J. R. *Solvent Extr. Ion Exch.* **1998**, *16*, 967.
(30) Bond, E. M.; Gan, X.; FitzPatrick, J. R.; Paine, R. T. *J. Alloys Compd.* **1998**, *271*−*273*, 172.
(31) Nash, K. L.; Lavallette, C.; Borkowski, M.; Paine, R. T.; Gan, X. *Inorg. Chem.* **2002**, *41*, 5849.
(32) Binyamin, I.; Pailloux, S.; Duesler, E. N.; Rapko, B. M.; Paine, R. T. *Inorg. Chem.* **2006**, *45*, 5886.
(33) Binyamin, I.; Pailloux, S.; Hay, B. P.; Rapko, B. M.; Duesler, E. N.; Paine, R. T. *J. Heterocycl. Chem.* **2007**, *44*, 99.
(34) Reich, H. E.; Levine, R. *J. Am. Chem. Soc.* **1955**, *77*, 4913.
(35) Murray, R. J. U.S. Pat. 4,847,301, July 11, 1989.
(36) Wang, J.-W.; Natalie, K. J., Jr.; Nwokogu, G. C.; Pispati, J. S.; Flaherty, P. T.; Greenwood, T. D.; Wolfe, J. F. *J. Org. Chem.* **1997**, *62*, 6152.
(37) Bentz, E.; Moloney, M. G.; Westaway, S. M. *Tetrahedron Lett.* **2004**, *45*, 7395.
(38) Kurashima, Y.; Miyata, H.; Momose, D. U.S. Pat. No. 4,877,795, Oct. 31, 1989.

SCHEME 1



coordination complexes. Therefore, we have explored two of the existing methods for the synthesis of **1**. Method 1 utilized the peptide coupling approach of Kurashima[38] and Method 2 involved carbanion substitution with diphenylcarbamoyl chloride without photostimulation.[34]

The peptide coupling approach (Method 1) is summarized in eq 1. Conditions described by Kurashima[38] were employed along with several variations; however, the best yields realized were only 30−40%. In addition, as is often the case with this methodology, it was relatively difficult to purify the product.



(1)

1

Given these shortcomings, a simplified nucleophilic substitution approach (Method 2) was examined as summarized in Scheme 1. Initially this reaction was performed in a 1:1 equiv picolylithium/diphenylcarbamoyl chloride reactant ratio; however, it was noted that significant amounts of 2-(pyridin-2-yl)-*N*,*N*,*N*′,*N*′-tetramethylmalonamide **3** also formed, probably due to the enhanced acidity of the acetamide, $-CH_2C(O)NPh_2$, protons following formation of **1**. Not only was the yield of **1** reduced by formation of the malonamide, but separation of the two products was difficult. A variety of conditions and reactant stoichiometries were explored and the optimum yield (83% based on diphenylcarbamoyl chloride) and purification were achieved with a 1:0.2 equiv picolylithium:carbamoylchloride ratio. With this combining ratio, no malonamide byproduct was produced and **1** was isolated as an analytically pure yellow-orange crystalline solid. The analogue, 2-(6-methyl-pyridin-2-yl)-*N*,*N*-diphenylamide, **2**, was prepared in a similar fashion and isolated as a yellow solid in 70% yield (based on diphenylcarbamoyl chloride).

Both **1** and **2** display an intense ($M + H^+$) ion in ESI-MS and IR spectra contain an adsorption at 1674 (**1**) or 1675 cm^{-1} (**2**) that are assigned to ν_{co}. The ^1H and $^{13}C\{^1H\}$ NMR spectra for **1** and **2** are consistent with the proposed structures, with diagnostic resonances for C_1 [δ 3.80 (2H); 45.6] and C_7 [δ 170.7] in **1** and C_1 [δ 3.74 (2H); 45.4], C_7 [δ 170.8], and C_8 [δ 2.45 (3H); 24.8] in **2**. In addition, the molecular structures of **1** and **2** were confirmed by single-crystal X-ray diffraction analyses and views of the molecules are shown in Figure 1.

As noted above, 2-(pyridin-2-yl)-*N*,*N*,*N*′,*N*′-tetramethylmalonamide **3** also formed in the reaction summarized in Scheme 1 when more than 0.2 equiv of $Ph_2NC(O)Cl$ was available. Indeed, **3** and the related compound **4** were isolated in 80% yield from a combining ratio of 2-picoline or 2,6-lutidine/BuLi/$Ph_2NC(O)Cl$ = 1/2/2 as shown in Scheme 2. Compounds **3** and **4** are crystalline solids that display ($M + H^+$) ions in ESI-MS and ν_{co} appears at 1682 and 1688 cm^{-1}, respectively, in the IR spectra. The ^1H and $^{13}C\{^1H\}$ NMR spectra are consistent with the proposed structures with the methine $-C(H)[C(O)NPh_2]_2$ group showing resonances for **3** at δ 5.2 (1H) and δ 60.1 and for **4** at δ 5.2 (1H) and δ 59.8, respectively. The structure of **4** was further confirmed by single-crystal X-ray diffraction analysis and a view of the molecule is shown in Figure 2.

It is interesting to compare the chemistry that produces **1**−**4** against related chemistry that results in formation of derivatives of the (phosphino)pyridine *P*-oxides, **C**.[21,22,26,28] In general, using similar reaction conditions, there seems to be no tendency to generate bis-phosphine oxide analogues of **3** and **4** with reactant ratios 2,6-lutidine/$Ph_2P(O)Cl$/BuLi of 1/2/0.1−1. There is a slight tendency to generate the bis-phosphine oxide with a combining ratio 1/2/2, but the optimum way to obtain double substitution is through stepwise formation/isolation of the monosubstitution product **C** followed by treatment of it with BuLi/$Ph_2P(O)Cl$, 1/1.[40,41] This suggests that the acidity of the methylene group separating the pyridine ring from the amide is greater than that for the methylene group attached to the phosphine oxide.

To further examine this point, deprotonation energies were computed at the MP2/aug-cc-pVDZ level of theory. The results are shown in Figure 3. For computational simplicity, the phenyl groups on the amide nitrogen atom and on the phosphorus atoms were replaced with methyl groups. Clearly, deprotonations of both the methylamide and methylphosphine oxide centers on the pyridine or pyridine oxide rings (eqs 2−7) are significantly favored over deprotonation of the nonacidic CH_4 (eq 8). This is due to resonance stabilization of the anions in the former. Then, deprotonation of either the pyridine or pyridine *N*-oxide-amides (eqs 2 and 6) is slightly favored over that of the respective phosphine oxides (eqs 3 and 7). The comparisons of energetics for eqs 2 and 3 support the experimental observation described above that the double substitution with formation of a malonamide is favored over formation of a bis-phosphine oxide. It is also interesting to note that the computed acidity of the 6-methyl group is slightly greater for the phosphine oxide compound compared to that for the amide analogue [eq 4 vs eq 5].

With satisfactory syntheses of **1** and **2** defined, attention was directed to formation of the respective *N*-oxide derivatives. Prior work on 2-(diphenylphosphinomethyl)pyridine *P*-oxide, **C**, indicated that pyridine *N*-oxidation was easily accomplished in high yield (>90%), without byproduct formation, by using *m*-chloroperbenzoic acid, peracetic acid, or OXONE and it was anticipated that each of these oxidants would provide a clean route to the *N*-oxides of **1** and **2**. However, this chemistry is more complex than expected. With each pyridine precursor **1** and **2** and each oxidant, four products are obtained as summarized in Scheme 3. Since *m*-chloroperbenzoic acid (*m*CPBA) provided the most complete conversions, further discussion is limited to its use as the oxidant.

Initially, oxidation of **1** with *m*CPBA was studied with a 1:1 combining ratio in $CHCl_3$ at 23 °C. TLC (ethyl acetate) of reaction mixtures indicated the formation of at least three products. This observation led to the study of substrate (**1** or

(39) The atom numbering system chosen for the X-ray crystal structures differs from that employed for the NMR assignments.

(40) Bodrin, G. V.; Matveeva, A. G.; Terekhova, M. I. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1991**, *4*, 912.

(41) Gan, X.; Paine, R. T. Unpublished results.

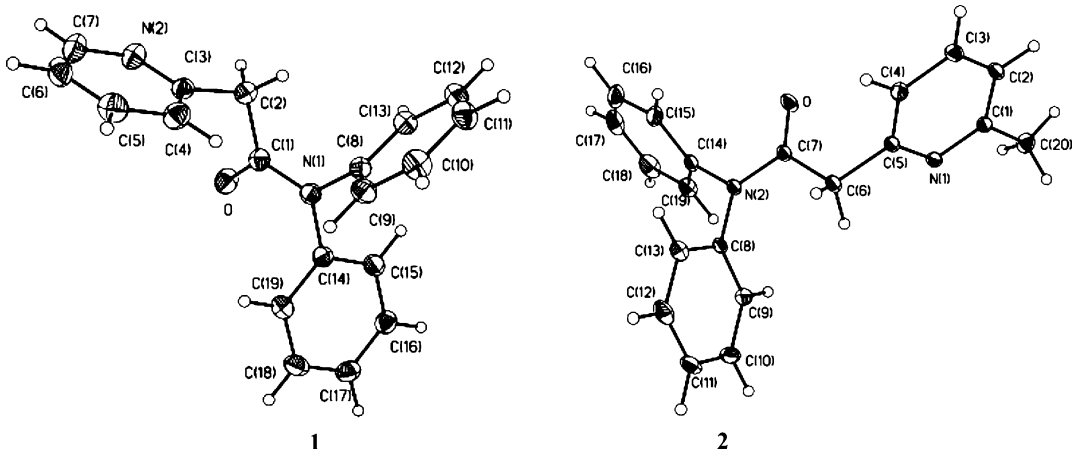


FIGURE 1. Molecular structure and atom labeling scheme for **1** and **2**.[39]

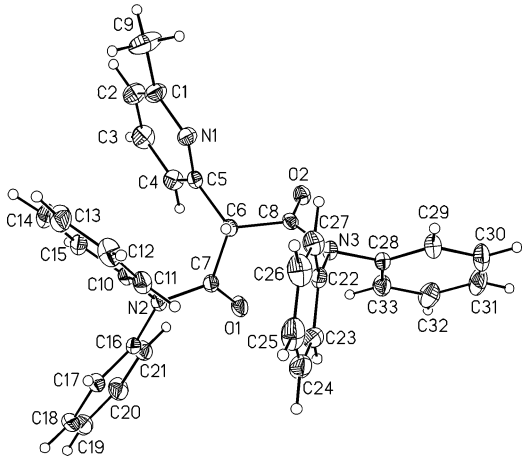
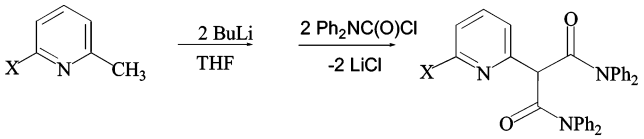


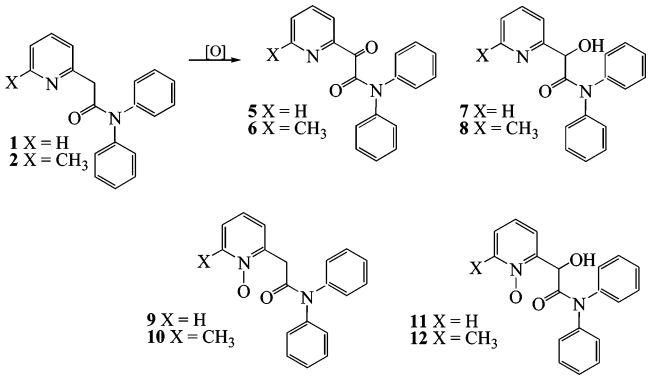
FIGURE 2. Molecular structure and atom labeling scheme for **4**.[39]

SCHEME 2



3 X = H
4 X = CH_3

SCHEME 3



2)/oxidant (*m*CPBA) combining ratios in the range 0.5−2 and the discovery that four products are formed in varying amounts. The details of results from ratios 0.87 and 1.2 are described since these led to the best product separations.

The combination of **1** (1 eq) with *m*CPBA (0.87 eq) in CH_2Cl_2 at reflux (12 h) gave a mixture that, following workup, displayed three spots by TLC (ethyl acetate). Subsequent column chromatography, using EtOAc as the eluant, showed that the first spot corresponds to **5** and it was isolated in 7% yield (based on *m*CPBA). The second fraction from the column initially contained **7** (45%) with a trace of starting material, and at the end of this fraction, pure **7** was obtained (19%). The third fraction was recovered by use of MeOH (2%) in CH_2Cl_2 as eluant and this contained **9** (19%). Compound **11** was not observed under these conditions. With a combining ratio of **1** (1 equiv) with *m*CPBA (1.2 equiv) in CH_2Cl_2 at 23 °C (12 h) three spots were observed in TLC (ethyl acetate) following workup. Column chromatography with EtOAc as the eluant provided a small amount (1%) of **5** in the first fraction and the major product **7** (71%) in the second fraction (based on **1**). The column was then eluted with 2% MeOH/CH_2Cl_2 and **9** (17%) and **11** (10%) were recovered. Alternatively, a gradient mixture of MeOH/CH_2Cl_2 was used to elute the column and similar product yields were obtained.

Given these results, two additional excess oxidant combinations were examined. A mixture of **1** (1 equiv) and *m*CPBA (3 equiv) in CH_2Cl_2 was refluxed (12 h) and, following workup, two spots were detected by TLC. Column chromatography with EtOAc as eluant gave **5** (1−3%) and a mixture of **11** (62%) and **9** (38%). In a similar manner, **1** (1 equiv) and *m*CPBA (5 equiv) gave a mixture of **11**, **9**, and a trace of **5**, but here the recrystallization of the product residue led to recovery of pure **11** (28%) as colorless crystals.

In summary, no conditions were found that led to high yield formation of the α-ketoamide **5**; however, it was isolated as colorless crystals, in low yield, with the deficient oxidant condition. Compound **7** was the dominant product when 1.2 equiv of oxidant was employed and it was isolated in pure form. Compound **9**, the most desired ligand target, was not obtained as a dominant product and it was very difficult to purify. Compound **11** was dominant when excess oxidant was supplied and it was isolated in modest yield. Using parallel reaction conditions, the oxidation of **2** proceeded in a nearly identical manner to give **6** (minor product), **8** (dominant product with 1 equiv of *m*CPBA), **10**, and **12** (dominant product with 3 equiv of *m*CPBA). It is also found that oxidation of pure, isolated samples of **7** (CH_2Cl_2, 1.3 equiv of *m*CPBA, reflux, 12 h) produced 100% conversion to **11** while identical treatment of

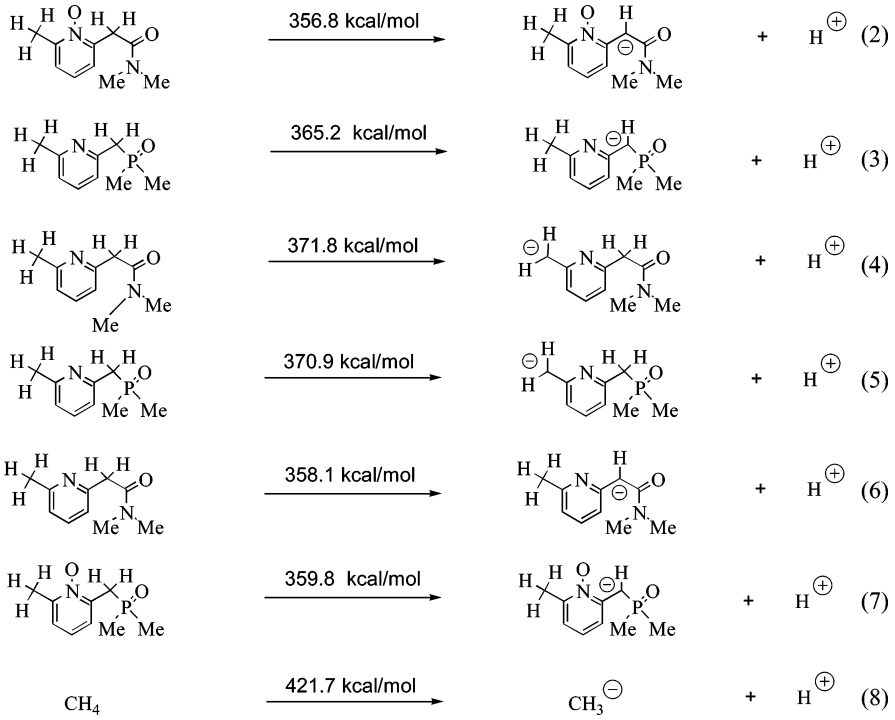


FIGURE 3. Computed deprotonation reaction energies for model compounds of **C** and **M**.

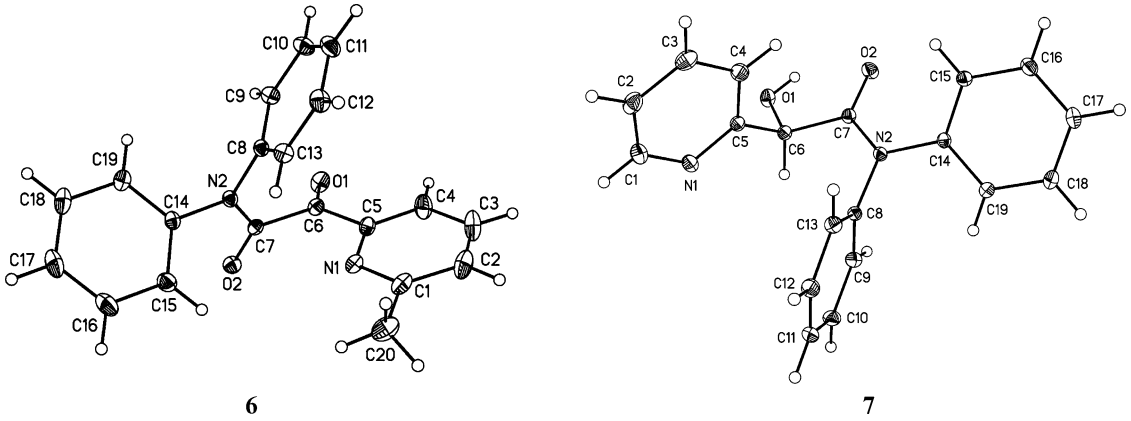


FIGURE 4. Molecular structures and atom labeling schemes for **6** and **7**.[39]

isolated samples of **9** gave **11** but more slowly (66% conversion in 12 h), and conversion was still incomplete after 24 h.

Spectroscopic characterization data (IR, NMR, MS) for each oxidation product **5**−**12** were collected. Each compound displays an intense [M + H$^+$] ion and infrared bands for the resident functional groups (C═O, N−O, and/or OH). The ^{1}H and ^{13}C{^{1}H} NMR spectra are consistent with the proposed structures. In addition, molecular structures for **6** and **7** (Figure 4) and for **12** and a mixture of **9** and **11** (Figure 5) were determined by X-ray diffraction techniques. As mentioned earlier, it is difficult to separate **9** and **11** and mixed crystals were typically obtained. In fact, the structure refinement for the mixed crystal was better behaved than that for the pure components and this is likely a result of more favorable packing even though no classical intermolecular hydrogen bonding is apparent. In all cases the crystal structures confirm the spectroscopically assigned structures.

Clearly, strong base-promoted substitution chemistry on 2-picoline and 2,6-lutidine by *N*,*N*-diphenylcarbamoyl chloride that initially produces **1** and **2** and then **3** and **4**, respectively, and the multichannel chemical oxidation chemistry for **1** and **2** differ from the chemistry involving the phosphine oxide analogues of **C**−**F**.[21,26] In the phosphine oxides, double substitution only occurs under more forcing conditions and oxidation chemistry results only in formation of *N*-oxides related to **9** and **10**. As noted above, computational analyses suggest that the methylene (C_1) protons are likely more acidic in **1** and **2** than in the phosphine oxide analogues making the (C_1) carbon more susceptible to the second substitution step or oxidation. It appears that there is a preference for initial oxidation to occur at the (C_1) carbon atom over the pyridine N atom since, with reactant ratios [O]:**1**(**2**) = 0.8−1.0, **7**(**8**) is the dominant product. The *N*-oxide **9**(**10**) forms under all conditions but in low yield, while **11**(**12**) results from mixtures rich in oxidant.

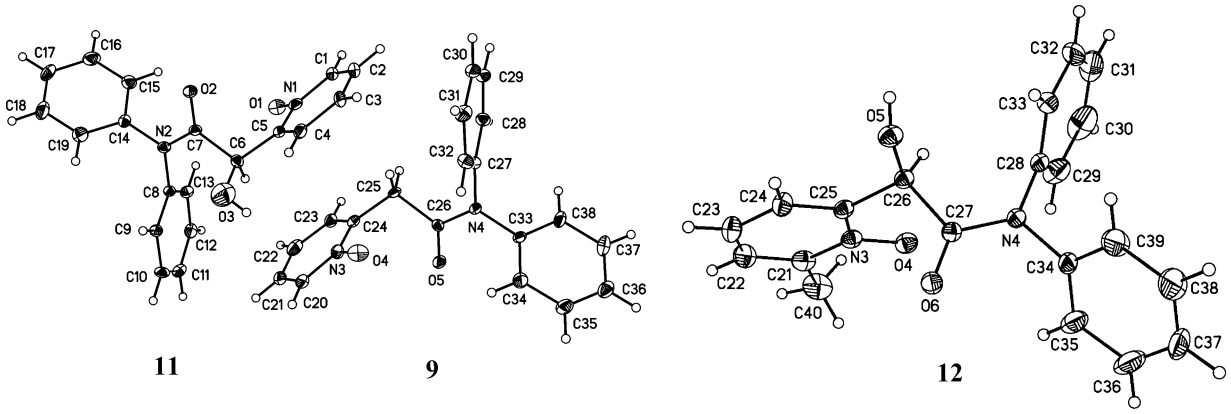


FIGURE 5. Molecular structures and atom labeling schemes for a mixture of **9** + **11** and **12**.[39]

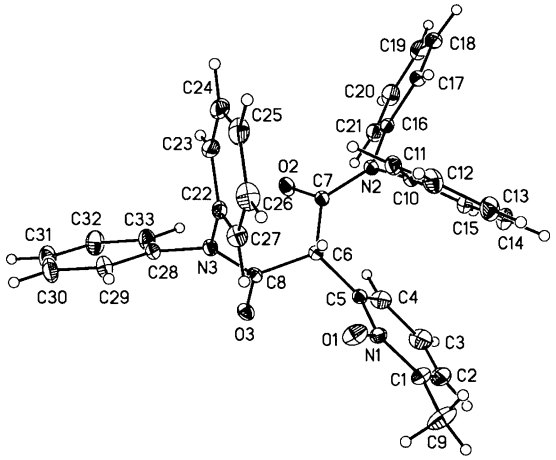
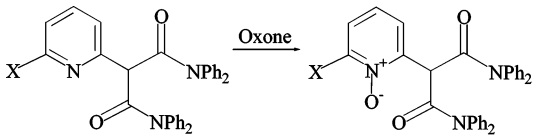


FIGURE 6. Molecular structure and atom labeling scheme for **14**.[39]

It is noted that *N*,*N*-dialkyl-2-pyridyl glyoxyl amides, alkylamido analogues of the α-ketoamide **5**, have been previously reported to be difficult to prepare.[42] The *N*,*N*-diethyl derivative is reported as a product of (a) SeO_2 induced ring opening of 3-*N*,*N*-diethylacetamido triazolopyridine,[43] (b) Pd-catalyzed α-ketoamido carbonylation of 2-iodopyridine,[44−47] and (c) a combination 2-pyridyl esters and amino acetonitrile followed by oxidation of the intermediate cyanoketone with bleach.[48] The last approach was also used to prepare a *n*-Pr analogue, but no examples of *N*,*N*-diaryl amide derivatives are reported. In addition, Jones[43] briefly described formation of *N*,*N*-diethyl-2-pyridyl glycolamide, an alkyl amido analogue of **7**, from acidic hydrolysis of its triazolopyridine precursor.

Further evidence that **7** and **8** are the key initial products in the oxidation processes for **1** and **2** is found in the outcome of the oxidation of the malonamides **3** and **4**. As shown in eq 9, only the *N*-oxidation products **13** and **14** are formed and there is no evidence for hydroxylation of the C_1 carbon. Compounds **13** and **14** were characterized by IR, MS, and NMR spectroscopy, and the molecular structure of **14** was confirmed by X-ray crystallography (Figure 6). The process by which the α-ketoamides **5** and **6** form is less clear, but they are always very minor products and therefore may result from an impurity oxidant. However, it has been previously noted that mandelamides, *p*-RC_6H_4-C(H)(OH)-C(O)N(H)R′, undergo oxidation with $BaMnO_4$ to give glyoxamides, *p*-RC_6H_4C(O)C(O)N(H)R′.[49] This supports the conclusion that **5**(**6**) results from oxidation of initially formed **7**(**8**).



3 X = H
4 X = Me

13 X = H
14 X = Me

(9)

Conclusion

This study has defined high-yield syntheses for 2-(pyridin-2-yl)-*N*,*N*-diphenylamides and 2-(pyridin-2-yl)-*N*,*N*,*N*′,*N*′-tetraphenylmalonamides. The chemical *N*-oxidation chemistry for the latter, **3** and **4**, is straightforward producing the trifunctional molecules **13** and **14** in high yields. The chemical *N*-oxidation chemistry of the former, **1** and **2**, is more complex, but the products have been identified and characterized. Compounds **1**, **2**, **9**, and **10** have the potential to act as bidentate bifunctional chelating ligands while trifunctional **3**−**8** and **11**−**14** may serve as tridentate ligands. From the ligand design perspective, optimal ligand architectures would adopt low-energy conformations in which all the binding sites are oriented to complement the metal ion. However, without exception the molecular structures obtained for these ligands reveal that the oxygen-bearing functional groups are rotated away from each other in the crystals placing the binding sites in a divergent rather than convergent orientation. Similar behavior observed in prior studies of phosphine oxide analogues has been attributed to minimizing dipole/electron pair repulsions.[21,26,41] To the extent that conformations observed in the solid state correspond to those present in solution, these results suggest that structural

(42) Abarca, A.; Gomez-Aldaravi, E.; Jones, G.; Sliskovic, D. R. *J. Chem. Res.* (*S*) **1983**, *144*, 1341.
(43) Jones, G.; Mouat, D. J.; Tonkinson, D. J. *J. Chem. Soc., Perkin Trans.* **1985**, 2719.
(44) Couve-Bonnaire, S.; Carpentier, J.-F.; Mortreux, A.; Castanet, Y. *Adv. Synth. Catal.* **2001**, *343*, 289.
(45) Couve-Bonnaire, S.; Carpentier, J.-F.; Castanet, Y.; Mortreux, A. *Tetrahedron Lett.* **1999**, *40*, 3717.
(46) Tsukada, N.; Ohba, Y.; Inoue, Y. *J. Organomet. Chem.* **2003**, *687*, 436.
(47) Ozawa, F.; Sugimoto, T.; Yuasa, Y.; Santra, M.; Yamamoto, T.; Yamamoto, A. *Organometallics* **1984**, *3*, 683.
(48) Yang, Z.; Zhang, Z.; Meanwell, N. A.; Kadow, J. F.; Wang, T. *Org. Lett.* **2002**, *4*, 1103.
(49) Haddadin, M. J.; Tannus, H. T. *Heterocycles* **1984**, *22*, 773.

reorganization will be required to achieve conformations that allow all binding sites to engage the metal ion. Further studies are now in progress to investigate the coordination chemistry for this new family of ligands.

Experimental Section

2-(Pyridin-2-yl)-*N*,*N*-diphenylacetamide (1): Method 1. 1,3-Dicyclohexylcarbodiimide (DCC) (3.2 g, 0.015 mol) was added to a mixture of 2-pyridyl acetic acid hydrochloride (2.065 g, 0.012 mol), diphenylamine (2.03 g, 0.012 mol), and 1-hydroxybenzotriazole hydrate (HOBT) (1.6 g, 0.012 mol) in dry pyridine (25 mL) and the mixture was stirred (23 °C, 18 h). The DCU formed was removed by filtration, the filtrate was evaporated, and the oily residue was treated with aqueous HCl (1 N, 50 mL). The aqueous phase was washed with Et_2O (3 × 25 mL) and then treated with aqueous NaOH solution (2 N) to pH 11. This solution was extracted with CH_2Cl_2 (100 mL) and the organic phase dried over Na_2CO_3. The volatiles were vacuum evaporated leaving a yellow oil, **1**. Yield: 1.3 g (37%). Chromatographic column purification was performed with silica gel 70−230 mesh and CH_2Cl_2:MeOH 100:3 as eluant. ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.79 (2H), 7.06 (d,d, J = 7.2 Hz, 1H), 7.20 (d,d, J = 7.3 Hz, 1H), 7.20−7.40 (m, 10H), 7.54 (d, d, J = 1.8, 7.7 Hz, 1H), 8.45 (d, J = 4.8 Hz, 1H). ^{13}C{^{1}H} NMR (62.5 Hz, $CDCl_3$): δ 45.6, 122.3, 124.7, 127.1, 129.8, 136.9, 143.4, 149.9, 156.4, 170.7. IR (KBr, cm^{-1}): 1674 (ν_{co}). MS (FAB$^+$): m/z 289.1 (M + H$^+$, 35%). Anal. Calcd for $C_{19}H_{16}N_2O$: C 79.14, H 5.59, N 9.71. Found: C 78.60, H 5.82, N 9.33.

Method 2. 2-Picoline (2 g, 21 mmol) in dry THF (15 mL) was treated dropwise with *n*-BuLi (13 mL, 1.6 M in THF, 21 mmol) at 0 °C. Following addition, the mixture was warmed to 23 °C and stirred (1 h). The resulting mixture was cooled (0 °C) and diphenylcarbamoyl chloride (0.99 g, 4.3 mmol) in THF (15 mL) was added dropwise. This mixture was stirred overnight (23 °C). The solvent was evaporated and the remaining residue carefully hydrolyzed (50 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL) and the organic phase was washed with water (50 mL) and dried over $MgSO_4$. The solvent was vacuum evaporated leaving a red oil. Chromatographic column purification was performed with silica gel 70−230 mesh and ethyl acetate or CH_2Cl_2:MeOH 99:1, then 98/2 as eluant. Solvent was evaporated leaving a yellow-orange solid, **1**. Yield: 0.79 g, 81%. Subsequent washing with hexane (2 × 10 mL) left a white solid (0.57 g, 59%). ^{1}H NMR ($CDCl_3$): δ 3.83 (s, 2H), 7.00 (d, J = 6.8 Hz, 1H), 7.15−7.45 (m, 11H), 7.55 (d,d, J = 2, 7.8 Hz, 1H), 8.50 (dd, J = 0.75, 4.0 Hz, 1H). ^{13}C{^{1}H} NMR (62.5 MHz, $CDCl_3$): δ 44.9, 121.6, 124.0, 126.5, 129.2, 136.2, 142.7, 149.2, 155.7, 170.0. HRMS: found 289.1330 (M + H$^+$). $C_{19}H_{17}N_2O$ requires 289.1341. Anal. Calcd for $C_{19}H_{16}N_2O$: C 79.14, H 5.59, N 9.72. Found: C 78.87, H 5.59, N 9.70.

2-(6-Methyl-pyridin-2-yl)-*N*,*N*-diphenylacetamide (2). *n*-BuLi solution (1.6 M in THF, 11.7 mL) was added dropwise to a stirred solution of 2,6-lutidine (2 g, 19 mmol) in dry THF (15 mL) at 0 °C. The mixture turned red and after stirring (30 min, 23 °C) diphenylcarbamoyl chloride (0.88 g, 3.8 mmol) in dry THF (15 mL) was added dropwise at 0 °C. The solution color turned yellow and stirring was continued overnight (23 °C). Solvent was vacuum evaporated and the residue was treated with a CH_2Cl_2 (50 mL)/H_2O (50 mL) mixture. The aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL) and the combined organic phases were dried over $MgSO_4$ and concentrated. The residue was flash chromatographed (silica gel) with EtOAc/hexane (3/7) as initial eluant. The amount of EtOAc was increased until the final eluant contained only EtOAc. The solvent was evaporated, the residue was recrystallized from MeOH (−20 °C), and a yellow solid, **2**, collected. Yield: 0.80 g, 70%. Mp 98−100 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.45 (s, 3H), 3.74 (s, 2H), 6.93 (d, J = 7.5 Hz, 1H), 6.98 (d, J = 6.9 Hz, 1H), 7.25 (m, 10H), 7.40 (d, d, J = 7.5 Hz, 1H). ^{13}C{^{1}H} (62.5 MHz, $CDCl_3$): δ 24.8, 45.4, 121.3, 121.6, 126.9, 128.1, 129.1, 136.9, 143.2, 155.3, 158.2, 168.2, 170.8. IR (KBr, cm^{-1}): 1675 (ν_{co}). HRMS: found 303.1432 (M + H$^+$). $C_{20}H_{19}N_2O$ requires 303.1497. Anal. Calcd for $C_{20}H_{18}N_2O$: C 79.44, H 6.00, N 9.26. Found: C 78.33, H 5.89, N 9.15.

2-(Pyridin-2-yl)-*N*,*N*,*N*′,*N*′-tetraphenylmalonamide (3). *n*-BuLi solution (1.6 M in THF, 7.5 mL, 12 mmol) was added dropwise to picoline (1.0 g, 12 mmol), then diluted in dry THF (10 mL) and held at 0 °C. The mixture was stirred, then warmed to 23 °C (1 h) and chilled again to 0 °C. Diphenylcarbamoyl chloride (5.57 g, 24 mmol) in dry THF (15 mL) was added dropwise with stirring and the mixture was heated overnight (50 °C). The mixture was then concentrated and the residue was hydrolyzed with water (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were dried over $MgSO_4$, and the residue was flash chromatographed (silica gel) with EtOAc as eluant. The solvent was removed and a yellow solid (**3**) was obtained (4.1 g, 80%). This was crystallized from MeOH to afford tan crystals. Yield: 3.0 g, 57%. Mp 120−124 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 5.22 (s, 1H), 6.75 (d, J = 7.1 Hz, 4H), 7.13 (4H), 7.25−7.30 (13H), 7.45 (d, J = 7.8 Hz, 1H), 7.63 (td, J = 6.0, 1.7 Hz, 1H), 8.33 (d, J = 4.2 Hz, 1H). ^{13}C{^{1}H} NMR (62.5 MHz, $CDCl_3$): δ 60.1, 122.2, 124.4, 125.2, 126.2, 128.1, 128.8, 129.4, 129.6, 136.1, 141.8, 142.4, 148.7, 154.5, 167.6. IR (KBr, cm^{-1}): 1682 (ν_{co}). HRMS: found 484.1989 (M + H$^+$). $C_{32}H_{26}N_3O_2$ requires 484.2025.

2-(6-Methylpyridin-2-yl)-N,N,N′,N′-tetraphenylmalonamide (4). *n*-BuLi solution (1.6 M in THF, 11.6 mL, 18 mmol) was added dropwise to 2,6-lutidine (1.0 g, 9.3 mmol) in dry THF (15 mL) at 0 °C. The stirred mixture turned red and was then warmed to 23 °C (30 min). The resulting mixture was cooled to 0 °C and diphenylcarbamoyl chloride (4.32 g, 18.6 mmol) in dry THF (15 mL) was added dropwise with stirring. The solution turned red and was stirred overnight (50 °C). Solvent was then vacuum evaporated and the residue was treated with CH_2Cl_2/H_2O (50 mL/50 mL), the phases separated, and the aqueous phase extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were dried ($MgSO_4$) and concentrated and the residue was flash chromatographed with EtOAc/hexane (1/1) as the initial eluant. During elution, the percent of EtOAc was increased to 100%. The solvent was evaporated and a colorless solid (**4**) was obtained. Yield: 3.68 g, 80%. Mp 150−152 °C. The solid was recrystallized from MeOH. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.4 (s, 3H), 5.2 (s, 1H), 6.8−7.5 (m, 23H). ^{13}C{^{1}H} NMR (62.5 MHz, $CDCl_3$): δ 23.9, 59.8, 121.0, 121.2, 125.8, 126.0, 127.6, 128.4, 129.2, 135.9, 141.7, 142.4, 153.5, 157.1, 167.7. IR (KBr, cm^{-1}): 1688 (ν_{co}). HRMS: found 498.2163 (major), 499.2257 (minor) (M + H$^+$). $C_{33}H_{28}N_3O_2$ requires 498.2182. Anal. Calcd for $C_{33}H_{27}N_3O_2$: C 79.66, H 5.47, N 8.44. Found: C 79.48, H 5.36, N 8.40.

2(1-Oxypyridin-2-yl)-*N*,*N*,*N*′,*N*′-tetraphenylmalonamide (13). A sample of **3** (0.4 g, 0.8 mmol) in CH_2Cl_2 (5 mL) was combined with *m*-CPBA (0.185 g, 1.07 mmol) and the mixture was refluxed overnight with periodic TLC monitoring of the reaction progress (CH_2Cl_2/MeOH, 99/1). The resulting mixture was quenched (sat. $NaHCO_3$, 3 × 10 mL) and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The organic phase was dried ($MgSO_4$) and concentrated and the residue was purified by flash chromatography with a gradient of MeOH in CH_2Cl_2. The product **13** was isolated as a white solid. Yield: 0.9 g, 88%. Mp 134−136 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.0 (s, 1H), 6.8 (d, J = 7.0 Hz, 4H), 7.2 (m, 4H), 7.2−7.4 (m, 14H), 7.7 (dd, J = 7.0, 2.0 Hz, 1H), 8.0 (d, J = 6.5 Hz, 1H). ^{13}C{^{1}H} (62.5 MHz, $CDCl_3$): δ 52.3, 125.2, 125.5, 126.5, 126.8, 127.4, 128.7, 129.3, 129.4, 130.2, 138.9, 141.9, 142.7, 146.8, 166.7. IR (KBr, cm^{-1}): 1681 (ν_{co}). HRMS: found 500.1949 (M + H$^+$). $C_{32}H_{26}N_3O_3$ requires 500.1974.

2-(6-Methyl-1-oxypyridin-2-yl)-N,N,N′,N′-tetraphenylmalonamide (14). A sample of **4** (0.6 g, 1.2 mmol) in MeOH/CH_2Cl_2 (15 mL/5 mL) was combined with OXONE (0.81 g, 1.32 mmol) and $NaHCO_3$ (0.21 g, 2.5 mmol) and refluxed (12 h). Solvent was evaporated and the residue was treated with CH_2Cl_2/H_2O (50

mL/50 mL). The aqueous phase was separated and extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic phases were dried over $MgSO_4$. The filtered organic phase was evaporated leaving a white solid that was further purified by column chromatography with EtOAc/hexane (1:1) as initial eluant followed by pure EtOAc. The *N*-oxide **14** was isolated as a white solid. Yield: 0.31 g, 50%. Mp 164−166 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.77 (s, 3H), 6.17 (s, 1H), 7.35 (s, 4H), 7.80 (m, 6H), 7.90 (m, 9H), 8.00 (d, J = 7.0 Hz, 2H), 8.12 (d, J = 7.0 Hz, 2H). ^{13}C{^{1}H} (62.5 MHz, DMSO-d_6): δ 17.7, 52.4, 124.3, 124.6, 125.7, 126.7, 128.3, 128.7, 129.2, 130.0, 141.5, 142.7, 145.3, 147.5, 166.28. IR (KBr, cm^{-1}): 1681 (ν_{co}). HRMS: found 514.2130 (M + H$^+$). $C_{33}H_{28}N_3O_3$ requires 514.2131. Solubility: CH_2Cl_2 (v. sol.), MeOH (sol.), EtOAc (sol.), hexane (insol.).

General Oxidation Procedure. A sample of **1** or **2** (1 equiv) was dissolved in CH_2Cl_2 (10 mL) and *m*-chloroperbenzoic acid (0.8−5 equiv) was added with stirring. The mixture was then refluxed overnight. The resulting mixture was quenched with aqueous saturated $NaHCO_3$ solution and the aqueous phase was extracted with CH_2Cl_2. Three spots were typically observed by TLC and the CH_2Cl_2 solution containing the products was chromatographed on silica gel (4 cm × 30 cm) with ethyl acetate as the eluant. Variations in the oxidation and purification procedures led to optimized yields for **5**, **7**, **9**, and **11** from **1** and **6**, **8**, **10**, and **12** from **2**. Details of these procedures are presented in the Supporting Information.

Selected Characterization Data for Oxidation Products: 2-Oxo-*N*,*N*-diphenyl-2-(pyridin-2-yl)acetamide (5). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.10−7.50 (m, 11H), 7.65−7.85 (m, 2H), 8.75 (d,d, J = 4.0, 0.8 Hz, 1H). ^{13}C{^{1}H} NMR (62.5 MHz, $CDCl_3$): δ 123.7, 126.4, 127.3, 128.3, 128.8, 129.5, 129.6, 130.0, 137.5, 140.8, 141.6, 150.2, 151.9, 167.8, 191.0. HRMS: found 303.1099 (M + H$^+$). $C_{19}H_{15}N_2O_2$ requires 303.1134.

2-Oxo-*N*,*N*-diphenyl-2-(6-methylpyridin-2-yl)acetamide (6). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.15 (s, 3H), 6.70−7.30 (m, 13H). ^{13}C{^{1}H} NMR (62.5 MHz, $CDCl_3$): δ 24.2, 120.0, 125.8, 126.6, 127.2, 127.9, 128.8, 128.9, 129.1, 136.8, 140.2, 141.1, 150.6, 158.4, 167.5, 190.8. HRMS: found 317.1264 (M + H$^+$). $C_{20}H_{17}N_2O_2$ requires 317.1290.

2-Hydroxy-*N*,*N*-dphenyl-2-(pyridin-2-yl)acaetamide (7). ^{1}H NMR (250 MHz, $CDCl_3$): δ 4.65 (s, 1H), 5.35 (s, 1H), 6.80 (d, J = 8.6 Hz, 1H), 6.95 (s, 1H), 7.10 (d,d, J = 4.0, 1.1 Hz, 1H), 7.2−7.4 (m, 9H), 7.45 (d,d, J = 7.8, 1.8 Hz, 1H), 8.50 (m, J = 4.8, J = 2.6, 1.8, J = 0.9 Hz, 1H). ^{13}C{^{1}H} NMR (62.5 MHz, $CDCl_3$): δ 73.3, 122.9, 123.3, 128.4, 128.6, 129.4, 137.0, 150.0, 158.0, 172.6. HRMS: found 305.1292 (M + H$^+$). $C_{19}H_{17}N_2O_2$ requires 305.1290.

2-Hydroxy-*N*,*N*-diphenyl-2-(6-methylpyridin-2-yl)acetamide (8). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.50 (s, 3H), 5.40 (s, 1H), 6.75 (d, J = 7.7 Hz, 1H), 7.00 (d, J = 7.7 Hz, 1H), 7.10−7.35 (m, 10H), 7.4 (d, d, J = 7.7 Hz, 1H), ^{13}C{^{1}H} NMR (62.5 MHz, $CDCl_3$): δ 24.2, 73.0, 119.1, 122.4, 127.6−130.1, 136.8, 157.2, 158.0, 172.5. HRMS: found 319.1446 [M + H$^+$]. $C_{20}H_{19}N_2O_2$ requires 319.1447.

2-(1-Oxy-pyridin-2-yl)-*N*,*N*-diphenylacetamide (9). ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.80 (s, 2H), 7.15−7.50 (m, 13H), 8.25 (d, d, J = 7.5, 4.2 Hz, 1H). ^{13}C{^{1}H} NMR (62.5 MHz, $CDCl_3$): δ 37.9, 124.2, 125.0, 126.1, 127.3, 127.7, 128.4, 129.4, 138.8, 142.4, 147.0, 167.7. HRMS: found 305.1291 (M + H$^+$). $C_{19}H_{17}N_2O_2$ requires 305.1290.

2-(6-Methyl-1-oxypyridin-2-yl)-*N*,*N*-diphenylacetamide (10). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.50 (s, 3H), 3.80 (s, 2H), 6.80−7.60 (m, 13H). ^{13}C{^{1}H} NMR (62.5 MHz, $CDCl_3$): δ 18.0, 38.6, 124.2, 124.7, 125.0, 126.7−129.5, 142.6, 146.8, 148.6, 168.1. HRMS: found 319.1443 (M + H$^+$). $C_{20}H_{19}N_2O_2$ requires 319.1447.

2-Hydroxy-2-(1-oxypyridin-2-yl)-*N*,*N*-diphenylacetamide (11). ^{1}H NMR (250 MHz, $CDCl_3$): δ 4.8 (s, 1H), 5.30 (s, 1H), 7.00 (d, J = 5.7 Hz, 1H), 7.05 (t, J = 6.7 Hz, 1H), 7.10 (t, J = 7.2 Hz, 1H), 7.15−7.40 (m, 10 H), 8.12 (d, J = 6.0 Hz, 1H). ^{13}C{^{1}H} NMR (62.5 MHz, DMSO-d_6): δ 67.5, 123.9, 124.7, 125.1, 126.9, 127.5, 128.8, 138.2, 142.9, 150.9, 168.6. HRMS: found 321.1213 (M + H$^+$). $C_{19}H_{17}N_2O_3$ requires 321.1239.

2-Hydroxy-2-(6-methyl-1-oxypyridin-2-yl)-*N*,*N*-diphenylacetamide (12). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.38 (s, 3H), 5.28 (s, 1H), 6.75 (d, J = 7.8 Hz, 1H), 6.85 (t, J = 7.8 Hz, 1H), 7.10 (d, J = 8.0 Hz, 1H), 7.15−7.50 (m, 10H). ^{13}C{^{1}H} NMR (62.5 MHz, $CDCl_3$): δ 17.6, 61.9, 123.5, 124.5, 125.1, 125−130, 148.1, 149.0, 170.0. HRMS: found 335.1389 (M + H$^+$). $C_{20}H_{18}N_2O_3$ requires 335.1396.

Electronic Structure Calculations. The energy change for the gas-phase reaction AH → A$^-$ + H$^+$ provides a measure of the intrinsic acidity of the AH proton. ΔE values, E(A$^-$) + E(H$^+$) − E(AH), were calculated for selected model compounds with the NWChem program,[50] using second-order Möller−Plesset perturbation theory (MP2).[51] Calculations were performed with the correlation consistent aug-cc-pVDZ basis set,[52] including all electrons in the correlation treatment.

Acknowledgment is made to the U.S. Department of Energy (DOE), Chemical Sciences, Geosciences and Biosciences Office, Office of Basic Energy Sciences (Grant DE-FG02-03ER15419) for financial support of this work (R.T.P.) and the DOE, Environmental Management Science Program, Office of Science (73759) (B.P.H.). Calculations were performed with the Molecular Science Computing Facility (MSCF) in the William R. Wiley Environmental Molecular Sciences Laboratory, a national scientific user facility sponsored by the DOE's Office of Biological and Environmental Research. We thank Dr. S.-J. Kim for his initial experimental contributions to this study.

Supporting Information Available: Experimental details for the formation and characterization of **4**−**11**, detailed data from the X-ray crystallographic structure determinations, and crystallographic information (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

JO701408Y

(50) (a) Straatsma, T. P.; Aprà, E.; Windus, T. L.; Bylaska, E. J.; de Jong, W.; Hirata, S.; Valiev, M.; Hackler, M. T.; Pollack, L.; Harrison, R. J.; Dupuis, M.; Smith, D. M. A.; Nieplocha, J.; Tipparaju, V.; Krishnan, M.; Auer, A. A.; Brown, E.; Cisneros, G.; Fann, G. I.; Fruchtl, H.; Garza, J.; Hirao, K.; Kendall, R.; Nichols, J.; Tsemekhman, K.; Wolinski, K.; Anchell, J.; Bernholdt, D.; Borowski, P.; Clark, T.; Clerc, D.; Dachsel, H.; Deegan, M.; Dyall, K.; Elwood, D.; Glendening, E.; Gutowski, M.; Hess, A.; Jaffe, J.; Johnson, B.; Ju, J.; Kobayashi, R.; Kutteh, R.; Lin, Z.; Littlefield, R.; Long, X.; Meng, B.; Nakajima, T.; Niu, S.; Rosing, M.; Sandrone, G.; Stave, M.; Taylor, H.; Thomas, G.; van Lenthe, J.; Wong, A.; Zhang, Z. *NWChem*, A Computational Chemistry Package for Parallel Computers, Version 4.6; Pacific Northwest National Laboratory: Richland, WA, 2004. (b) Kendall, R. A.; Aprà, E.; Bernholdt, D. E.; Bylaska, E. J.; Dupuis, M.; Fann, G. I.; Harrison, R. J.; Ju, J.; Nichols, J. A.; Nieplocha, J.; Straatsma, T. P.; Windus, T. L.; Wong, A. T. *Comput. Phys. Commun.* **2000**, *128*, 260−283.

(51) Moller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618.

(52) (a) Dunning, T. H., Jr. *J. Chem. Phys.* **1989**, *90*, 1007. (b) Kendall, R. A.; Dunning, T. H., Jr.; Harrison, R. J. *J. Chem. Phys.* **1992**, *96*, 6796.