

# A Tunable Route for the Synthesis of Azomethine Imines and $\beta$ -Aminocarbonyl Compounds from Alkenes

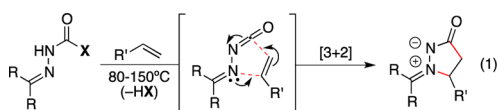
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## Supporting Information

**ABSTRACT:** Cyclic azomethine imines possessing a  $\beta$ -aminocarbonyl motif are accessed from simple alkene and hydrazone starting materials. A thermal, concerted alkene aminocarbonylation pathway involving an imino-isocyanate intermediate is proposed and supported by DFT calculations. A notable feature of the process is the steric shielding present in the dipoles formed, which allows for facile purification of the products by chromatography or crystallization. In addition, a fluorenone-derived reagent is reported, which provides reactivity with several alkene classes and allows for mild derivatization of the dipoles into  $\beta$ -aminoamides,  $\beta$ -aminoesters, and  $\beta$ -amino acids.

$\beta$ -Aminocarbonyl motifs are privileged structures in medicinal chemistry,<sup>1</sup> peptidomimetics,<sup>2</sup> molecular recognition,<sup>3</sup> and natural products.<sup>4</sup> In many pharmaceuticals (e.g.,  $\beta$ -lactam antibiotics) and synthetic peptides (e.g.,  $\beta$ -peptides) this functionality is intimately associated with desired therapeutic properties, for example by allowing enzyme inhibition or leading to improved pharmacokinetic properties.<sup>5</sup> While the importance of this structure has led to many synthetic developments, a general aminocarbonylation route to convert readily available alkenes into  $\beta$ -aminocarbonyl compounds has yet to emerge. Currently, mild but specific intramolecular variants have been developed using transition metal catalysis,<sup>7</sup> and intermolecular variants rely on the use of chlorosulfonyl isocyanate to afford  $\beta$ -lactams.<sup>8</sup> The latter approach is limited by the reactive nature of the reagent, which operates *via* an ionic [2 + 2] mechanism and displays poor functional group compatibility. To address current limitations, we initiated efforts toward novel intermolecular alkene aminocarbonylation reactivity. Herein, we report a straightforward synthesis of azomethine imines possessing  $\beta$ -aminocarbonyl motifs from hydrazones and alkenes (eq 1) and the derivatization of these adducts into  $\beta$ -aminocarbonyl compounds.



In 2009, we reported intramolecular aminocarbonylation reactions using hydrazine derivatives and provided evidence for a

concerted mechanism involving an amino-isocyanate intermediate.<sup>9</sup> To achieve an intermolecular variant, we became interested in the analogous reactivity of imino-isocyanates.<sup>10</sup> While pioneering work from Jones showed that C–C  $\pi$ -bonds provide the desired  $\beta$ -aminocarbonyl motif embedded in a cyclic azomethine imine product,<sup>11</sup> the efficiency of this approach or the likelihood of generating imino-isocyanates upon thermolysis of simple hydrazone precursors remained speculative. Thus, we embarked on the evaluation of this reactivity using an excess of a reactive alkene (norbornene) and various hydrazones. Gratifyingly, we observed the formation of the desired product upon thermolysis and therefore systematically surveyed the reactivity profile of several hydrazones (Table 1).

**Table 1. Survey of Leaving Groups for an Aminocarbonylation Reagent<sup>a</sup>**

Entry	X	Yields (%) <sup>b</sup>			
		150 °C	120 °C	100 °C	80 °C
1	Ot-Bu (1a)	99	69	23	7
2	OEt (1b)	99	8	0	0
3	OCH <sub>2</sub> CF <sub>3</sub> (1c)	82	55	30	9
4	OPh (1d)	92	85	84	38
5	SEt (1e)	98	64	46	11
6	SPh (1f)	90	69	60	31
7	N( <i>i</i> -Pr) <sub>2</sub> (1g)	90	69	46	13

<sup>a</sup>Conditions: hydrazone (1 equiv), alkene (10 equiv) in PhCF<sub>3</sub> (0.05 M) heated in a sealed vial (microwave reactor). <sup>b</sup>NMR yield using 1,3,5-trimethoxybenzene as an internal standard.

Selected *bis*-isopropyl hydrazones were evaluated at temperatures ranging from 80 to 150 °C, to probe the effect of the leaving group on imino-isocyanate generation and overall reaction efficiency (Table 1). We were delighted to observe high yields with all hydrazones at 150 °C and that some leaving groups led to encouraging unoptimized reactivity at or below 100 °C. As expected, the use of better oxygen and sulfur leaving groups led to increased yields at lower temperature [entries 2–3 (OEt vs OCH<sub>2</sub>CF<sub>3</sub>) and entries 5–6 (SEt vs SPh)]. In agreement with

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recent work by Booker–Milburn, Lloyd–Jones et al.,<sup>12</sup> we observed that sterically hindered hydrazone leaving group **1g** also led to mild generation of the desired isocyanate and allowed the use of diisopropyl amine as a leaving group. Given their excellent level of reactivity at 150 °C (*Or*-Bu, **1a**, entry 1) and 100 °C (OPh, **1d**, entry 4), these leaving groups were selected for investigating the impact of hydrazone structure (Table 2).

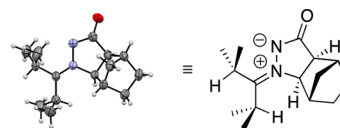
**Table 2. Hydrazone Scope of Aminocarbonylation Reactivity<sup>a</sup>**

Entry	R <sup>1</sup> , R <sup>2</sup>	X	Product	Yield (%) <sup>b</sup>
1	R <sup>1</sup> =H, R <sup>2</sup> =Ph	OPh, <b>2a</b>	R <sup>1</sup> =Ph, R <sup>2</sup> =H, <b>3a</b>	50 <sup>c</sup>
2	R <sup>1</sup> =R <sup>2</sup> =Me	<i>Or</i> -Bu, <b>2b</b>	R <sup>1</sup> =R <sup>2</sup> =Me, <b>3b</b>	70
3	R <sup>1</sup> =R <sup>2</sup> =Et	<i>Or</i> -Bu, <b>2c</b>	R <sup>1</sup> =R <sup>2</sup> =Et, <b>3c</b>	67 <sup>d</sup>
4	R <sup>1</sup> =R <sup>2</sup> =Ph	<i>Or</i> -Bu, <b>2d</b>	R <sup>1</sup> =R <sup>2</sup> =Ph, <b>3d</b>	70
5	"	OPh, <b>2e</b>	"	25 <sup>e</sup>
6		<i>Or</i> -Bu, <b>2f</b>		70
7		<i>Or</i> -Bu, <b>2g</b>		95
8	R <sup>1</sup> =R <sup>2</sup> = <i>i</i> -Pr	<i>Or</i> -Bu, <b>1a</b>		95
9	"	OPh, <b>1d</b>		92
10		OPh, <b>2h</b>		99 <sup>c,f</sup>

<sup>a</sup>Conditions: hydrazone (1 equiv), alkene (10 equiv) in PhCF<sub>3</sub> (0.05 M) heated in a sealed vial (microwave reactor, 150 °C, 3 h). <sup>b</sup>Isolated yield. <sup>c</sup>Reaction at 120 °C. <sup>d</sup>15 equiv of C<sub>7</sub>H<sub>10</sub>. <sup>e</sup>Reaction at 100 °C. <sup>f</sup>Solvent-free reaction; 2 equiv of C<sub>7</sub>H<sub>10</sub>.

Subsequently, we tested the reactivity of various hydrazones toward norbornene (Table 2). Smaller hydrazone reagents (**2a–2d**) provided the norbornene-derived azomethine imines in good yields, but complete consumption of starting material suggested the presence of competing side reactions.<sup>13</sup> Thus, we explored more hindered reagents and were pleased that hydrazones derived from adamantanone, diisopropyl ketone, and fluorenone (Table 2, entries 7–10) resulted in excellent yields of the aminocarbonylation products. While all entries were performed in a microwave reactor to allow for somewhat shorter reaction times, several gram-scale reactions were also performed under thermal conditions with excellent efficiency (see Supporting Information for details).

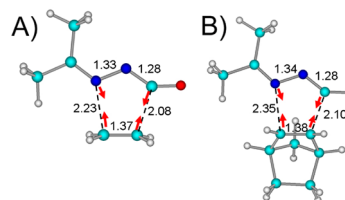
Despite their dipolar nature, these useful<sup>14</sup> azomethine imine products are bench-stable.<sup>15</sup> In addition, the majority of adducts reported herein are crystalline and are readily isolated by chromatography (except **3b** and **3c**). Analysis of the crystal structure of adduct **3g** (Figure 1) suggests that steric shielding is responsible for this stability, and this likely also prevents competing [3 + 2] side reactions that could occur with the excess alkene present under the reaction conditions. Indeed, [3 + 2]-adducts derived



**Figure 1.** X-ray crystal structure of azomethine imine **3g**.

from the least hindered dipoles **3a–3c** are minor byproducts (Table 2, entries 1–3).

After exploring the impact of hydrazone structure on intermolecular aminocarbonylation reactivity, we surveyed the synthetic scope of the reaction with various alkene classes (Table 3). Special emphasis was placed on fluorenone-derived hydrazone **2h**, since it affords dipoles that can be transformed into several  $\beta$ -aminocarbonyl compounds (*vide infra*). Using this versatile reagent,<sup>16</sup> we were pleased to observe that simple terminal alkenes such as 1-hexene and allyltrimethylsilane reacted in good yields (Table 3, entries 1–3). Cyclohexene (entry 4) and several dienes provided the desired adducts in yields ranging from modest to very good, in a trend suggesting that conjugated and strained dienes are more reactive (entries 5–8). We were also encouraged by the yields obtained for vinylarenes (entries 9–11) and related cyclic derivatives (entries 12–13). In contrast, electron-rich alkenes such as vinylferrocene, enamine **5m**, and vinyl ethers proved to be more reactive substrates and afforded cycloadducts at 80 °C (entries 14–25). Using hindered diisopropyl hydrazone **1d** (X = OPh), vinyl pyrrolidinone (entry 16) as well as linear and cyclic vinyl ethers (entries 17–25) provided the corresponding adducts efficiently, and slightly lower yields were observed with hydrazone **2h**. As previously, the identity of the azomethine imines formed using electron-rich alkenes was secured through X-ray crystallography of dihydrofuran cycloadduct **5w** (see Supporting Information for details). Finally, an important trend present in Table 3 is the high Markovnikov regioselectivity observed with all substrates. To obtain additional insight on the mechanism of this transformation, DFT calculations at the B3LYP/TZVP level<sup>17</sup> were performed to probe the pathway involving an imino-isocyanate presented in eq 1.



**Figure 2.** Transition state structure for the intermolecular aminocarbonylation of ethylene (A) and norbornene (B) using dimethyl imino-isocyanate. Relevant bond distances (Å) are shown. Red arrows indicate the atomic movements which correspond to the imaginary normal mode.

The potential energy surface has been calculated for the reaction of norbornene (see Figure S2, Supporting Information). Figure 2 presents the transition state structure determined for the reaction between dimethyl imino-isocyanate and both ethylene and norbornene. Gibbs free energies of activation ( $\Delta G^\ddagger_{298K}$ ) for concerted processes in the gas phase were calculated to be 36.1 and 35.5 kcal/mol for C<sub>2</sub>H<sub>4</sub> and C<sub>7</sub>H<sub>10</sub> respectively, which is consistent with a reaction requiring heat to proceed. These barriers remain fairly unchanged when concerted aminocarbonylation occurs in solvent ( $\Delta G^\ddagger_{298K}$  is 36.3 kcal/mol for the reaction with C<sub>7</sub>H<sub>10</sub> in MeOH). The asynchronous transition

Table 3. Alkene Scope of Aminocarbonylation Reactivity

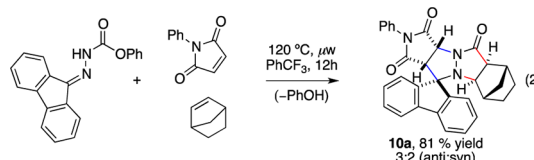
$  \begin{array}{c}  \text{R}=\text{i-Pr (1d)} \\  \text{R}=\text{Ph (2e)} \\  \text{R,R}=\text{Fluorenone (2h)}  \end{array}  $					$  \begin{array}{c}  \text{R}^1 \\  \text{R}^2 \\  \text{4a-q} \\  \xrightarrow[\text{(-HOPh)}]{\mu\text{w, PhCF}_3, 3-6 \text{ h}}  \end{array}  $				
Entry <sup>a</sup>	Alkene	Hydrazone	Product	Yield (%) <sup>b</sup>	Entry <sup>f</sup>	Alkene <sup>g</sup>	Hydrazone	Product	Yield (%) <sup>b</sup>
1	R <sup>1</sup> =(CH <sub>2</sub> ) <sub>3</sub> CH <sub>3</sub> , <b>4a</b>	<b>2h</b>	R <sup>1</sup> =(CH <sub>2</sub> ) <sub>3</sub> CH <sub>3</sub> , <b>5a</b>	73	14		<b>2h</b>		93
2	R <sup>1</sup> =CH <sub>2</sub> TMS, <b>4b</b>	<b>2h</b>	R <sup>1</sup> =CH <sub>2</sub> TMS, <b>5b</b>	81	15		<b>2h</b>		40
3	R <sup>1</sup> =(CH <sub>2</sub> ) <sub>2</sub> OBn, <b>4c</b>	<b>2h</b>	R <sup>1</sup> =(CH <sub>2</sub> ) <sub>2</sub> OBn, <b>5c</b>	52	16		<b>1d</b>		77
4		<b>2h</b>		49 <sup>e</sup>					
5		<b>2h</b>		52 <sup>c</sup>	17	R <sup>4</sup> = <i>n</i> -Bu, <b>4n</b>	<b>2h</b>	R <sup>4</sup> = <i>n</i> -Bu, <b>5q</b>	75
6		<b>1d</b>		60 <sup>c,d</sup>	18	R <sup>4</sup> =Cy, <b>4o</b>	<b>2h</b>	R <sup>4</sup> =Cy, <b>5r</b>	68
7		<b>2h</b>		86	19	R <sup>4</sup> = <i>n</i> -Bu, <b>4n</b>	<b>1d</b>	R <sup>4</sup> = <i>n</i> -Bu, <b>5s</b>	75
8		<b>1d</b>		78 <sup>d</sup>	20	R <sup>4</sup> =Cy, <b>4o</b>	<b>1d</b>	R <sup>4</sup> =Cy, <b>5t</b>	87
9		<b>2h</b>		64	21		<b>2h</b>		57
10	R <sup>3</sup> =F, <b>4h</b>	<b>2h</b>	R <sup>3</sup> =F, <b>5j</b>	54	22	"	<b>1d</b>		99
11	R <sup>3</sup> =OMe, <b>4i</b>	<b>2h</b>	R <sup>3</sup> =OMe, <b>5k</b>	74	23	"	<b>2e</b>		75
12		<b>2h</b>		41 <sup>c</sup>	24		<b>2h</b>		77
13		<b>2h</b>		51 <sup>c</sup>	25	"	<b>1d</b>		70

<sup>a</sup>Conditions: hydrazone (1.0 equiv.), alkene (10 equiv.), heated in a sealed vial (80–150 °C, see SI) in PhCF<sub>3</sub> at 0.05 M. <sup>b</sup>Isolated yield. <sup>c</sup>Isolated as a mixture of regioisomers [14:1 (**5e**), 7:1 (**5f**), 6:1 (**5l**), 3:2 (**5m**)]. <sup>d</sup>Solvent-free reaction. <sup>e</sup>Cyclohexene as solvent. <sup>f</sup>Conditions: hydrazone (1.0 equiv.), alkene (1.0 to 12 equiv.), heated in a sealed vial (80–100 °C; see SI). <sup>g</sup>Using 2 equiv of alkene with reagent **2h** and 10 equiv with **1d** and **2e**, except for **5n** (1), **5o** (5), and **5p** (12).

state is also in line with the high Markovnikov selectivity observed experimentally. Overall, these results support the pathway presented in eq 1, and efforts are ongoing to secure conclusive experimental evidence.

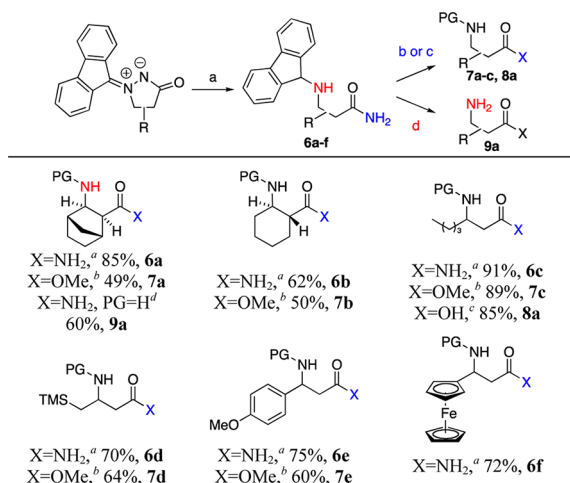
Subsequent efforts focused on the derivatization of the azomethine imine adducts derived from hydrazone **2h** into several β-aminocarbonyl compounds (Scheme 1). Reagent **2h** was developed to allow subsequent N–N bond cleavage under mild reducing and basic conditions, in an analogy to the Fmoc protecting group.<sup>18</sup> Gratifyingly, we observed that various aminocarbonylation products provided fluorenyl-protected<sup>19</sup> β-aminoamides upon treatment with KBH<sub>4</sub> and Raney Nickel in MeOH.<sup>20</sup> β-Aminoesters and β-amino acids could also be obtained from the β-aminoamides using literature procedures.<sup>21</sup> The fluorenyl protecting group could also be removed under standard conditions.<sup>19</sup> Overall, these derivatization procedures establish that hydrazone **2h** provides access to several types of β-aminocarbonyl compounds from simple alkenes. Finally,

exploratory studies building on the [3 + 2] reactivity of closely related azomethine imines<sup>22</sup> suggest the reactivity described herein holds potential for multicomponent reactions (eq 2).



In summary, we have developed a modular route for the synthesis of valuable azomethine imines from simple alkene and hydrazone starting materials. This reactivity allows the functionalization of alkenes into β-aminocarbonyl motifs, which are embedded in the structure of stable and crystalline cyclic dipole products. The results are consistent with a concerted aminocarbonylation event between an alkene and an in situ

Scheme 1. Derivatization of Azomethine Imines



<sup>a</sup> Conditions:  $\text{KBH}_4$ ,  $\text{Ra-Ni}$ ,  $\text{MeOH}$ ,  $60^\circ\text{C}$ , 3 h. <sup>b</sup>  $\text{SOCl}_2$ ,  $\text{MeOH}$ ,  $60^\circ\text{C}$ , 12 h. <sup>c</sup>  $\text{SOCl}_2$ ,  $\text{MeOH}$ ,  $60^\circ\text{C}$ , 12 h; then 10 M  $\text{NaOH}$ , rt. <sup>d</sup>  $\text{DDQ}$ ,  $\text{THF}$ ,  $0^\circ\text{C}$ , 2 h;  $\text{HCl}$  (1 M).

generated imino-isocyanate intermediate. In addition, a simple fluorenone-derived reagent (**2h**) yields azomethine imine adducts that can be converted into  $\beta$ -aminoamides and other derivatives after mild reductive cleavage of the N–N bond. Improvements and applications of this reactivity are under active investigation and will be reported in due course.

## ■ ASSOCIATED CONTENT

### ■ Supporting Information

Complete experimental procedures and characterization, reversibility studies, computational details, X-ray crystal structures, 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.

## ■ ACKNOWLEDGMENTS

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## ■ REFERENCES

- (1) For a review, see: Kuhl, A.; Hahn, M. G.; Dumic, M.; Mittendorf, J. *Amino Acids* **2005**, 29, 89.
- (2) For selected reviews, see: (a) Steer, D. L.; Lew, R. A.; Perlmutter, P.; Smith, A. I.; Aguilar, M.-I. *Curr. Med. Chem.* **2002**, 9, 811. (b) Seebach, D.; Gardiner, J. *Acc. Chem. Res.* **2008**, 41, 1366.
- (3) Disney, M. D.; Hook, D. F.; Namoto, K.; Seeberger, P. H.; Seebach, D. *Chem. Biodiversity* **2005**, 2, 1624.
- (4) Review: Lelais, G.; Seebach, D. *Biopolymers* **2004**, 76, 206.

(5) For selected reviews, see: (a) Cheng, R. P.; Gellman, S. H.; DeGrado, W. F. *Chem. Rev.* **2001**, 101, 3219. (b) Horne, W. S.; Gellman, S. H. *Acc. Chem. Res.* **2008**, 41, 1399.

(6) Selected reviews: (a) Juaristi, E.; Soloshonok, V. A. *Enantioselective Synthesis of  $\beta$ -Amino Acids*, 2nd ed.; Wiley: New York, 2005. (b) Cardillo, G.; Tomasini, C. *Chem. Soc. Rev.* **1996**, 117.

(7) (a) Hegedus, L. S.; Allen, G. F.; Olsen, D. J. *J. Am. Chem. Soc.* **1980**, 102, 3583. (b) Hegedus, L. S.; McKearin, J. M. *J. Am. Chem. Soc.* **1982**, 104, 2444. (c) Tamura, Y.; Hojo, M.; Higashimura, H.; Yoshida, Z. *J. Am. Chem. Soc.* **1988**, 110, 3994. (d) Cernak, T. A.; Lambert, T. H. *J. Am. Chem. Soc.* **2009**, 131, 3124. (e) Ambrosini, L. M.; Cernak, T. A.; Lambert, T. H. *Synthesis* **2010**, 870. (f) Ambrosini, L. M.; Cernak, T. A.; Lambert, T. H. *Tetrahedron* **2010**, 66, 4882. (g) For a review, see: Beccalli, E. D.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Chem. Rev.* **2007**, 107, 5318.

(8) For reviews, see: (a) Rasmussen, J. K.; Hassner, A. *Chem. Rev.* **1976**, 76, 389. (b) Dhar, D. N.; Murthy, K. S. K. *Synthesis* **1986**, 437. (c) Furman, B.; Borsuk, K.; Kaluza, Z.; Lysek, R.; Chmielewski, M. *Curr. Org. Chem.* **2004**, 8, 463.

(9) (a) Roveda, J.-G.; Clavette, C.; Hunt, A. D.; Gorelsky, S. I.; Whipp, C. J.; Beauchemin, A. M. *J. Am. Chem. Soc.* **2009**, 131, 8740. (b) For a seminal review, see: Reichen, W. *Chem. Rev.* **1978**, 78, 569.

(10) For a recent review, see: Wentrup, C.; Finnerty, J. J.; Koch, R. *Curr. Org. Chem.* **2011**, 15, 1745.

(11) Jones, D. W. *J. Chem. Soc., Chem. Commun.* **1982**, 766.

(12) Hutchby, M.; Houlden, C. E.; Ford, J. G.; Tyler, S. N. G.; Gagné, M. R.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *Angew. Chem., Int. Ed.* **2009**, 48, 8721.

(13) In addition to a competing [3 + 2] with  $\text{C}_7\text{H}_{10}$ , a plausible decomposition pathway involves dimerization of the imino-isocyanate intermediate: for related reactivity, see: Lockley, W. J. S.; Ramakrishnan, V. T.; Lwowski, W. *Tetrahedron Lett.* **1974**, 2621.

(14) Recent examples: (a) Na, R.; Jing, C.; Xu, Q.; Jiang, H.; Wu, X.; Shi, J.; Zhong, J.; Wang, M.; Benitez, D.; Tkatchouk, E.; Goddard, W. A., III; Guo, H.; Kwon, O. *J. Am. Chem. Soc.* **2011**, 133, 13337 (and cited references). (b) Hashimoto, T.; Kimura, H.; Kawamata, Y.; Maruoka, K. *Nat. Chem.* **2011**, 3, 642. (c) Shintani, R.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, 125, 10778. (d) Suárez, A.; Downey, C. W.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, 127, 11244. (e) Shintani, R.; Hayashi, T. *J. Am. Chem. Soc.* **2006**, 128, 6330. (f) Chen, W.; Yuan, X.-H.; Li, R.; Du, W.; Wu, Y.; Ding, L.-S.; Chen, Y.-C. *Adv. Synth. Catal.* **2006**, 348, 1818. (g) Chan, A.; Scheidt, K. A. *J. Am. Chem. Soc.* **2007**, 129, 5334. (h) Shapiro, N. D.; Shi, Y.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, 131, 11654.

(15) For reviews, see: (a) Struckwisch, C. G. *Synthesis* **1973**, 469. (b) Rodina, L. L.; Kolberg, A.; Schulze, B. *Heterocycles* **1998**, 49, 587. (c) Schantl, J. G. In *Science of Synthesis*; Padwa, A., Bellus, D., Eds.; Thieme Verlag: Stuttgart, 2004; Vol. 27, pp 731–824.

(16) Preliminary investigations with reagents **1a** and **1d** showed reduced aminocarbonylation reactivity in comparison with reagent **2h**. Typically the use of solvent-free conditions and excess alkene with reagents **1a** and **1d** provides higher yields of the azomethine imines.

(17) (a) Becke, A. D. *J. Chem. Phys.* **1993**, 98, 5648. (b) Lee, C. T.; Yang, W. T.; Parr, R. G. *Phys. Rev. B* **1988**, 37, 785. (c) Schafer, A.; Huber, C.; Ahlrichs, R. *J. Chem. Phys.* **1994**, 100, 5829.

(18) For related reactivity, see: Magnus, P.; Garizi, N.; Seibert, K. A.; Ornhold, A. *Org. Lett.* **2009**, 11, 5646.

(19) Takamura, M.; Hamashima, Y.; Usuda, H.; Kanai, M.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2000**, 39, 1650.

(20) Alexakis, A.; Lensen, N.; Mangeney, P. *Synlett* **1991**, 625.

(21) Li, L.-C.; Ren, J.; Liao, T.-G.; Jiang, J.-X.; Zhu, H.-J. *Eur. J. Org. Chem.* **2007**, 1026.

(22) (a) Dorn, H.; Otto, A. *Chem. Ber.* **1968**, 101, 3287. (b) Pezdirc, L.; Glošelj, U.; Meden, A.; Stanovnik, B.; Svete, J. *J. Heterocycl. Chem.* **2008**, 45, 181.