# Multilevel Selectivity in the Mild and High-Yielding Chlorosilane-Induced Cleavage of Carbamates to Isocyanates

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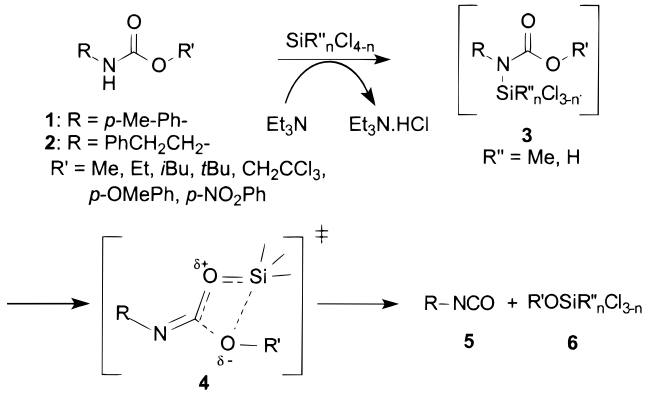
The silane-induced cleavage of a series of *N*-*p*-tolylcarbamates and *N*-phenethylcarbamates to isocyanates has been investigated as a function of chlorosilane, carbamate substituent, and reaction conditions. Reaction yields were determined from the isolated ureas, which were formed by trapping the corresponding isocyanates with isobutylamine. Under room-temperature conditions, multilevel selectivity in carbamate activation has been demonstrated. This selectivity together with the generality of the methodology enhances the utility of carbamates as synthetic intermediates and protecting groups. To demonstrate the effectiveness of this selectivity, a series of biscarbamates were selectively monoactivated to isocyanates in excellent yields.

Carbamates that act as useful synthetic intermediates and protecting groups find widespread use in organic synthesis. For example, the *tert*-butoxycarbonyl (*t*-Boc) group is one of the most frequently used amino protecting groups.[1] However, the general manipulation of carbamates is limited in both quantity and scope.[2−5] Mild and high-yielding methods for the cleavage of carbamates, which are both selective and general in scope, would represent a set of novel and useful transformations in organic synthesis.[4,6,7] The chlorosilane-induced cleavage of carbamates to isocyanates has previously been shown to proceed under relatively mild conditions.[8−11] Herein, we report a systematic study of the reactivity of a series of substrates with various chlorosilanes under mild reaction conditions. This study uses the dependence of the ease of cleavage on the reagents and substrates to effect selective carbamate cleavage. Thus, we demonstrate for the first time, multi-level selectivity in the cleavage of a range of carbamates under the mildest conditions yet reported.

The methodology involves the treatment of a carbamate with a chlorosilane in the presence of triethylamine to produce an isocyanate **5** and an alkoxysilane **6** (Scheme 1). The reaction is thought to proceed by formation of the *N*-silylated species **3**, which was previously isolated.[9] Although silane-induced carbamate cleavage is known, the full scope and utility of the reaction were never explored in depth.[12]

**Scheme 1**




The substrates investigated were the *N*-arylcarbamates **1** (R = *p*-MePh−) and the *N*-alkylcarbamates **2** (R = $PhCH_2CH_2$−), which sterically and electronically alter R′. Cleavage was initiated by adding 1.2 equiv of triethylamine and one of four chlorosilanes (trichlorosilane, methyltrichlorosilane, dichlorodimethylsilane, or chlorotrimethylsilane) to a solution of the substrate in benzene. Three sets of reaction conditions were examined: 70 °C for 4 h, 70 °C for 24 h, and room temperature for 24 h. The reaction progress was determined for each carbamate using a combination of GC−MS,[13] $^1$H NMR spectroscopy,[14] and isolation of a urea derivative of the isocyanate.[15] The degree of cleavage was easily followed due to the absence of any side reactions. Representative selections of our results for the cleavage of the *N*-*p*-tolylcarbamates **1** and *N*-phenethylcarbamates **2** are shown in Table 1.

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**Table 1. Yields[a] (%) for Silane-Induced Cleavage of *N*-*p*-Tolylcarbamates 1 and *N*-Phenethylcarbamates 2 under Various Silane and Reaction Conditions**

| | | $HSiCl_3$ | | | $MeSiCl_3$ | | | $Me_2SiCl_2$ | | | $Me_3SiCl$ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| entry | R | 70/4 | 70/24 | rt/24 | 70/4 | 70/24 | rt/24 | 70/4 | 70/24 | rt/24 | 70/4 | 70/24 | rt/24 |
| **1a** | Me | 95 | 91 | 86 | ± | 100 | 71[b] | ± | 90 | 6[b] | 0[b] | 0[b] | − |
| **1e** | *t*-Bu | ± | 90 | 20[b] | − | − | 0[b] | − | − | − | − | − | − |
| **1g** | $CH_2CCl_3$ | 85 | 88 | 72[b,d] | ± | 91 | 0[b] | 4[b] | ± | − | 0[b] | 8[b] | − |
| **1h**[c] | *p*-OMePh | 96 | 85 | 89 | 85[b] | 100 | 90[b] | 51[b] | 89[b] | 26[b] | 37[b] | 68[b] | 7[b] |
| **1j**[c] | *p*-$NO_2$Ph | 88 | 81 | 78 | 99 | 99 | 100 | 97 | 97 | 99 | 97 | 97 | 98 |
| **2b** | Et | 99 | 86 | ± | ± | 99 | − | ± | 81 | − | − | − | − |
| **2d** | *i*-Bu | 88 | 84 | 88 | ± | 97 | 5[b] | ± | ± | − | − | − | − |
| **2e** | *t*-Bu | ± | 94 | 60[b] | − | − | − | − | − | − | − | − | − |
| **2g** | $CH_2CCl_3$ | 92 | 87 | ± | − | ± | − | − | 0[b] | − | − | − | − |
| **2j**[c] | *p*-$NO_2$Ph | 97 | 85 | 96 | 100 | 98 | 99 | 99 | 97 | 100 | 86[b] | 88[b] | 97 |

[a] Yields reported are isolated yields of the urea derivatives. Otherwise, they are $^1$H NMR-determined yields. [b] $^1$H NMR-determined yields. [c] The isolated yields reported for this carbamate were obtained only when $^1$H NMR showed complete conversion to the isocyanate. Otherwise, NMR-determined yields are reported. [d] Isolated yield was 71%. −: Yield estimated by GC−MS <20%. ±: yield estimated by GC−MS was between 20 and 80%. 70/4: 70 °C for 4 h. 70/24: 70 °C for 24 h. rt/24: room temperature for 24 h.

The reactivity of the silane was found to decrease with increasing methyl substitution and decreasing Cl substitution at the silicon atom. This finding is consistent with previous observations that trichlorosilane-induced cleavage occurs at temperatures lower than those observed with chlorotrimethylsilane.[9,10] Mironov and coworkers have proposed that the increasing Cl substitution introduces competing p→d $\pi$ interactions, which leads to a weakening of the N−Si bond, thereby lowering the thermal stability of intermediate **3**.[8b]

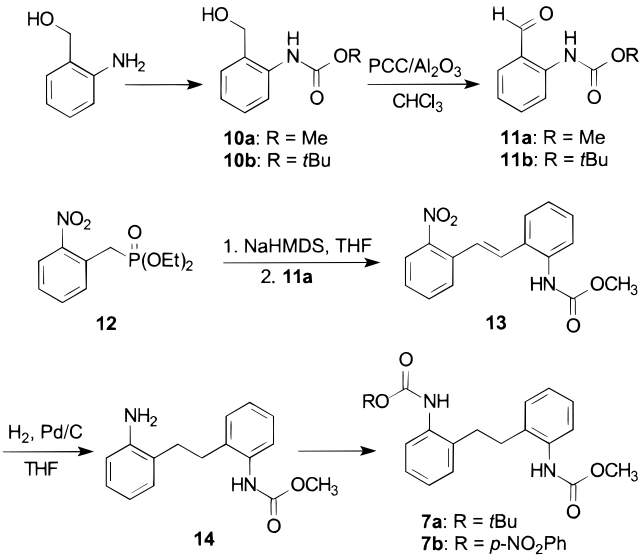
Cleavage of the alkyl carbamates was found to be strongly affected by the steric properties of the alkyl substituent, R′. This conclusion is based on the observed reactivity pattern: Me ≈ Et > *i*-Bu > $CH_2CCl_3$ > *t*-Bu. Increasing the steric bulk of R′ presumably destabilizes the proposed transition state **4**[9d] due to increased nonbonding interactions between R′ and the Si ligands.

Comparison of the reactivities of the aryl carbamates allowed for the assessment of the effect of the electronic character of the substituent. The rate of carbamate cleavage increases with the stability of the aryl oxide anion; the *p*-nitrophenyl carbamate is more reactive than the *p*-methoxyphenyl carbamate. It is clear that the electron-withdrawing nature of the substituent on the phenyl moiety assists in the cleavage, presumably by stabilizing the partial negative charge that develops at the neighboring oxygen atom in the transition state **4**. This observation has been reported with the chlorotrimethylsilane-assisted cleavage,[9] and our studies found it to be general for the chlorosilanes. Of particular note are the *p*-nitrophenyl carbamates, which were activated to the isocyanates under all of our reaction conditions and represent an easily cleaved isocyanate-masking group that is stable during chromatographic purification.

Our data show that, under mild conditions, selective carbamate cleavage can be achieved by choosing the appropriate silane for the substituents R′. This selectivity has been demonstrated on biscarbamates **7a**−**d** (Scheme 4), designed using the results in Table 1. The biscarbamates **7a** and **7b** were synthesized by Horner−Wadsworth−Emmons coupling of carbamate aldehyde **11a** with *o*-nitrobenzylphosphonate **12**, simultaneous hydrogenation of the styrene double bond and the nitro group to result in **13**, and carbamoylation of **14** to **7a** and **7b** (Scheme 2).

The anion of the *o*-nitrobenzylphosphonate **12** proved too nucleophilic for the *p*-methoxyphenyl carbamate to survive the reaction conditions and so the Boc protecting

**Scheme 2**

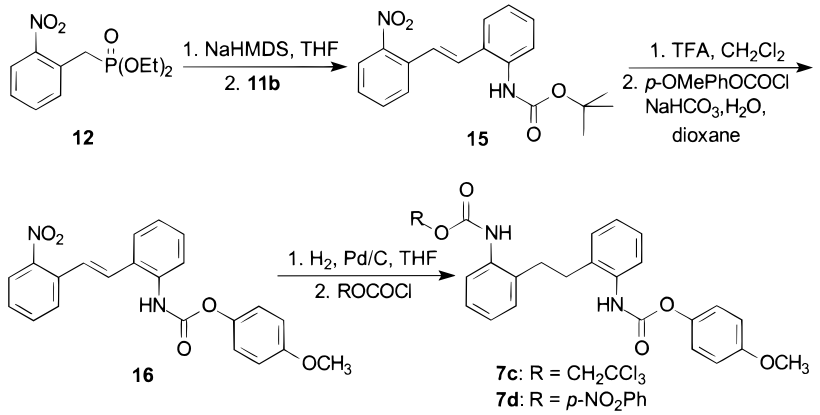



group was used during the Horner−Wadsworth−Emmons coupling in the synthesis of **7c** and **7d** (Scheme 3). Aldehyde **11b** was coupled with the *o*-nitrobenzylphosphonate **12** to yield the *o*-nitrostyrene **15**. The Boc group in **15** was removed with TFA in methylene chloride, and the resulting free amine was carbamoylated to yield **16**. The *o*-nitrostyrene **16** was hydrogenated, and the resulting bibenzylamine was carbamoylated to yield **7c** and **7d**.

The biscarbamates **7a**−**d** were selectively transformed to the monoisocyanates **8a**−**d** (Scheme 4, Table 2). The internal selectivities in each case were determined by the isolation of ureas **9a**−**d**. Due to the tendency of some aryl carbamates to undergo aminolysis to produce ureas, the consumption of substrates **7b**−**d** was monitored by $^1$H NMR during the course of the reaction. The presence of the isocyanates in the reaction mixture was subsequently verified by IR spectroscopy.

Selective carbamate cleavages (Table 2) have been effected in excellent yields at room temperature. In biscarbamate **7a**, the methyl carbamate was selectively activated in the presence of the *tert*-butyl carbamate (Scheme 5). Correspondingly, the *p*-nitrophenyl carbamate in **7b** was selectively cleaved over the methyl carbamate using chlorotrimethylsilane to give **9b** in 98% yield. The selective cleavage of the *p*-methoxyphenyl carbamate over the 2,2,2-trichloroethyl carbamate in **7c** was achieved with methyl trichlorosilane and mild heat-

**Scheme 3**




**Scheme 4**

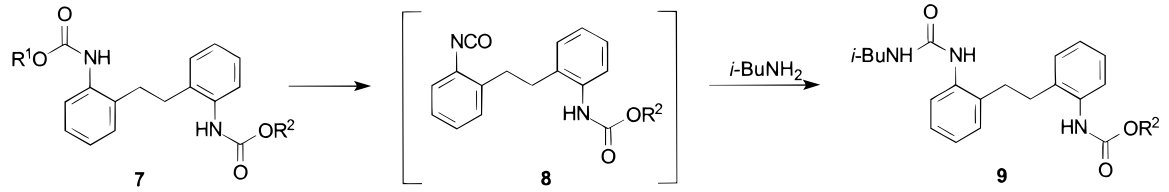



**Table 2. Yields of Urea 9 for the Internal Selective Cleavage of Biscarbamates 7**

| entry | silane | $R^1$ | $R^2$ | yield of **9** (%) |
|---|---|---|---|---|
| **7a** | $HSiCl_3$ | Me | *t*-Bu | 95[b] |
| **7b**[a] | $Me_2SiCl_2$ | *p*-$NO_2$Ph | Me | 98[c] |
| **7c** | $MeSiCl_3$ | *p*-MeOPh | $CH_2CCl_3$ | 88[d] |
| **7d**[a] | $Me_3SiCl$ | *p*-$NO_2$Ph | *p*-MeOPh | 90[e] |

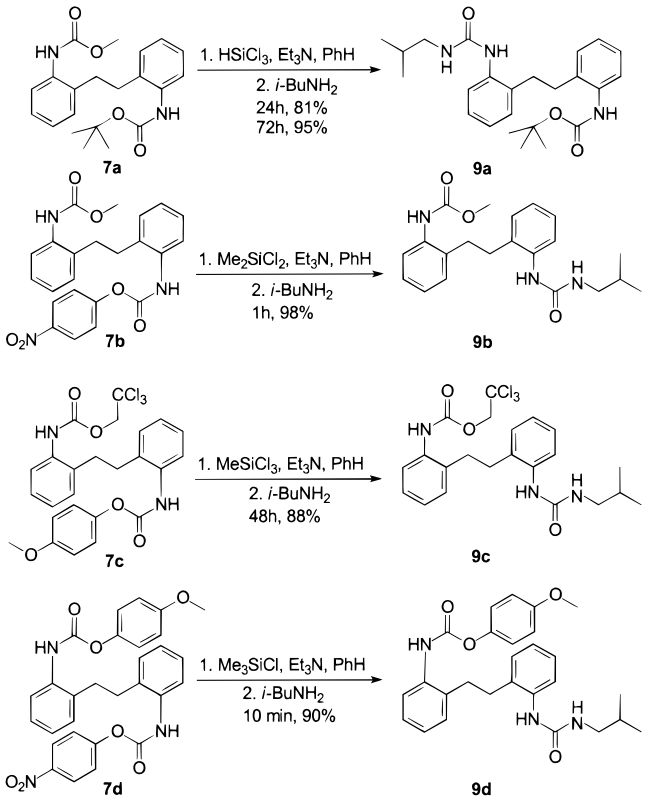
[a] These reactions were determined by $^1H$ NMR to reach completion, and the presence of the isocyanates was verified by IR spectroscopy. [b] Conditions: rt, 72 h. [c] Conditions: rt, 1 h. [d] Conditions: 40 °C, 53 h. [e] Conditions: rt, 10 min.

ing at 40 °C to afford **9c** in 88% yield. The ease of *p*-nitrophenyl carbamate cleavage in the presence of the *p*-methoxyphenyl carbamate was demonstrated by the short reaction time for the monoactivation of biscarbamate **7d**. The reaction of biscarbamates **7b**−**d**, carried out in chloroform,[16] suggests that the solvent has little effect on the selectivity of carbamate cleavage and that the results from our survey can probably be extended to reactions in other solvents.

In addition, these results show two levels of selectivity for the *tert*-butyl, methyl, and *p*-nitrophenyl carbamates (**7a** and **7b**) as well as for the 2,2,2-trichloroethyl, *p*-methoxyphenyl, and *p*-nitrophenyl carbamates (**7c** and **7d**). Therefore, in the presence of these sets of three carbamates, the appropriate chlorosilanes can be used to selectively cleave one carbamate at a time under mild conditions.

It is worth noting an important outcome of the selective cleavage of a sterically less demanding carbamate (e.g., R′ = Me) over a *t*-Boc-protected amine. This methodology, together with well-known methods for cleaving *t*-Boc-protected amines in the presence of alkyl carbamates, makes the two protecting groups orthogonal. Likewise, the 2,2,2-trichloroethyl carbamate, which is useful for the protection of amino groups due to its facile removal,[17,18] can act as a protecting group orthogonal to other less sterically demanding alkyl or aryl carbamates.

**Scheme 5**




In conclusion, we have demonstrated selectivity in the silane-induced cleavage of carbamates under mild conditions. Moreover, we have illustrated the effectiveness of this selectivity in the monoactivation of biscarbamates to the isocyanates, thereby demonstrating proof-of-concept.

(12) The traditional reaction conditions employ chlorotrimethylsilane and high reaction temperatures (>100 °C). See ref 9.

(13) Although accurate quantitative information was not obtained, the GC−MS traces provided us with estimates of the progress of reaction.

## Experimental Section

**General Experimental Methods.** All elemental analyses were performed by the University of Illinois Elemental Analysis Lab. All mass spectrometry data were obtained by the University of Illinois Mass Spectrometry Lab. $CH_2Cl_2$, $Et_3N$, and pyridine were distilled from $CaH_2$ prior to use as reaction solvents. Benzene and THF were distilled from sodium benzophenone ketyl.

Analytical thin-layer chromatography (TLC) was performed using Merck silica gel 60 F254 precoated plates with a fluorescent indicator. Visualization was accomplished by UV illumination and ninhydrin solution. Flash chromatography was performed using silica gel 60 (230−400 mesh) from Merck. 2-(*tert*-Butyloxycarbonyl)aminobenzyl alcohol (**10b**) was prepared according to Liu and Hood's procedure.[19] $PCC/Al_2O_3$ was prepared according to the procedure in *Vogel's Textbook of Practical Organic Chemistry*.[20]

**General Procedure for the Preparation of Carbamates 1a−j and 2a−j.** Carbamates were synthesized by reaction of either *p*-toluidine or phenethylamine with the chloroformate by the following representative procedure, except for the *tert*-butyl carbamates, **1e** and **2e**, which were synthesized by the reaction of the amine with 1.1 equiv of $(t\text{-Boc})_2O$ in $CH_2Cl_2$. All carbamates were characterized by $^1H$ NMR, $^{13}C$ NMR, mass spectrometry, and elemental analyses and, when possible, further verified by comparison with literature-reported values.

**Representative Procedure for the Synthesis of *N*-*p*-Tolylcarbamates.**[21] To a stirring solution of *p*-toluidine (2.1 g, 19.62 mmol) and pyridine (1.7 mL, 21.02 mmol, 1.1 equiv) in $CH_2Cl_2$ (100 mL) was added phenyl chloroformate (2.6 mL, 20.72 mmol, 1.1 equiv) dropwise. The resulting solution was stirred at room temperature for 3 h, washed with water, 5% aqueous HCl and 5% aqueous NaOH, dried ($MgSO_4$), and evaporated under reduced pressure. The residue was crystallized from EtOAc/hexane to afford phenyl *N*-*p*-tolylcarbamate (4.2 g, 94%) as white crystalline needles.

**Methyl *N*-*p*-tolylcarbamate (1a):** mp 94−95 °C (EtOAc/cyclohexane) (lit.[22] mp 96−98 °C). Anal. Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.24; H, 6.76; N, 8.43.

**Ethyl *N*-*p*-tolylcarbamate (1b):** purified by distillation bp 95−98 °C/0.15 mmHg; 49−50 °C; (lit.[19] mp 49−51 °C). Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.02; H, 7.31; N, 7.84.

**Isopropyl *N*-*p*-tolylcarbamate (1c):** purified by distillation bp 97−98 °C/0.11 mmHg; 50−51 °C (lit.[24] mp 51−52 °C). Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.46; H, 7.86; N, 7.27.

**Isobutyl *N*-*p*-tolylcarbamate (1d):** mp 49−51 °C; (lit.[25] 52.5−53 °C). Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.66; H, 8.28; N, 6.79.

***tert*-Butyl *N*-*p*-tolylcarbamate (1e):** mp 89−90 °C (cyclohexane) (lit.[26] mp 88−88.5 °C, lit.[27] mp 91−93 °C). Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.54; H, 8.31; N, 6.77.

**Benzyl *N*-*p*-tolylcarbamate (1f):** mp 79−81 °C (hexane) (lit.[28] mp 81−83 °C). Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.92; H, 6.43; N, 5.85.

**2,2,2-Trichloroethyl-*N*-*p*-tolylcarbamate (1g):** yield 79%; mp 77−78 °C (hexane); $^{13}C$ NMR ($CDCl_3$, 126 MHz) $\delta$ 151.79, 134.63, 134.04, 129.91, 119.22, 95.53, 74.67, 21.00; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 7.30 (br d, 2H, $J$ = 7.8 Hz), 7.14 (br d, 2H, $J$ = 7.9 Hz), 6.83 (br s, 1H), 4.82 (s, 2H), 2.32 (s, 3H); HRMS calcd for $C_{10}H_{10}Cl_3NO_2$ ($M^+$) 280.9777, found 280.9785. Anal. Calcd for $C_{10}H_{10}Cl_3NO_2$: C, 42.51; H, 3.57; N, 4.96. Found: C, 42.68; H, 3.69; N, 4.85.

***p*-Methoxyphenyl *N*-*p*-tolylcarbamate (1h):** yield 90%; mp 158−160 °C (benzene); $^{13}C$ NMR ($CDCl_3$, 101 MHz) $\delta$ 157.29, 144.29, 135.02, 133.52, 129.76, 122.70, 118.94, 114.56, 55.76, 20.95; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 7.32 (br d, 2H, $J$ = 8.0 Hz), 7.10 (*AA*′BB′, 2H, $J_{AA'} = J_{BB'} = 3.0$ Hz, $J_{AB} = J_{A'B'} = 9.0$ Hz, $\nu_A = \nu_{A'} = 3547.9$ Hz, $\nu_B = \nu_{B'} = 3547.9$ Hz), 6.90 (AA′*BB*′, 2H, as above), 6.86 (br s, 1H), 3.80 (s, 3H), 2.32 (s, 3H); HRMS calcd for $C_{15}H_{15}NO_3$ ($M^+$) 257.1052, found 257.1059. Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 70.03; H, 5.82; N, 5.48.

**Phenyl *N*-*p*-tolylcarbamate (1i):** mp 114−115 °C (EtOAc/hexane) (lit.[29] mp 113−114 °C, lit.[30] mp 115 °C). Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.94; H, 5.72; N, 6.18.

***p*-Nitrophenyl *N*-*p*-tolylcarbamate (1j):** yield 76%; mp 139−140 °C (benzene) (lit.[31] mp 135−136 °C); $^{13}C$ NMR ($CDCl_3$, 126 MHz) $\delta$ 155.68, 150.47, 145.18, 134.46, 134.24, 129.97, 125.38, 122.31, 119.34, 20.97; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 8.44 (*AA*′BB′, 2H, $J_{AA'} = J_{BB'} = 3.0$ Hz, $J_{AB} = J_{A'B'} = 9.1$ Hz, $\nu_A = \nu_{A'} = 4125.7$ Hz, $\nu_B = \nu_{B'} = 3681.0$ Hz), 7.37 (AA′*BB*′, 2H, as above), 7.32 (br d, 2H, $J$ = 7.9 Hz), 7.15 (br d, 2H, $J$ = 8.4 Hz), 7.06 (br s, 1H), 2.33 (s, 3H); HRMS calcd for $C_{14}H_{12}N_2O_4$ ($M^+$) 272.0797, found 272.0799. Anal. Calcd for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44; N, 10.29. Found: C, 61.60; H, 4.30; N, 10.24.

**Methyl *N*-phenethylcarbamate (2a):** purified by distillation bp 90−92 °C/0.11 mmHg (lit.[32] bp 94−95 °C/0.3 mmHg). Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 66.63; H, 7.27; N, 7.84.

**Ethyl *N*-phenethylcarbamate (2b):** purified by distillation bp 100−103 °C/0.16 mmHg (lit.[32] bp 100−102 °C/0.15 mmHg); mp 32−34 °C (lit.[32] mp 31−34 °C, lit.[33] mp 33.5 °C, lit.[34] mp 34−35 °C). Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.22; H, 7.79; N, 7.24.

**Isopropyl *N*-phenethylcarbamate (2c):** purified by distillation bp 98−101 °C/0.16 mmHg (lit.[35] bp 115−116 °C/0.6 mmHg). Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.36; H, 8.27; N, 6.80.

**Isobutyl *N*-phenethylcarbamate (2d):** purified by distillation bp 117−120 °C/0.17 mmHg (lit.[36] bp 119−120 °C/0.8 mmHg). Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.30; H, 8.62; N, 6.40.

***tert*-Butyl *N*-phenethylcarbamate (2e):** mp 54−55 °C (hexane) (lit.[37] mp 54−55 °C, lit.[38] mp 55−56 °C). Anal. Calcd

(14) For the cleavage of some of the aryl carbamates, the reaction progress was studied by $^1H$ NMR since the substrates react with isobutylamine.

(15) Isocyanates were derivatized by reaction with isobutylamine.

(16) Reactions of biscarbamates **7b**−**d** were carried out in chloroform due to their poor solubilities in benzene.

(17) The trichloroethoxycarbonyl group is easily removed by reduction with zinc metal in acetic acid or hot ethanol. See refs 1 and 3.

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(19) Liu, J.; Hood, R. H. *J. Heterocyc. Chem.* **1995**, *32*, 523.

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(21) All carbamates were synthesized by reaction of either *p*-toluidine or phenethylamine with the chloroformate by this representative procedure, except for the *tert*-butyl carbamates, which were synthesized by reaction of the amine with 1.1 equiv of $(t\text{-Boc})_2O$.

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for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.28; H, 8.60; N, 6.30.

**Benzyl *N*-phenethylcarbamate (2f):** mp 60−62 °C (EtOAc/cyclohexane); (lit.[37a] mp 56−58 °C). Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.34; H, 6.71; N, 5.50.

**2,2,2-Trichloroethyl *N*-phenethylcarbamate (2 g):** mp 58−59 °C (EtOAc/cyclohexane); $^{13}$C NMR ($CDCl_3$, 101 MHz) $\delta$ 154.58, 138.49, 128.85, 128.70, 126.64, 74.40, 42.50, 35.92; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.35−7.29 (m, 2H), 7.25−7.18 (m, 3H), 4.98 (br s, 1H), 4.72 (s, 2H), 3.50(q, 2H, $J$ = 6.7 Hz), 2.85 (t, 2H, $J$ = 7.0 Hz); HRMS calcd for $C_{10}H_{10}Cl_3NO_2$ ($M^+$) 294.9934, found 294.9937. Anal. Calcd for $C_{11}H_{12}Cl_3NO_2$: C, 44.55; H, 4.08; N, 4.72. Found: C, 44.50; H, 4.04; N, 4.59.

***p*-Methoxyphenyl *N*-phenethylcarbamate (2h):** yield 94%; mp 87−88 °C (hexane); $^{13}$C NMR ($CDCl_3$, 126 MHz) $\delta$ 157.15, 155.19, 144.75, 138.80, 129.03, 128.93, 126.83, 122.66, 114.54, 55.79, 42.55, 36.13; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.36−7.21 (m, 5H), 7.01 (*AA*′BB′, 2H, $J_{AA'} = J_{BB'} = 3.0$ Hz, $J_{AB} = J_{A'B'} = 8.9$ Hz, $\nu_A = \nu_{A'} = 3505.2$ Hz, $\nu_B = \nu_{B'} = 3428.4$ Hz), 6.86 (AA′*BB*′, 2H, as above), 4.98 (br s, 1H), 3.79 (s, 3H), 3.53 (q, 2H, $J$ = 6.6 Hz), 2.89 (t, 2H, $J$ = 6.8 Hz); HRMS calcd for $C_{16}H_{17}NO_3$ ($M^+$) 271.1208, found 271.1202). Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.77; H, 6.08; N, 5.14.

**Phenyl *N*-phenethylcarbamate (2i):** mp 90−91 °C (EtOAc/cyclohexane) (lit.[39] mp 89−90 °C). Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.56; H, 6.18; N, 5.80.

***p*-Nitrophenyl *N*-phenethylcarbamate (2j):** yield 90%; mp 106−107 °C (benzene); $^{13}$C NMR ($CDCl_3$, 126 MHz) $\delta$ 156.11, 153.25, 144.91, 138.38, 128.99, 128.98, 127.00, 125.30, 122.14, 42.59, 35.95. $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 8.23 (*AA*′BB′, 2H, $J_{AA'} = J_{BB'} = 3.0$ Hz, $J_{AB} = J_{A'B'} = 9.2$ Hz, $\nu_A = \nu_{A'} = 4112.2$ Hz, $\nu_B = \nu_{B'} = 3638.7$ Hz), 7.37−7.21 (m, 5H), 7.28 (AA′*BB*′, 2H, as above), 5.18 (br s, 1H), 5.57 (q, 2H, $J$ = 6.7 Hz), 2.91 (t, 2H, $J$ = 6.9 Hz); HRMS calcd for $C_{15}H_{14}N_2O_4$ ($M^+$) 286.0954, found 286.0952. Anal. Calcd for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.93; N, 9.79. Found: C, 62.53; H, 4.77; N, 9.68.

**General Procedure for the Silane-Induced Cleavage of Carbamates.** To a solution of the carbamate (approximately 0.5 mmol) in 2 mL of benzene was added 1.2 equiv of $Et_3N$ and 1.2 equiv of the chlorosilane. The reaction was shaken in a sealed vial and subjected to the appropriate reaction conditions. The isocyanate was trapped by addition of 0.2 mL of isobutylamine and the urea purified by flash column chromatography. All ureas were characterized by $^1$H and $^{13}$C NMR. Purity and composition were verified by elemental analyses and mass spectral analyses.

**2-(Methyloxycarbonyl)aminobenzyl Alcohol (10a).** To a stirring solution of 2-aminobenzyl alcohol (4.01 g, 32.5 mmol) in 20 mL of dioxane, 20 mL of saturated $NaHCO_3$ solution, and 8 mL of water at 0 °C was added methyl chloroformate (2.5 mL, 32.4 mmol) dropwise. The resulting mixture was stirred at room temperature for 15 h, and then more methyl chloroformate (0.5 mL, 6.5 mmol) was added dropwise while the reaction mixture was cooled to 0 °C. After being warmed to room temperature, the reaction was diluted with brine and extracted with $CHCl_3$ (4×). The organic layers were pooled, dried ($MgSO_4$), and evaporated under reduced pressure. The residue was chromatographed (1:25 EtOAc/$CHCl_3$) to afford **10a** (5.49 g, 93%) as a light yellow syrup: $^{13}$C NMR ($CDCl_3$, 101 MHz) $\delta$ 154.82, 137.78, 129.37, 129.02, 123.65, 121.14, 64.39, 52.54; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 7.96 (br s, 1H), 7.89 (br d, 1H, $J$ = 7.1 Hz), 7.31 (td, 1H, $J$ = 7.8, 1.6 Hz), 7.14 (dd, 1H, $J$ = 7.6, 1.5 Hz), 7.03 (td, 1H, $J$ = 7.4, 1.1 Hz), 4.66 (d, 2H, $J$ = 5.7 Hz), 3.75 (s, 3H), 2.54 (t, 1H, $J$ = 5.7 Hz); HRMS calcd for $C_9H_{11}NO_3$ ($M^+$) 181.0739, found 181.0737. Anal. Calcd for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.44; H, 6.15; N, 7.57.

**2-(Methyloxycarbonyl)aminobenzaldehyde (11a).** To a solution of methyl carbamate **10a** (5.49 g, 30.3 mmol) in 230 mL of $CHCl_3$ was added PCC/$Al_2O_3$ (45 g). The reaction mixture was stirred at room temperature for 30 min and then filtered through a bed of silica. The filtrate was concentrated under reduced pressure and chromatographed (300:4 $CHCl_3$:EtOH) to give **11a** (3.96 g, 73%) as a white solid: mp 90−92.5 °C; $^{13}$C NMR ($CDCl_3$, 101 MHz) $\delta$ 195.22, 154.19, 141.31, 136.14, 122.06, 121.38, 118.30, 52.54; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 10.60 (br s, 1H), 9.88 (s, 1H), 8.44 (d, 1H, $J$ = 8.7 Hz), 7.60 (m, 2H), 7.15 (td, 1H, $J$ = 7.6, 0.9 Hz), 3.79 (s, 3H); HRMS calcd for $C_9H_9NO_3$ ($M^+$) 179.0582, found 179.0584. Anal. Calcd for $C_9H_9NO_3$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.41; H, 5.05; N, 7.77.[40]

**2-(*tert*-Butyloxycarbonyl)aminobenzaldehyde (11b).** To a solution of 2-(*tert*-butyloxycarbonyl)aminobenzyl alcohol (**10b**) (6.72 g, 30.1 mmol) in 350 mL of $CHCl_3$ was added PCC/$Al_2O_3$ (33 g). The reaction mixture was stirred at room temperature for 30 min, after which time TLC indicated that the reaction was incomplete. More PCC/$Al_2O_3$ (18 g) was added, and the reaction mixture was stirred for another 30 min and then filtered through a bed of silica. The filtrate was concentrated under reduced pressure and chromatographed (300:4 $CHCl_3$/EtOH) to give a yellow oil that was crystallized from hexane to afford **11b** (3.73 g, 56%) as an off-white solid: mp 54.5−56.5 °C; $^{13}$C NMR ($CDCl_3$, 126 MHz) $\delta$ 195.26, 153.08, 141.99, 136.28, 136.15, 121.68, 121.39, 118.41, 81.13, 28.44; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 10.39 (br s, 1H), 9.89 (s, 1H), 8.45 (d, 1H, $J$ = 8.4 Hz), 7.61 (dd, 1H, $J$ = 7.6, 1.5 Hz), 7.56 (m, 1H), 7.12 (m, 1H), 1.53 (s, 9H); HRMS calcd for $C_{12}H_{15}NO_3$ ($M^+$) 221.1052, found 221.1058. Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.16; H, 6.95; N, 6.18.

**(2-Nitrobenzyl)phosphonic Acid Diethyl Ester (12).** A mixture of 1-(bromomethyl)-2-nitrobenzene (5.35 g, 24.8 mmol) and triethyl phosphite (4.7 mL, 27.4 mmol) was heated in a simple distillation apparatus to 110 °C. Ethyl bromide was collected for 40 min and the reaction mixture was maintained at 110 °C for another 1 h. After being cooled to room temperature, the reaction mixture was purified by Kugehlrohr distillation (150 °C/0.25 mmHg) to give **12** (6.55 g, 97%) as a yellow liquid: $^{13}$C NMR ($CDCl_3$, 126 MHz) $\delta$ 149.48 ($C_q$, $J_{CP}$ = 7.0 Hz), 133.31 (CH, $J_{CP}$ = 4.9 Hz), 133.10 (CH, $J_{CP}$ = 2.6 Hz), 128.14 (CH, $J_{CP}$ = 4.0 Hz), 127.39 ($C_q$, $J_{CP}$ = 9.0 Hz), 125.32 (CH, $J_{CP}$ = 3.5 Hz), 62.46 ($CH_2$), 30.57 ($CH_2$, $J_{CP}$ = 137.9 Hz), 16.32 ($CH_3$, $J_{CP}$ = 6.2 Hz); $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.90 (br d, 1H, $J$ = 8.2 Hz), 7.51 (br t, 1H, $J$ = 7.6 Hz), 7.42 (m, 1H, $J$ = 7.8 Hz), 7.37 (m, 1H, $J$ = 7.8 Hz), 3.98 (m, 4H), 3.66 (d, 2H, $J$ = 22.6 Hz), 1.18 (t, 6H, $J$ = 7.0 Hz).[43]

***N*-[(2′-nitrostilben-2-yl)phenyl]methylcarbamate (13).** To a solution of **12** (2.01 g, 7.4 mmol) in 10 mL of THF at 0 °C was added 7.8 mL of a 1 M solution of NaHMDS in THF dropwise. The reaction mixture was stirred at 0 °C for 10 min, **11a** (1.32 g, 7.4 mmol) was then added in one portion, and stirring was continued for another 20 min. The mixture was diluted with 100 mL of $Et_2O$, washed with brine (2×), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed (100:3 $CHCl_3$/EtOH) to yield **13** (1.87 g, 85%) as a yellow solid; $^{13}$C NMR ($CDCl_3$, 101 MHz) $\delta$ 147.95, 135.14, 133.41, 132.94, 129.28, 128.67, 128.61, 128.48, 127.22, 127.03, 125.29, 124.88, 52.69; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.99 (dd, 1H, $J$ = 8.2, 1.1 Hz), 7.73 (dd, 2H, $J$ = 7.9, 0.7 Hz), 7.62 (t, 1H, $J$ = 7.6 Hz), 7.55 (br d, 1H, $J$ = 7.7 Hz), 7.48 (d, 1H, $J$ = 16.2 Hz), 7.44 (td, 1H, $J$ = 7.7, 1.4 Hz), 7.33 (td, 1H, $J$ = 7.7, 1.4 Hz), 7.19 (br t, 1H, $J$ = 7.8 Hz), 7.13 (d, 1H, $J$ = 15.9 Hz), 6.65 (br s, 1H), 3.79 (s, 3H); HRMS calcd for $C_{16}H_{14}N_2O_4$ ($M^+$) 298.0954, found 298.0957. Anal. Calcd for $C_{16}H_{14}N_2O_4$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.35; H, 4.73; N, 9.29.

***N*-(2′-aminobibenzyl-2-yl)methylcarbamate (14).** A solution of **13** in 30 mL of THF was stirred vigorously under hydrogen (65 psi) with 5% Pd/C for 4 h. The catalyst was filtered off, and the filtrate was concentrated under reduced

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pressure to give **14** (1.66 g, 98%) as an off-white residue: mp 85−87 °C; $^{13}$C NMR ($CDCl_3$, 101 MHz) $\delta$ 144.10, 135.68, 129.89, 129.71, 127.58, 127.14, 126.10, 125.01, 119.50, 116.51, 52.47, 32.52, 30.83; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.66 (br s, 1H), 7.23 (m, 2H), 7.13 (dd, 1H, $J$ = 7.4, 1.1 Hz), 7.08 (td, 1H, $J$ = 7.6, 1.5 Hz), 6.98 (dd, 1H, $J$ = 7.6, 1.4 Hz), 6.76 (td, 2H, $J$ = 7.5, 1.1 Hz), 6.70 (d, 1H, $J$ = 7.9, 1.1 Hz), 3.74 (s, 3H), 2.89 (*AA*′BB′, 2H, $\nu_A = \nu_{A'} = 1156.9$ Hz, $\nu_B = \nu_{B'} = 1117.3$ Hz, $J_{AA'} = J_{BB'} = 14.0$ Hz, $J_{AB} = J_{A'B'} = 6.0$ Hz, $J_{AB'} = J_{A'B} = 9.5$ Hz), 3.59 (br s, 2H), 2.79 (AA′*BB*′, 2H, as above); HRMS calcd for $C_{16}H_{18}N_2O_2$ ($M^+$) 270.1368, found 270.1365. Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 70.83; H, 6.77; N, 10.38.

***N*-(2′-(Methylcarbamate)bibenzyl-2-yl)-*tert*-butylcarbamate (7a).** To a stirring solution of **14** (0.64 g, 2.3 mmol) in 6 mL of $CH_2Cl_2$ at room temperature was added ($t$-Boc)$_2$O (0.54 g, 2.5 mmol) in one portion. The resulting mixture was stirred at room temperature overnight and then filtered, evaporated under reduced pressure, and recrystallized (EtOAc/petroleum ether) to yield **7a** (0.71 g, 82%) as a white solid: $^{13}$C NMR ($CDCl_3$, 101 MHz) $\delta$ 155.13, 153.82, 135.80, 135.46, 132.65, 129.80, 129.71, 127.39, 127.29, 125.41, 125.02, 123.66, 80.47, 52.52, 32.19, 31.96, 28.43; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.61 (br d, 2H, $J$ = 7.9 Hz), 7.26−7.17 (m, 3H), 7.16−7.10 (m, 2H), 7.08 (td, 1H, $J$ = 7.4, 1.3 Hz), 6.29 (br s, 1H), 6.08 (br s, 1H), 3.72 (s, 3H), 2.87 (*AA*′BB′, 2H, $\nu_A = \nu_{A'} = 1436.0$ Hz, $\nu_B = \nu_{B'} = 1428.7$ Hz, $J_{AA'} = J_{BB'} = 15.0$ Hz, $J_{AB} = J_{A'B'} = 6.5$ Hz, $J_{AB'} = J_{A'B} = 9.0$ Hz), 2.86 (AA′*BB*′, 2H, as above), 1.48 (s, 9H); HRMS calcd for $C_{21}H_{26}N_2O_4$ ($M^+$) 370.1893, found 370.1887. Anal. Calcd for $C_{21}H_{26}N_2O_4$: C, 68.09; H, 7.07; N, 7.56. Found: C, 67.94; H, 7.10; N, 7.32.

***N*-(2′-(Methylcarbamate)bibenzyl-2-yl)-*p*-nitrophenylcarbamate (7b).** A mixture of **14** (0.64 g, 2.4 mmol), *p*-nitrochloroformate (0.48 g, 2.4 mmol), and 0.20 mL of pyridine in 6.5 mL of $CH_2Cl_2$ was stirred at room temperature overnight. The reaction mixture was diluted with 100 mL of $CHCl_3$, washed with 1% $KHSO_4$ (pH ∼4), dried ($MgSO_4$), and evaporated under reduced pressure. The yellow residue was recrystallized (EtOAc/petroleum ether) to yield **7b** (0.77 g, 74%) as a white solid: mp 157−161 °C; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 8.26 (d, 2H, $J$ = 9.0 Hz), 7.68 (br d, 1H, $J$ = 6.0 Hz), 7.51 (br d, 1H, $J$ = 7.0 Hz), 7.35 (d, 2H, $J$ = 8.5 Hz), 7.30−7.17 (m, 4H), 7.14 (d, 2H, $J$ = 4.4 Hz), 6.91 (br s, 1H), 6.21 (br s, 1H), 3.71 (s, 3H), 3.03 (*AA*′BB′, 2H, $\nu_A = \nu_{A'} = 1514.5$ Hz, $\nu_B = \nu_{B'} = 1479.3$ Hz, $J_{AA'} = J_{BB'} = 16.0$ Hz, $J_{AB} = J_{A'B'} = 6.5$ Hz, $J_{AB'} = J_{A'B} = 7.5$ Hz), 2.96 (AA′*BB*′, 2H, as above); HRFABMS calcd for $C_{23}H_{22}N_3O_6$ ($M + H)^+$ 436.1509, found 436.1509. Anal. Calcd for $C_{23}H_{21}N_3O_6$: C, 63.44; H, 4.86; N, 9.65. Found: C, 63.25; H, 4.88; N, 9.52.[44]

***N*-[(2′-Nitrostilben-2-yl)phenyl]-*tert*-butylcarbamate (15).** To a solution of **12** (2.00 g, 7.3 mmol) in 10 mL of THF at 0 °C was added 7.7 mL of a 1 M solution of NaHMDS in THF dropwise. The reaction was stirred at 0 °C for 10 min, **11b** (1.63 g, 7.4 mmol) was added in one portion, and the reaction mixture was allowed to warm to room temperature overnight. The reaction mixture was diluted with 100 mL of $CHCl_3$, washed with brine (2×), dried ($MgSO_4$), and evaporated under reduced pressure. The yellow residue was recrystallized (EtOAc/petroleum ether) to yield **15** (2.00 g, 80%) as yellow crystals: mp 130−132 °C; $^{13}$C NMR ($CDCl_3$, 126 MHz) $\delta$ 135.78, 133.47, 133.22, 129.41, 129.16, 128.83, 128.56, 127.55, 127.15, 125.04, 124.86, 28.50; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 8.00 (dd, 1H, $J$ = 8.2, 1.2 Hz), 7.76 (d, 2H, $J$ = 7.7 Hz), 7.63 (t, 1H, $J$ = 7.7 Hz), 7.54 (br d, 1H, $J$ = 7.6 Hz), 7.48 (d, 1H, $J$ = 16.1 Hz), 7.45 (td, 1H, $J$ = 7.7, 1.4 Hz), 7.32 (td, 1H, $J$ = 7.8, 1.5 Hz), 7.16 (br t, 1H, $J$ = 7.6 Hz), 7.14 (d, 1H, $J$ = 16.0 Hz), 6.47 (br s, 1H), 1.53 (s, 9H); HRMS calcd for $C_{19}H_{20}N_2O_4$ ($M^+$) 340.1423, found 340.1417. Anal. Calcd for $C_{19}H_{20}N_2O_4$: C, 67.05; H, 5.92; N, 8.23. Found: C, 67.12; H, 5.73; N, 8.01.

***N*-[(2′-Nitrostilben-2-yl)phenyl]-*p*-methoxyphenylcarbamate (16).** A solution of **15** (1.93 g, 5.7 mmol) in 10 mL of $CH_2Cl_2$ and 5 mL of TFA was stirred at room temperature. Stirring was continued for 20 min after $CO_2$ evolution ceased. The reaction mixture was evaporated under reduced pressure to give the corresponding amine as a yellow solid (2.05 g, 5.7 mmol) that was used without further purification.

To a suspension of the above amine in 15 mL of dioxane was added 30 mL of saturated $NaHCO_3$ slowly, and the rapidly stirred reaction mixture was cooled to 0 °C. *p*-Methoxyphenyl chloroformate (0.89 mL, 5.9 mmol) was introduced by dropwise addition to the reaction mixture. After $CO_2$ evolution ceased, stirring was continued at 0 °C for another 30 min. The solution was diluted with water to a final volume of 100 mL. The resultant yellow solid was filtered, washed with water, air-dried, and recrystallized (EtOAc/petroleum ether) to yield **16** as yellow needles (1.69 g, 75%): mp 168−170 °C; $^{13}$C NMR ($CDCl_3$, 101 MHz) $\delta$ 157.38, 148.12, 144.28, 134.85, 133.58, 132.98, 129.55, 128.86, 128.74, 128.52, 128.06, 127.67, 125.06, 122.61, 114.60, 55.79; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.01 (dd, 1H, $J$ = 8.3, 1.2 Hz), 7.87 (br s, 1H), 7.77 (dd, 1H, $J$ = 8.0, 1.0 Hz), 7.64 (td, 1H, $J$ = 7.6, 1.0 Hz), 7.57 (br d, 1H, $J$ = 7.3 Hz), 7.52 (d, 1H, $J$ = 16.0 Hz), 7.46 (td, 1H, $J$ = 7.8, 1.3 Hz), 7.36 (td, 1H, $J$ = 6.7, 1.4 Hz), 7.21 (m, 1H), 7.19 (d, 1H, $J$ = 16.4 Hz), 7.12 (*AA*′BB′, 2H, $\nu_A = \nu_{A'} = 2848.4$ Hz, $\nu_B = \nu_{B'} = 2754.7$ Hz, $J_{AA'} = J_{BB'} = 3.0$ Hz, $J_{AB} = J_{A'B'} = 8.7$ Hz, $J_{AB'} = J_{A'B} = 0$ Hz), 7.00 (br s, 1H), 6.89 (AA′*BB*′, 2H, as above), 3.80(s, 3H); HRFABMS calcd for $C_{22}H_{19}N_2O_5$ ($M + H)^+$ 391.1294, found 391.1294. Anal. Calcd for $C_{22}H_{18}N_2O_5$: C, 67.69; H, 4.65; N, 7.18. Found: C, 67.68; H, 4.66; N, 7.18.

***N*-(2′-(2,2,2-Trichloroethylcarbamate)bibenzyl-2-yl)-*p*-methoxyphenylcarbamate (7c).** A solution of **16** (0.53 g, 1.4 mmol) in 20 mL of THF was stirred vigorously under hydrogen (60 psi) with 5% Pd/C for 1 h. To the solution at atmospheric pressure were added pyridine (0.12 mL, 1.5 mmol) and 2,2,2-trichloroethyl chloroformate (0.20 mL, 1.4 mmol). The reaction mixture was stirred at room temperature for 30 min, and the catalyst was filtered off and washed with 100 mL $CHCl_3$. The filtrate was diluted with 100 mL of $CHCl_3$, washed with 5% aqueous $KHSO_4$ and saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and evaporated under reduced pressure. The white residue was recrystallized (EtOAc/hexane) to yield **7c** (0.62 g, 85%) as a white solid: mp 159.5−164.5 °C; $^{13}$C NMR ($CDCl_3$, 101 MHz) $\delta$ 157.27, 153.01, 144.34, 135.23, 134.60, 130.25, 130.09, 127.75, 127.66, 126.65, 122.64, 114.53, 74.70, 55.80, 32.50; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.72 (br s, 1H), 7.50 (br d, 1H, $J$ = 7.1 Hz), 7.29−7.18 (m, 5H), 7.14 (br t, 1H, $J$ = 7.4 Hz), 7.06 (*AA*′BB′, 2H, $\nu_A = \nu_{A'} = 3529.0$ Hz, $\nu_B = \nu_{B'} = 3437.9$ Hz, $J_{AA'} = J_{BB'} = 2.5$ Hz, $J_{AB} = J_{A'B'} = 9.0$ Hz, $J_{AB'} = J_{A'B} = 0$ Hz), 6.87 (AA′*BB*′, 2H, as above), 6.67 (br s, 1H), 6.37 (br s, 1H), 4.75 (s, 2H), 3.79 (s, 3H), 2.98 (*AA*′BB′, 2H, $\nu_A = \nu_{A'} = 1488.4$ Hz, $\nu_B = \nu_{B'} = 1469.1$ Hz, $J_{AA'} = J_{BB'} = 14.0$ Hz, $J_{AB} = J_{A'B'} = 7.0$ Hz, $J_{AB'} = J_{A'B} = 7.5$ Hz), 2.94 (AA′*BB*′, 2H, as above); HRFABMS calcd for $C_{25}H_{24}Cl_3N_2O_5$ ($M + H)^+$ 537.0751, found 537.0749. Anal. Calcd for $C_{25}H_{23}Cl_3N_2O_5 \cdot ?H_2O$: C, 54.91; H, 4.42; N, 5.12. Found: C, 55.22; H, 4.27; N, 4.94.

***N*-(2′-(*p*-Nitrophenylcarbamate)bibenzyl-2-yl)-*p*-methoxyphenylcarbamate (7d).** A solution of **16** (0.51 g, 1.3 mmol) in 20 mL of THF was stirred vigorously under hydrogen (60 psi) with 5% Pd/C for 1 h. To this solution at atmospheric pressure were added pyridine (0.12 mL, 1.5 mmol) and *p*-nitrophenyl chloroformate (0.28 g, 1.4 mmol). The reaction mixture was stirred at room temperature for 30 min, and the catalyst was filtered off and washed with 100 mL of $CHCl_3$. The filtrate was diluted with 400 mL of $CHCl_3$, washed with 3% aqueous $KHSO_4$ (100 mL) and saturated aqueous $NaHCO_3$ (100 mL), dried ($MgSO_4$), and evaporated under reduced pressure. The white residue was recrystallized (EtOAc/hexane) to yield **7d** (0.61 g, 88%) as a white solid: mp 193−195 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 8.84 (br d, 1H, $J$ = 5.4 Hz), 8.18 (d, 1H, $J$ = 9.0 Hz), 7.63 (br m, 2H), 7.38−7.28 (m, 3H), 7.24−7.14 (m, 4H), 7.01 (*AA*′BB′, 2H, $\nu_A = \nu_{A'} = 2802.1$ Hz, $\nu_B = \nu_{B'} = 2729.0$ Hz, $J_{AA'} = J_{BB'} = 2.5$ Hz, $J_{AB} = J_{A'B'} = 8.7$ Hz, $J_{AB'} = J_{A'B} = 0$ Hz), 6.82 (AA′*BB*′, 2H, as above), 6.82 (br s, 1H), 6.55 (br s, 1H), 3.76 (s, 3H), 3.00 (br s, 4H); HRFABMS calcd for $C_{29}H_{26}N_3O_7$ ($M + H)^+$ 528.1771, found

528.1772. Anal. Calcd for $C_{29}H_{25}N_3O_7 \cdot ?H_2O$: C, 64.92; H, 4.88; N, 7.83. Found: C, 64.99; H, 4.75; N, 7.90.[41]

**Selective Monoactivation of Biscarbamates. *N*-(2′-(*tert*-Butylcarbamate)bibenzyl-2-yl)isobutylurea (9a).** To a solution of **7a** (50 mg, 0.13 mmol) in 2 mL of benzene were added $Et_3N$ (23 $\mu$L, 1.2 equiv) and $HSiCl_3$ (16 $\mu$L, 1.2 equiv). The reaction mixture was shaken and allowed to react in a sealed vial at room temperature for 72 h. The isocyanate was then trapped by the addition of 0.3 mL of isobutylamine. The resultant urea was purified by chromatography (1:7 EtOAc/$CHCl_3$) to yield **9a** (52.7 mg, 95%) as a white solid; mp >320 °C; $^{13}$C NMR (DMSO-$d_6$, 101 MHz) $\delta$ 155.66, 154.16, 137.64, 136.15, 135.93, 131.15, 129.28, 128.70, 126.23, 126.12, 125.02, 122.19, 121.66, 78.65, 46.62, 30.68, 28.56, 28.17, 20.06; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.84 (br d, 1H, $J$ = 8.2 Hz), 7.31 (dd, 1H, $J$ = 7.9, 1.0 Hz), 7.21−7.13 (m, 3H), 7.01 (td, 1H, $J$ = 7.5, 1.3 Hz), 7.00 (td, 1H, $J$ = 7.6, 1.1 Hz), 6.63 (br s, 1H), 6.32 (s, 1H), 6.19 (s, 1H), 5.36 (br s, 1H), 2.90 (m, 2H), 2.88 (*AA*′BB′, 2H, $\nu_A = \nu_{A'}$ = 1150.2 Hz, $\nu_B = \nu_{B'}$ = 1122.5 Hz, $J_{AA'} = J_{BB'}$ = 16.0 Hz, $J_{AB} = J_{A'B'}$ = 5.5 Hz, $J_{AB'} = J_{A'B}$ = 7.5 Hz), 2.81 (AA′*BB*′, 2H, as above), 1.68 (non, 1H, $J$ = 6.7 Hz), 1.53 (s, 9H), 0.86 (d, 6H, $J$ = 6.7 Hz); HRFABMS calcd for $C_{24}H_{34}N_3O_3$ $(M + H)^+$ 412.2600, found 412.2598. Anal. Calcd for $C_{24}H_{33}N_3O_3$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.67; H, 8.11; N, 10.04.

***N*-(2′-(Methylcarbamate)bibenzyl-2-yl)isobutylurea (9b).** To a solution of **7b** (48.7 Mg, 0.11 mmol) in 2 mL of $CHCl_3$ were added $Et_3N$ (31 $\mu$L, 2 equiv) and $Me_2SiCl_2$ (27 $\mu$L, 2 equiv). The reaction mixture was shaken and allowed to react at room temperature in a sealed vial for 1 h. The reaction was determined by NMR to reach full conversion within this time, and although the isocyanate was not isolated, its presence was confirmed by IR spectroscopy (Ar NCO asymmetric stretch 2275.6 cm$^{-1}$ (lit.[45] PhNCO asymmetric stretch ~2275 cm$^{-1}$)). The isocyanate was trapped by addition of 0.3 mL of isobutylamine to form the urea **9b**, which was chromatographed (1:4 EtOAc/$CHCl_3$), washed with 10% NaOH (2×) and water, dried ($MgSO_4$), and rechromatographed (1:5 EtOAc/$CHCl_3$) to yield **9b** (40.3 mg, 98%) as a white solid: $^{13}$C NMR (DMSO-$d_6$, 101 MHz) $\delta$ 155.69, 155.31, 137.61, 135.91, 135.62, 131.20, 129.39, 128.70, 126.38, 126.15, 125.16, 122.30, 121.80, 51.74, 46.65, 30.80, 30.43, 28.58, 20.08; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 7.69 (br d, 1H, $J$ = 7.9 Hz), 7.36 (br d, 1H, $J$ = 7.9 Hz), 7.24−7.16 (m, 3H), 7.10−7.03 (m, 2H), 6.85 (br s, 1H), 6.51 (s, 1H), 6.12 (s, 1H), 5.21 (br s, 1H), 3.79 (s, 3H), 2.96 (t, 2H, $J$ = 6.1 Hz), 2.86 (*AA*′BB′, 2H, $\nu_A = \nu_{A'}$ = 1454.3 Hz, $\nu_B = \nu_{B'}$ = 1439.3 Hz, $J_{AA'} = J_{BB'}$ = 14.0 Hz, $J_{AB} = J_{A'B'}$ = 7.0 Hz, $J_{AB'} = J_{A'B}$ = 7.5 Hz), 2.83 (AA′*BB*′, 2H, as above), 1.70 (non, 1H, $J$ = 6.7 Hz), 0.88 (d, 6H, $J$ = 6.5 Hz); HRFABMS calcd for $C_{21}H_{28}N_3O_3$ $(M + H)^+$ 370.2131, found 370.2131. Anal. Calcd for $C_{21}H_{27}N_3O_3$: C, 68.27; H, 7.37; N, 11.37. Found: C, 67.99; H, 7.46; N, 11.06.

***N*-(2′-(2,2,2-Trichloroethylcarbamate)bibenzyl-2-yl)-isobutylurea (9c).** To a solution of **7c** (49.0 mg, 0.091 mmol) in 2 mL of $CHCl_3$ were added $Et_3N$ (15 $\mu$L, 1.2 equiv) and $MeSiCl_3$ (13 $\mu$L, 1.2 equiv). The reaction mixture was heated at 40 °C in a sealed vial for 49 h, after which time the reaction was allowed to cool to room temperature and 0.3 mL of isobutylamine was added. The reaction was determined by NMR to reach full conversion within this time. After the isobutylamine was allowed to react with the isocyanate for 1 min, the reaction mixture was poured into a 1:2 solution of 10% HCl/10% $(NH_4)_2SO_4$. The organic layer was washed with 10% NaOH (2×), dried ($MgSO_4$), and evaporated under reduced pressure in the presence of silica gel. The silica with adsorbed residue was loaded onto a column, and the residue was chromatographed (1:5 EtOAc/$CHCl_3$). The product fractions were combined, washed with 10% NaOH (2×) and water, dried ($MgSO_4$), and concentrated under reduced pressure to yield **9c** (39.2 mg, 88%) as a white solid: mp 206−208 °C; $^{13}$C NMR (DMSO-$d_6$, 101 MHz) $\delta$ 155.65, 153.38, 137.60, 136.78, 135.18, 131.01, 129.53, 128.63, 126.50, 126.15, 126.07, 122.35, 122.20, 121.68, 96.19, 73.45, 46.63, 30.75, 30.50, 28.55, 20.08; $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$ 9.56 (br s, 1H), 7.76 (d, 1H, $J$ = 8.1 Hz), 7.62 (s, 1H), 7.29 (td, 2H, $J$ = 8.1, 1.6 Hz), 7.23 (td, 1H, $J$ = 7.5, 1.7 Hz), 7.18 (td, 1H, $J$ = 7.3, 1.6 Hz), 7.10 (m, 2H), 6.91 (td, 1H, $J$ = 7.5, 1.3 Hz), 6.55 (t, 1H, $J$ = 5.9 Hz), 4.92 (s, 2H), 2.92 (t, 2H, $J$ = 6.3 Hz), 2.84 (*AA*′BB′, 2H, $\nu_A = \nu_{A'}$ = 1137.0 Hz, $\nu_B = \nu_{B'}$ = 1095.3 Hz, $J_{AA'} = J_{BB'}$ = 14.0 Hz, $J_{AB} = J_{A'B'}$ = 5.0 Hz, $J_{AB'} = J_{A'B}$ = 9.5 Hz), 2.74 (AA′*BB*′, 2H, as above), 1.86 (non, 1H, $J$ = 6.7 Hz), 0.87 (d, 6H, $J$ = 6.7 Hz); HRFABMS calcd for $C_{22}H_{27}Cl_3N_3O_3$ $(M + H)^+$ 486.1118, found 486.1119. Anal. Calcd for $C_{22}H_{26}Cl_3N_3O_3$: C, 54.28; H, 5.38; N, 8.63. Found: C, 54.43; H, 5.70; N, 8.38.

***N*-(2′-(*p*-Methoxyphenylcarbamate)bibenzyl-2-yl)isobutylurea (9d).** To a solution of **7d** (22.8 mg, 0.043 mmol) in 1 mL of $CHCl_3$ were added $Et_3N$ (8 $\mu$L, 1.3 equiv) and $Me_3SiCl$ (6 $\mu$L, 1.1 equiv). The reaction was shaken and kept at room temperature. After 10 min, 0.2 mL of isobutylamine was added. The reaction was determined by NMR to reach full conversion within this time, and although the isocyanate was not isolated, its presence was confirmed by IR spectroscopy (Ar NCO asymmetric strech 2272.5 cm$^{-1}$ (lit.[42] PhNCO asymmetric stretch ~2275 cm$^{-1}$)). After the isobutylamine was allowed to react with the isocyanate for 1 min,[46] the reaction mixture was poured into a 1:2 mixture of 10% HCl/10% $(NH_4)_2SO_4$. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure, and the resulting white solid was dissolved in $CHCl_3$ and evaporated in the presence of silica gel. The silica with adsorbed residue was loaded onto a column, and the residue was chromatographed (1:5 EtOAc/$CHCl_3$). The product fractions were combined, washed with 10% NaOH (2×) and water, dried ($MgSO_4$), and concentrated under reduced pressure to yield **9d** (17.9 mg, 90%) as a white solid: mp >320 °C; $^{13}$C NMR (DMSO-$d_6$, 101 MHz) $\delta$ 156.54, 155.72, 153.55, 144.22, 137.65, 135.50, 131.20, 129.55, 128.74, 126.52, 126.21, 125.62, 122.76, 122.34, 121.83, 114.30, 55.41, 46.65, 30.92, 30.55, 28.58, 20.08; $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$ 9.50 (br s, 1H), 7.76 (dd, 1H, $J$ = 8.2, 1.1 Hz), 7.67 (s, 1H), 7.44 (dd, 1H, $J$ = 7.9, 1.0 Hz), 7.30 (dd, 1H, $J$ = 7.5, 1.5 Hz), 7.23 (td, 1H, $J$ = 7.7, 1.6 Hz), 7.20−7.06 (m, 5H), 6.97−6.91 (m, 3H), 6.53 (t, 1H, $J$ = 5.8 Hz), 3.75 (s, 3H), 2.90 (t, 2H, $J$ = 6.1 Hz), 2.90 (*AA*′BB′, 2H, $\nu_A = \nu_{A'}$ = 1161.6 Hz, $\nu_B = \nu_{B'}$ = 1114.8 Hz, $J_{AA'} = J_{BB'}$ = 14.0 Hz, $J_{AB} = J_{A'B'}$ = 5.5 Hz, $J_{AB'} = J_{A'B}$ = 11.0 Hz), 2.79 (AA′*BB*′, 2H, as above), 1.66 (non, 1H, $J$ = 6.7 Hz), 0.86 (d, 6H, $J$ = 6.7 Hz); HRFABMS calcd for $C_{27}H_{32}N_3O_4$ $(M+H)^+$ 462.2393, found 462.2394. Anal. Calcd for $C_{27}H_{31}N_3O_4 \cdot {}^1/_3H_2O$ : C, 69.36; H, 6.83; N, 8.99. Found: C, 69.35; H, 6.78; N, 9.02.

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