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Chlorotrimethylsilane Activation of Acylcyanamides for the Synthesis of Mono-*N*-acylguanidines

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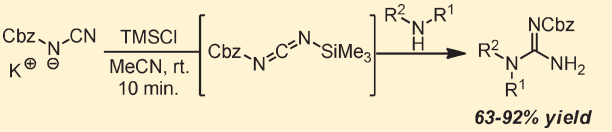
Supporting Information

ABSTRACT: A simple and efficient one-pot method for the synthesis of monoprotected guanidines is presented. Treatment of an acylcyanamide with chlorotrimethylsilane generates a reactive *N*-silylcarbodiimide capable of guanylating a variety of amines. Typically the reaction is complete in 15 min for primary and secondary aliphatic amines at rt. Hindered amines and anilines are also competent nucleophiles but require extended reaction times.



The guanidinium ion represents an important molecular architecture, valuable for its ability to engage receptors electrostatically and through diverse hydrogen bond topologies.[1] This has made the guanidine a valuable synthetic target for applications as varied as natural products chemistry,[2] medicinal chemistry,[3] supramolecular chemistry,[4] and asymmetric catalysis.[5] As a result there have been a large number of synthetic methods developed to introduce the guanidine unit. Most of these methods rely on the introduction of a diacylated guanidine unit to circumvent problems associated with the reactivity or purification of this basic functional group (Figure 1). In concert with a thiophilic metal salt (typically Hg(II), Cu(I), or Ag(I)), the di-Boc-*S*-Me-pseudothiourea (**1**) is by far the most commonly utilized reagent to install the guanidine unit.[6] The parent thiourea **2** can also be used in conjunction with an activating agent (typically Mukaiyama's reagent[7] (**3**) or other suitable peptide coupling reagents[8]). Goodman's reagent[9] (**4**) has also found wide utility since it is capable of guanylating weakly nucleophilic amines. The pyrazole transfer reagents **5** and **6** have also been developed to obviate the use of toxic metals.[10]

These reagents are typically used to install the guanidine unit, which after protecting group removal reveals a terminal mono- or *N*,*N*-disubstituted guanidine. There have been a number of recent reports however, aimed at developing chemistry to generate peripheral C−N bonds around the intact guanidine unit.[11] These methods target more highly substituted guanidinium ion structures but still incorporate the diacylated guanidine unit. We became interested in the use of mono-*N*-acylguanidines in these methodologies, anticipating the ability to exploit open nitrogen valences for subsequent functionalization reactions.

The synthesis of mono-*N*-acylguanidines is typically accomplished by the acylation of guanidines with anhydrides or activated acid derivatives. This method is frequently complicated by over acylation due to the increased acidity of the initially formed mono-*N*-acylguanidine.[12] Alternatively they can be accessed by the controlled hydrolysis of polyacyl or acyl-protected guanidines.[13] Several methods have also been developed for their synthesis from *N*-acyl-thioureas[14] or *N*-acyl-pseudothioureas.[14c] The use of the monoprotected versions of the pyrazole reagent **5** have also been

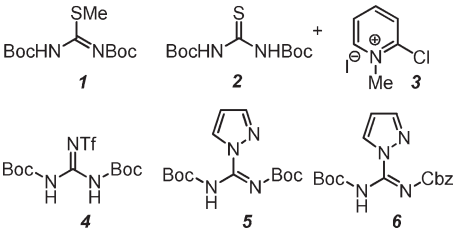


Figure 1. Common guanylation reagents.

reported, but are unreactive or poorly reactive toward amines.[10,11i] Alternatively, the differentially protected pyrazole **6** can be employed followed by selective removal of either the Boc or Cbz group.[15] These methods suffer from poor yields, require multiple synthetic manipulations, or utilize costly reagents.

We were interested in a disconnection that relies on the addition of an amine to an acylcyanamide. While it is known that amines undergo addition to acylcyanamides, these reactions typically require forcing conditions, are limited to anilines,[16] and are complicated by cyanamide decomposition thus limiting their utility. Since acylcyanamides typically have pK_a's ∼ 2−4,[17] this renders them unreactive toward aliphatic amines *via* salt formation. We considered the possibility that treatment of the acylcyanamide with a temporary activating agent might form a reactive carbodiimide intermediate, lacking the acidic proton rendering it capable of guanylating aliphatic or basic amines. Herein we report our finding that silylation is particularly effective strategy to activate acylcyanamides for nucleophilic addition.

We first began examining the direct activation of the cyanamide **7**[18] and its reaction with benzylamine (Table 1). As anticipated, there was no reaction in the absence of an activating agent or in the presence of an exogenous base (entries 1 and 2). Trifluoromethanesulfonic anhydride was capable of activating the cyanamide, however, these conditions led to complex reaction mixtures and low yields of the guanidine **3** (entry 3).

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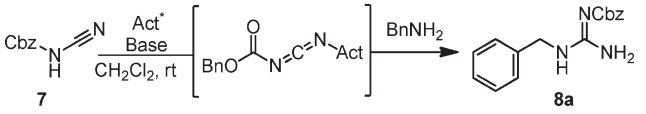
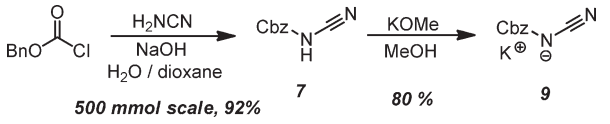
Table 1. Survey of Activation Conditions



entry	activating agent	base	% yield
1	none	none	0
2	none	*i*-Pr_2NEt	0
3	Tf_2O	pyridine	0
4	TMSCl	pyridine	68
5	TMSCl	*i*-Pr_2NEt	91

Scheme 1. Preparation of Benzyloxycarbonylcyanamide Potassium Salt

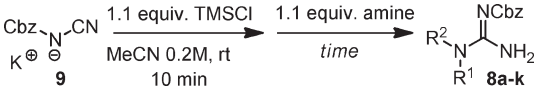


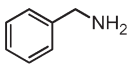
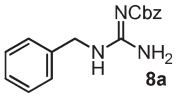
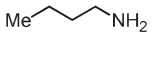
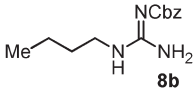
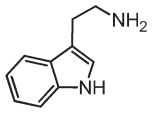
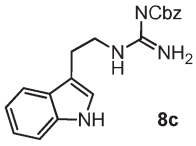
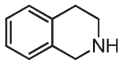
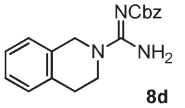
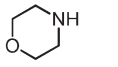
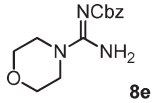
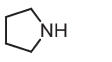
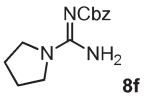
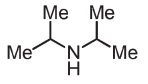
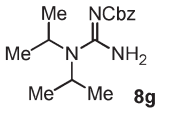
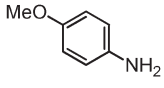
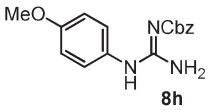
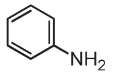
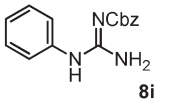
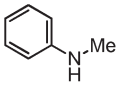
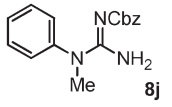
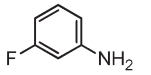
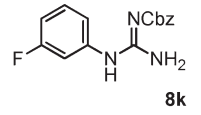
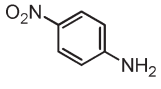
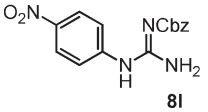
The best results (entries 4 and 5) were obtained using chlorotrimethylsilane as the activating agent.

We were excited by these initial experiments for several reasons. (1) The reaction was very rapid, reaching completion in just 15 min, (2) washing the crude reaction mixture with aqueous acid and then base removed any unreacted amine or acylcyanamide respectively, delivering high purity material after workup, and (3) the mono-Cbz guanidines are amenable to normal-phase purification methods. One drawback, however, was the instability of reagent **7** which in our hands would decompose significantly after 2−3 days of storage at room temperature. It has previously been observed that these acylcyanamides decompose to generate a variety of diacyl- and cyanoguanidine byproducts.[18] We anticipated that the alkali salts of the cyanamide might provide a convenient, shelf-stable version of this reagent. We developed an efficient scalable preparation of the potassium salt of **7** (Scheme 1).[19] Precipitation of the salt from methanol was found to be optimal for producing **9** as a fine powder that could easily be manipulated. Other recrystallization solvents or the sodium and lithium counterions gave the corresponding salt as a fluffy solid or fine plates which were difficult to handle or solubilize in subsequent reaction conditions.

The potassium salt **9** has very poor solubility in THF, CH_2Cl_2, toluene, and acetonitrile. However, treatment of a suspension of the reagent in acetonitrile with TMSCl rapidly forms a milky solution suggesting the formation of precipitated potassium chloride. After approximately 10 min, the original solid reagent **9** appeared to have been completely solubilized. To our delight, addition of benzylamine to this mixture gave the guanidine **8a** as quickly and cleanly as our previous reaction conditions (Table 1, entry 5), this time in 85% isolated yield after recrystallization (Table 2, entry 1). Surveying the reactivity of this reagent showed that it was quite general, reacting with other primary amines to give the guanidines **8b,c** in high yield after short reaction times (entries 1−3). Secondary amines were also reactive, giving the guanidines **8d**−**f** in just 15 min (entries 4−6). Guanylation of a hindered secondary amine, for example, diisopropylamine, was also successful providing the guanidine **8g** in 73% yield, but required more time to reach completion (entry 7). Guanylation of anilines required significantly longer reaction times (entries 8−11). Isolated yields of the guanidines **8h**−**k** were well aligned with the relative nucleophilicity of the parent aniline. While electron deficient anilines can react (entry 11), the reagent is not

Table 2. Scope of the Guanylation Reaction



entry	amine	product	time	Yield (%)
1		 8a	15 min	85%
2		 8b	15 min	91%
3		 8c	15 min	91%
4		 8d	15 min	88%
5		 8e	15 min	92%
6		 8f	15 min	90%
7		 8g	1 h	73%
8		 8h	8 h	83%
9		 8i	16 h	71%
10		 8j	16 h	68%
11		 8k	16 h	63%
12		 8l	--	N.R

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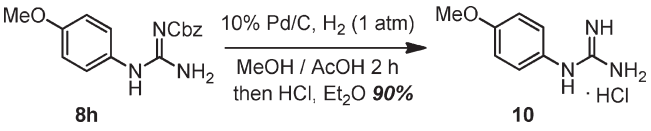
Scheme 2. Guanidine Deprotection



capable of guanylating extremely electron poor substrates such as *p*-nitroaniline under these conditions (entry 12).

Deprotection of these mono-Cbz protected guanidines can be carried out under standard hydrogenolysis conditions to provide the free guanidines or their HCl salts as exemplified by the conversion of **8h** to **10** (Scheme 2).

In summary, we have demonstrated that the activation of acylcyanamides with chlorotrimethylsilane generates an efficient reagent for the guanylation of aliphatic and aromatic amines. The method is operationally simple, high yielding at room temperature, and adequate purification is usually achieved through aqueous acid/base work up.

EXPERIMENTAL SECTION

Benzyloxycarbonylcyanamide (7). The title compound was prepared according to Kwon with minor modifications.[18] To a solution of sodium hydroxide (46.9 g, 1.17 mol) in distilled water (750 mL) was added cyanamide (49.6 g, 1.17 mol) in portions over 15 min. The mixture was stirred for 30 min at which time dioxane (100 mL) was added and the mixture cooled to 0 °C. Benzylchloroformate (95% purity) (83.5 mL, 0.58 mol) was added dropwise via an additional funnel over 1 h. The cooling bath was removed and the mixture stirred for 5 h at room temperature. The mixture was then transferred to a separatory funnel and washed with diethyl ether (3 × 100 mL). The aqueous phase was acidified with concd HCl to pH = 2 and extracted with dichloromethane (3 × 400 mL). The combined organics were then dried with Na_2SO_4, filtered through a short plug of silica gel and concentrated to give the cyanamide as a colorless oil that was used without further purification (90.2 g, 92%). Physical data were identical with those previously reported.

Benzyloxycarbonylcyanamide Potassium Salt (9). Potassium metal (8.64 g, 0.221 mol, 0.95 equiv) was added carefully to methanol (300 mL) at 0 °C. After all of the metal was consumed the benzyloxycarbonylcyanamide (41.0 g, 0.232 mol) was added. After 10 min, a white precipitate was formed. Toluene (300 mL) was added and the mixture stirred at 0 °C for 30 min. The solids were collected on a Büchner funnel, rinsed with toluene (2 × 100 mL), hexanes (2 × 100 mL) and air-dried to give the potassium salt as a white microscrystalline solid (34.7 g, 73%). A second crop could be obtained from the mother liquor (3.21 g, 7%). R_f = 0.28 (ethyl acetate). mp = 222−224 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.34−7.24 (m, 5H), 4.87 (s, 2H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 162.6, 138.7, 128.1, 127.3, 127.2, 122.1, 65.2. IR (powder): 3059, 3034 (both w), 2189 (s) 2144 (m), 1622 (s), 1394, 1338, 1306, 1177, 1145 (all m), 778, 758, 697 (all s). HRMS (ESI$^-$) calculated for $C_9H_7N_2O_2$ [M−] *m/z*, 175.0508; obsd, 175.0511.

General Procedure for the Guanylation of Amines with ***9****. N-Benzyloxycarbonyl-N′-benzylguanidine (****8a****).* Benzyloxycarbonylcyanamide potassium salt (300 mg, 1.40 mmol) was slurried in acetonitrile (7.0 mL to be 0.2 M). Chlorotrimethylsilane (194 μL, 1.50 mmol) was then added and the mixture stirred for 10 min [or until all of the solids have dissolved]. NOTE: The reaction mixture turns from a suspension to a milky white consistency. Benzylamine (164 μL, 1.50 mmol) was then added. After 15 min, TLC analysis showed that the reaction was complete and the reaction was concentrated under reduced pressure to approximately one-third of the original volume. The mixture was then diluted with ethyl acetate (50 mL) and washed with 10% Na_2CO_3 (50 mL), brine (50 mL) and the organics dried over Na_2SO_4. Concentration under reduced pressure gave a white solid which was recrystallized from toluene/ethyl acetate to give the title compound as white microplates (337 mg, 85% yield). R_f = 0.07 (1:1) hexanes/ethyl acetate. mp = 168−170 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 7.33−7.23 (m, 10H), 4.96 (s, 2H), 4.37 (br s, 2H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 163.8, 162.1, 138.7, 129.6, 129.04, 128.9, 128.3, 128.1, 127.8, 127.6, 65.9, 44.1. IR (powder): 3472, 3282 (both m), 1640, 1616, 1588, 1558 (all s), 1424 (m), 1272, 1120 (both s). HRMS (ESI) calculated for $C_{16}H_{18}N_3O_2$ *m/z* (M + H), 284.1399; obsd, 284.1402.

*N-Benzyloxycarbonyl-N′-butylguanidine (****8b****).* Prepared according to the general procedure with purification on silica gel eluting with (1:1) hexanes/ethyl acetate to give the title compound as a white solid (91% yield). R_f = 0.15 (1:1) hexanes/ethyl acetate. mp = 73−75 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.80−8.40 (br s, 1H), 7.35−7.24 (m, 5H), 7.00−6.40 (br s, 1H), 5.06 (s, 2H), 3.01 (t, *J* = 7.0 Hz, 2H), 1.47 (quint, *J* = 7.0 Hz, 2H), 1.26 (sextet, *J* = 7.0 Hz, 2H), 0.86 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.9, 161.9, 137.7, 128.5, 127.8, 127.8, 66.1, 41.0, 31.1, 20.1, 13.8. IR (neat): 3407, 2957, 2931, 2872 (all w), 1622, 1582, 1278, 1103, 731 (all s). HRMS (ESI+) calculated for $C_{13}H_{20}N_3O_2$ *m/z* (M + H), 250.1556; obsd, 250.1552.

*N-Benzyloxycarbonyl-N′-ethylindoleguanidine (****8c****).* Prepared according to the general procedure with purification on silica gel eluting with 15% MeOH in CH_2Cl_2 to give the title compound as a white solid (91% yield). R_f = 0.51 (15% MeOH in CH_2Cl_2). mp = 156−157.5 °C. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.83 (br s, 1H), 7.57 (br s, 1H), 7.34−7.28 (m, 7H), 7.15 (br s, 2H), 7.07 (t, J=7.6 Hz, 1H), 6.95 (br s, 1H), 6.70 (br s, 1H), 4.97 (br s, 2H), 3.40 (br s, 2H), 2.86 (br s, 2H). ^{13}C NMR (DMSO-d_6, 125 MHz, mixture of rotamers): δ 163.8, 162.1, 138.8, 136.9, 128.9, 128.3, 128.1, 123.4, 121.6, 119.1, 118.9, 112.3, 112.1, 66.0, 65.5, 42.0, 41.3, 26.1, 25.3. IR: 3407, 3313, 2941, 2361, 2339, 1617, 1119, 742.1. HRMS (ESI+) calculated for $C_{19}H_{20}N_4O_2$ *m/z* (M + H), 337.1665; obsd, 337.1665.

*N-Benzyloxycarbonyl-N′-1,2,3,4-tetrahydroisoquinoline-guanidine (****8d****).* Prepared according to the general procedure and purified by recrystallization from hexanes/acetone to give the title compound as white plates (88% yield). R_f = 0.25 (1:1) hexanes/ethyl acetate. mp = 117−119 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.43 (d, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.28−7.26 (m, 2H), 7.22−7.20 (m, 2H), 7.17−7.14 (m, 2H), 5.15 (s, 2H), 4.68 (s, 2H), 3.72 (br t, *J* = 5.0 Hz, 2H), 2.90 (t, *J* = 5.0 Hz, 2H). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 163.9, 160.6, 137.6, 134.8, 132.7, 128.3, 128.0, 127.9, 127.7, 126.9, 126.6, 126.4, 66.6, 45.6, 41.6, 28.6. IR (neat): 3404, 3304, 3220 (all w), 1643 (m), 1583, 1537, 1438, 1295, 1240, 1216, 1091 (all s). HRMS (ESI) calculated for $C_{18}H_{20}N_3O_2$ *m/z* (M + H), 310.1556; obsd, 310.1558.

*N-Benzyloxycarbonyl-N′-morpholinoguanidine (****8e****).* Prepared according to the general procedure with purification on silica gel eluting with 1:1 hexanes/ethyl acetate to give the title compound as a white foam (92% yield). R_f = 0.21 (1:1) hexanes/ethyl acetate. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.37 (d, *J* = 7.5 Hz, 2H); 7.32 (t, *J* = 7.5 Hz, 2H); 7.26 (t, *J* = 7.5 Hz, 1H); 5.10 (s, 2H); 3.64 (t, *J* = 6.5, 4H); 3.48 (t, *J* = 6.5, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.2, 160.9, 137.4, 66.9, 66.3, 44.0. IR (neat): 3397 (br), 2964, 2857, 1645, 1589, 1535, 1443, 1374, 1292, 1256, 1094 cm^{-1}. HRMS (ESI) calculated for $C_{13}H_{18}N_3O_3$ *m/z* (M + H), 264.1348; obsd, 264.1349.

*N-Benzyloxycarbonyl-N′-pyrrolidinoguanidine (****8f****).* Prepared according to the general procedure with purification on silica gel eluting with 1:1 hexanes/ethyl acetate to give the title compound as a white solid (90% yield). R_f = 0.16 (1:1) hexanes/ethyl acetate. mp = 147−149 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.39 (d, *J* = 7.5 Hz, 2H); 7.30 (t, *J* = 7.5 Hz, 2H); 7.24 (t, *J* = 7.5 Hz, 1H); 5.10 (s, 2H); 3.52 (br s, 2H); 3.26 (br s, 2H); 1.91 (bs s, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.0, 159.4, 137.9, 128.4, 128.2, 66.6, 47.2 (br), 25.3 (br). IR (neat): 3338, 3166, 2974, 2949, 2871, 1652, 1596, 1561, 1453, 1276, 1101 cm^{-1}. HRMS

(ESI) calculated for $C_{13}H_{18}N_3O_2$ m/z (M + H), 248.1399; obsd, 248.1401.

*N-Benzyloxycarbonyl −N′, N′-diisopropylguanidine (**8g**).* Prepared according to the general procedure with recrystallization from hexanes/acetone to give the title compound as a light yellow solid (73% yield). R_f = 0.50 (1:1) hexanes/ethyl acetate. mp = 101−103 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.40 (d, J = 7.5 Hz, 2H); 7.31 (t, J = 7.5 Hz, 2H); 7.25 (t, J = 7.5 Hz, 1H); 5.10 (s, 2H); 4.37 (br s, 2H); 1.23 (d, J = 7.2 Hz, 12H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.3, 160.6, 138.9, 128.4, 128.1, 127.6, 66.6, 45.4, 20.9. IR (neat): 3477, 3294 (both br), 3031, 2945, 1644, 1581, 1522, 1404, 1377, 1245, 1085 cm^{-1}. HRMS (ESI) calculated for $C_{15}H_{24}N_3O_2$ m/z (M + H), 278.1869; obsd, 278.1869.

*N-Benzyloxycarbonyl-N′-4-methoxyphenylguanidine (**8h**).* Prepared according to the general procedure with recrystallization from toluene/ethyl acetate to give the title compound as a light purple solid (83% yield). R_f = 0.10 (1:1) hexanes/ethyl acetate. mp = 172−173 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.3−7.2 (m, 5H), 7.13 (d, J = 8.7 Hz, 2H), 6.82 (d, J = 8.2 Hz, 2H), 4.98 (s, 2H), 3.79 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.0, 161.6, 158.7, 137.5, 128.7, 128.4, 128.3, 127.8, 127.7, 115.0, 66.1, 55.6. IR (neat): 3475, 3272, 3067, 1640, 1606, 1574, 1391, 1276 cm^{-1}. HRMS (ESI) calculated for $C_{16}H_{18}N_3O_3$ m/z (M + H), 300.1348; obsd, 300.1349.

*N- Benzyloxycarbonyl-N′-phenylguanidine (**8i**).* Prepared according to the general procedure with recrystallization from toluene/ethyl acetate to give the title compound as a white solid (71% yield). R_f = 0.15 (1:1) hexanes/ethyl acetate. mp = 167−170 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.35−7.15 (m, 10H), 4.96 (s, 2H). ^{13}C NMR ($CDCl_3$, 500 MHz): δ 163.8, 160.8, 137.4, 136.6, 129.9, 128.5, 127.9, 127.7, 127.1, 126.2, 66.2. IR: 3470, 3301, 3032, 2945, 1624, 1561, 1232, 1065, 697 cm^{-1}. HRMS (ESI) calculated for $C_{15}H_{16}N_3O_2$ m/z (M + H), 270.1243; obsd, 270.1243.

*N-Benzyloxycarbonyl-N′-methyl-N′-phenylguanidine (**8j**).* Prepared according to the general procedure with purification on silica gel eluting with 1:1 hexanes/ethyl acetate to give the title compound as a colorless oil (68% yield). R_f = 0.43 (1:1 hexanes/ethyl acetate). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.48−7.42 (m, 4H); 7.38 (t, J = 7.5 Hz, 1H); 7.34 (t, J = 7.5 Hz, 2H); 7.29−7.25 (m, 3H); 5.16 (s, 3H); 3.39 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.1, 160.7, 141.8, 137.6, 130.4, 128.4, 128.3, 128.1, 127.6, 127.4, 66.7, 38.6. IR (neat): 3477, 3294 (both br), 3031, 2945, 1644, 1581, 1522, 1404, 1377, 1245, 1085 cm^{-1}. HRMS (ESI) calculated for $C_{16}H_{18}N_3O_2$ m/z (M + H), 284.1399; obsd, 284.1408.

*N-Benzyloxycarbonyl-N′-3-fluorophenylguanidine (**8k**).* Prepared according to the general procedure with recrystallization from hexanes/acetone to give the title compound as a light purple solid (63% yield). R_f = 0.18 (1:1) hexanes/ethyl acetate. mp = 131−132 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.29−7.23 (m, 6H), 6.97−6.90 (m, 3H), 5.00 (s, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.5 (d, J_{CF} = 249.5 Hz) 162.7 (br), 159.4 (br), 139.6 (br), 137.0, 131.0 (d, J_{CF} = 9.1 Hz), 128.5, 127.9, 121.2 (d, J_{CF} = 3.0 Hz), 113.4 (d, J_{CF} = 20.5 Hz), 113.0 (d, J_{CF} = 22.8 Hz), 66.4. IR (neat): 3473, 3305, 3065 (all w), 1627, 1595, 1563, 1263 (all s), 1145, 1078, 1063 (all m). HRMS (ESI) calculated for $C_{15}H_{15}N_3O_2F$ m/z (M + H), 288.1148; obsd, 288.1132.

1-(4-Methoxyphenyl)guanidine (10). A 25 mL round-bottom flask was charged with *N*-benzyloxycarbonyl-*N′*-4-methoxyphenylguanidine (**8h**) (100 mg, 0.33 mmol) and 10% palladium on charcoal (15 mg). The flask was flushed with nitrogen and then MeOH (5 mL) and AcOH (150 μL) was added. The mixture was stirred under a hydrogen atmosphere for 2 h at which time TLC showed the reaction to be complete. The mixture was filtered through a plug of cotton and concentrated under reduced pressure. The crude mixture was taken up in MeOH (2 mL) and 4 M HCl in diethyl ether (4 mL) was added. The mixture was again concentrated and the resulting solid triturated with diethyl ether (3 × 5 mL). The solids was then collected to give the title compound as a white powder (61 mg, 90%). Spectral data was identical to that previously reported.[20]

■ ASSOCIATED CONTENT

Supporting Information. General experimental details, ^{1}H, ^{13}C spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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