Articles

Palladium-Catalyzed Synthesis of 2-Substituted Indoles

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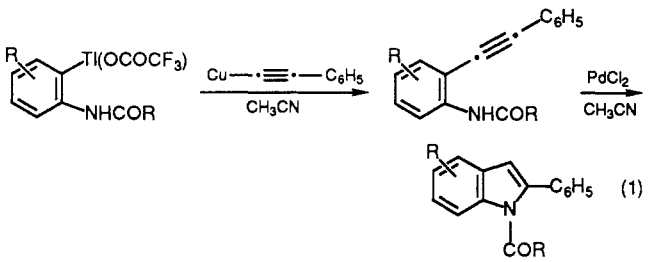
The palladium(0)-catalyzed cross-coupling reaction of alkynylstannanes with 2-bromoanilines or 2-trifloxyanilines results in the formation of 2-alkynylanilines. The coupling reaction tolerates substituents on the anilines, including ester, ether, chloro, and trifloxy groups. A palladium(II)-catalyzed intramolecular cyclization provides 2-substituted indoles. The cyclization proceeds without the need to reoxidize the metal and is most efficient with aliphatic substituents on the alkynyl terminus.

Introduction

The palladium-catalyzed intramolecular cyclization reactions of amines with alkynes and alkenes has been utilized for the synthesis of a number of nitrogen heterocycles, including pyrroles,[1] uracils,[2] and indoles.[3,4] The catalytic coupling of aryl halides with organostannanes[5] has been applied to the synthesis of indoles,[6] the final step in the procedure involving the palladium-catalyzed ring closure of *N*-tosyl-2-vinylanilines. In an effort to develop synthetic procedures for the preparation of 2-substituted indoles, the synthesis and cyclization reactions of acetylenic anilines was explored.

The palladium-catalyzed cyclization of 2-*N*-acylaminotolanes has been shown[7] to yield 2-phenylindoles. The preparation of 2-(phenylethynyl)anilines was achieved via ortho thallation of aniline and coupling with an alkynylcopper reagent (eq 1).



(1)

Recently several other 2-alkynylanilines and their cyclization reactions were reported.[8] Because the palladium-catalyzed cross-coupling of organostannanes with various electrophiles has been shown to be a highly efficient method for the formation of carbon–carbon bonds,[9] and since alkynylstannanes undergo the coupling reaction rapidly under the most mild conditions, the coupling cyclization sequence appeared to be an efficient method for the preparation of various 2-substituted indoles.

Results and Discussion

In order to optimize the coupling reaction conditions, 2-bromoaniline was used as a model for the coupling with alkynylstannanes. The amine was protected as the *N*-acetyl, *N*-tosyl, and *N*-trifluoroacetyl derivatives. The coupling reactions of the protected anilines with 1.2 equiv of tributylalkynylstannane, in the presence of 3% tetrakis(triphenylphosphine)palladium, in toluene at 100 °C

Table I. Alkynylstannane Coupling with *N*-Acetyl-2-bromoaniline[a]

product	R	*t*, h	% yield[b]
2a	n-C_3H_7	2.5	76.9
2b	i-C_3H_7	2.5	67.9
2c	n-C_4H_9	2	84.4
2d	C_6H_5	5	94.2
2e	CH_2OTHP	6[c]	76.0
2f	TMS	3.5	87.8
2g	$CH{=}CHOCH_3$	4.5	50.6
2h	$(CH_2)_2OSi(CH_3)_2C(CH_3)_3$	1.75	53.4
2i	CH_2OCH_3	3.5	60.0

[a] Reactions were carried out at 100 °C using 2–5 mmol of reactant, 1.2 equiv of alkynylstannane, and 3 mol % $Pd(Ph_3P)_4$ in 20–30 mL of toluene. The reaction was stopped upon disappearance of starting material as observed by TLC. [b] Isolated yields are reported for all reactions. [c] The reaction was heated at 110 °C.

Table II. Palladium-Catalyzed Cyclization of *N*-Acetyl-2-alkynylanilines[a]

product	R	cat. %	*t*, h	% yield[b]
3a	n-C_3H_7	10	1.5	84.3
3b	i-C_3H_7	5	1.5	91.0
3c	n-C_4H_9	10	1.5	93.0
3d	C_6H_5	13	2.5	69.3
3e	CH_2OTHP	10	12	–[c]
3f	$Si(CH_3)_3$	10	3	–[c]
3g	H	10	6	–[c]

[a] Reactions were run in acetonitrile at 80 °C using 10 mol % $nCH_3CN)_2PdCl_2$. The reaction was complete when TLC showed disappearance of starting material. [b] Yields are based on isolated material. [c] No indole was obtained; starting material decomposed.

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(1) (a) Trost, B. M.; Keinan, E. *J. Org. Chem.* **1980**, *45*, 2741. (b) Murahashi, S.; Shimamura, T.; Moritani, I. *J. Chem. Soc., Chem. Commun.* **1974**, 931. (c) Utimoto, K.; Miwa, H.; Nazaki, H. *Tetrahedron Lett.* **1981**, *22*, 4277.

(2) (a) Mizutani, M.; Sanemitsu, Y.; Tamaru, Y.; Yoshida, Z. *Tetrahedron Lett.* **1985**, *26*, 1237. (b) Mitzutani, M.; Sanemitsu, Y. *Tetrahedron* **1986**, *42*, 305.

(3) (a) Kasahara, A.; Izumi, T.; Murakami, S.; Yanai, H.; Takatori, M. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 927. (b) Yokoyama, Y.; Ito, S.; Takahashi, Y.; Murakami, Y. *Tetrahedron Lett.* **1985**, *26*, 6457. (c) Murakami, Y.; Yokoyama, A.; Aoki, T. *Heterocycles* **1984**, *22*, 1493. (d) Tischler, A. N.; Lanza, T. J. *Tetrahedron Lett.* **1986**, *27*, 1653. (e) Sakamoto, T.; Kondo, Y.; Yamanaka, H. *Heterocycles* **1986**, *24*, 31. (f) Tremont, S. J.; Rahman, H. U. *J. Am. Chem. Soc.* **1984**, *106*, 5759. (g) Harrington, P. J.; Hegedus, L. S.; McDaniel, K. F. *J. Am. Chem. Soc.* **1987**, *109*, 4335. (h) Hegedus, L. S.; Allen, G. F.; Bozell, J. J.; Waterman, E. L. *J. Am. Chem. Soc.* **1978**, *100*, 5800.

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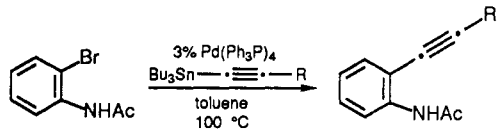
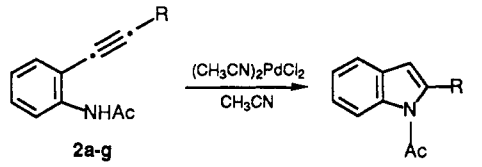
were monitored by TLC and were stopped when starting material had been consumed. The *N*-acetyl-protected aniline (**1**) consistently gave better yields than the other protected aniline derivatives. In addition, *N*-tosyl and *N*-trifluoroacetyl derivatives did not undergo cyclization to the indole, vide infra. To explore the generality of the coupling reaction, a number of different substituents on the alkynylstannanes were utilized (eq 2, Table I).



(2)

1 **2a-i**

The cyclization reactions of the 2-alkynylanilines were effected with bis(acetonitrile)palladium dichloride in acetonitrile at reflux (eq 3). For the *N*-trifluoroacetyl and the *N*-tosyl analogues, no cyclization occurred, only unchanged alkynes being obtained. The cyclization of *N*-



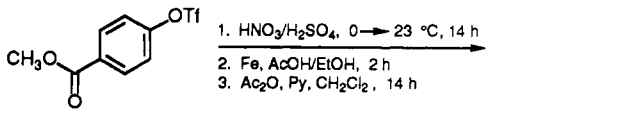
(3)

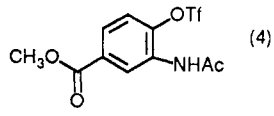
2a-g **3a-g**

acetyl-2-alkynylanilines proceeded rapidly (Table II), except that the tetrahydropyran-protected propargyl alcohol and the trimethylsilyl-substituted alkyne did not cyclize. In these cases, only unchanged starting material was recovered. Cyclization of the unsubstituted alkynylaniline (**2j**) did not take place, resulting in the decomposition of starting material.

Other palladium catalysts, such as bis(triphenylphosphine)palladium dichloride, bis(diphenylferrocenyl)palladium dichloride, and other reaction conditions, including varying the temperature from 23 °C to 100 °C in dimethylformamide, gave only decomposition or unchanged alkyne. No indoles were obtained in dimethylformamide, tetrahydrofuran, or acetonitrile with bis(triphenylphosphine)palladium dichloride.

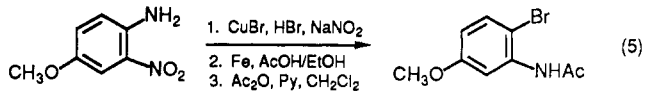
To investigate the influence that substituents on the phenyl ring would have in the coupling and cyclization reactions, several different 2-bromo- and 2-trifloxyanilines were prepared. Triflate (**4**) can be prepared from the commercially available phenol in several steps (eq 4). Formation of the triflate[10] was followed by nitration, reduction, and protection of the secondary amine as the acetyl derivative. *N*-Acetyl-2-bromo-5-methoxyaniline (**5**) was prepared from 5-methoxy-2-nitroaniline by first replacing the amine with bromine[11] followed by reduction of the nitro group to an amine and its protection as the *N*-acetyl derivative (eq 5).





(4)

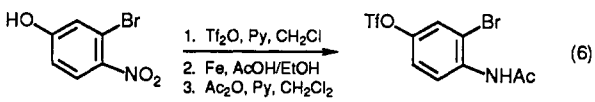
4
(52% overall yield)



(5)

5
(74% overall yield)

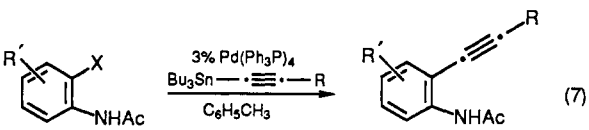
For the synthesis of 5-substituted indoles, different 4-substituted anilines were prepared. *N*-Acetyl-2-bromo-4-methylaniline was prepared from *p*-toluidine in a one-pot reaction in 83% yield.[12] Triflate **6** was prepared by first converting the phenol to the triflate, followed by reduction of the nitro group to the amine and protection as the *N*-acetyl derivative (eq 6).



(6)

6
(67% overall yield)

Coupling at the bromo position can be carried out selectively in the presence of the aryl triflate by the exclusion of lithium chloride.[10] The coupling reactions of the ring-substituted trifloxy- or bromoanilines using 3% Pd(0) catalysis in toluene at 10 °C yielded various *N*-acetyl-2-alkynylanilines (eq 7, Table III).



(7)

7-12

The yields for the 5-methoxy-2-alkynylanilines (**8a–d**) were somewhat lower than those for the 5-carbomethoxy-2-alkynylanilines (**7a–e**). The electron-donating ability of the *p*-methoxy group apparently decreases the rate of the oxidative addition step, and consequently decreases the yield, relative to the unsubstituted *N*-acetyl-2-bromoanilines. In addition, the oxidative addition of phenyl triflate (**7a–e**) to the palladium(0) catalyst has been shown to be more facile than aryl bromides[10] and therefore contribute to higher yields.

The position of the triflate, relative to the amine function, also influences the coupling reaction. The yields of the coupling reactions of alkynylstannanes with 3-trifloxy-2-bromoanilines (**12a,b**) were lower than those obtained from 4-trifloxy-2-bromoanilines (**11a–c**). It is not clear whether this is a reflection of a steric or electronic problem, or both.

(4) For a recent review on organometallic methods for indole synthesis, see: (a) Hegedus, L. S. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1113. (b) Sakamoto, T.; Konda, Y.; Yamanaka, H. *Heterocycles* **1988**, *27*, 2225.
(5) McKean, D. R.; Parrinello, G.; Renaldo, A. F.; Stille, J. K. *J. Org. Chem.* **1987**, *52*, 422.
(6) Krolski, M. E.; Renaldo, A. F.; Rudisill, D. E.; Stille, J. K. *J. Org. Chem.* **1988**, *53*, 1170.
(7) Taylor, E. C.; Katz, A. H.; Salgado-Zamora, H. *Tetrahedron Lett.* **1985**, *26*, 5963.
(8) (a) Iritani, K.; Matsubara, S.; Utimoto, K. *Tetrahedron Lett.* **1988**, *29*, 1799. (b) Sakamoto, T.; Kondo, Y.; Iwashita, S.; Nagano, T.; Yamanaka, H. *Chem. Pharm. Bull.* **1988**, *36*, 1305. (c) Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron Lett.* **1989**, *30*, 2581.
(9) (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. (b) Stille, J. K. *Pure Appl. Chem.* **1985**, *57*, 1771.
(10) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478.
(11) Doyle, M. P.; Sigfried, B.; Dellaria, J. F. *J. Org. Chem.* **1977**, *42*, 2426.
(12) Johnson, J. R.; Sandborn, L. T. *Organic Syntheses*; Wiley: New York, 1951; Collect. Vol. I, p 111.

Table III. Coupling Reactions of Alkynylstannanes with Substituted 2-Bromo- and 2-Trifloxyanilines[a]

R′	R	X	product	t, h	% yield[c]
5-CO_2CH_3	i-C_3H_7	OTf[b]	**7a**	3	73.1
5-CO_2CH_3	i-C_3H_7	OTf[b]	**7b**	1.75	77.1
5-CO_2CH_3	n-C_4H_9	OTf[b]	**7c**	3	88.2
5-CO_2CH_3	C_6H_5	OTf[b]	**7d**	2	83.5
5-CO_2CH_3	$Si(CH_3)_3$	OTf[b]	**7e**	1	97.3
5-OCH_3	n-C_3H_7	Br	**8a**	5.5	60.2
5-OCH_3	i-C_3H_7	Br	**8b**	3.5	56.5
5-OCH_3	n-C_4H_9	Br	**8c**	6	61.5
5-OCH_3	C_6H_5	Br	**8d**	5	75.7
4-CH_3	n-C_3H_7	Br	**9a**	3.5	64.7
4-CH_3	n-C_4H_9	Br	**9b**	2	80.7
4-CH_3	C_6H_5	Br	**9c**	2	89.3
4-CH_3	$(CH_2)_2OSi(CH_3)_2C(CH_3)_3$	Br	**9d**	2	43.2
4-CH_3	$(CH_2)_3OSi(CH_3)_2C(CH_3)_3$	Br	**9e**	1.5	71.4
4-CH_3	$(CH_2)_4C{\equiv}CSi(CH_3)_3$	Br	**9f**	4	51.9
4-Cl	n-C_3H_7	Br	**10a**	3.5	81.2
4-Cl	i-C_3H_7	Br	**10b**	2	76.4
4-Cl	n-C_4H_9	Br	**10c**	1.5	81.0
4-Cl	C_6H_5	Br	**10d**	1.5	77.1
4-OTf	i-C_3H_7	Br	**11a**	2	79.9
4-OTf	n-C_4H_9	Br	**11b**	2	83.9
4-OTf	C_6H_5	Br	**11c**	3	96.4
3-OTf	n-C_4H_9	Br	**12a**	3	36.2
3-OTf	C_6H_5	Br	**12b**	3	67.0

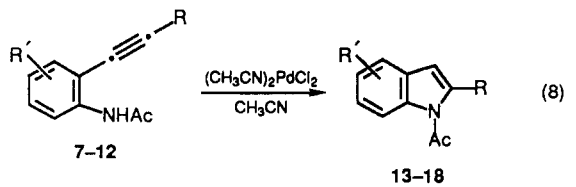
[a] Reactions were carried out at 100 °C using 2–5 mmol of reactant, 1.2 equiv of alkynylstannane, and 3 mol % $Pd(Ph_3P)_4$ in 20–40 mL of solvent. Dioxane was the solvent used for triflate coupling reactions with alkynylstannanes; toluene for all others. [b] 3 equiv of lithium chloride was added to the reactions in which the coupling at the triflate was effected to yield **7a–c**. [c] Yields are reported for isolated products and are unoptimized.

Table IV. Palladium-Catalyzed Cyclization of Substituted 2-Alkynylanilines to Indoles[a]

R′	R	product	t, h	% yield
6-CO_2CH_3	i-C_3H_7	**13a**	1.5	82.2
6-CO_2CH_3	n-C_4H_9	**13b**	1.75	71.4
6-CO_2CH_3	C_6H_5	**13c**	1.5	75.9
6-OCH_3	n-C_3H_7	**14a**	0.5	75.0
6-OCH_3	i-C_3H_7	**14b**	1	78.0
6-OCH_3	n-C_4H_9	**14c**	1.5	66.1
6-OCH_3	C_6H_5	**14d**	3	34.6[b]
5-CH_3	n-C_3H_7	**15a**	1	81.5
5-CH_3	n-C_4H_9	**15b**	0.5	77.4
5-CH_3	C_6H_5	**15c**	1.25	80.3
5-CH_3	$(CH_2)_2OSi(CH_3)_2C(CH_3)_3$	**15d**	1.5	37.0[b]
5-CH_3	$(CH_2)_3OSi(CH_3)_2C(CH_3)_3$	**15e**	2.5	35.2[b]
5-CH_3	$(CH_2)_4C{\equiv}CSi(CH_3)_3$	**15f**	5	40.0[b]
5-Cl	n-C_3H_7	**16a**	2.75	75.7
5-Cl	i-C_3H_7	**16b**	1.5	80.0
5-Cl	n-C_4H_9	**16c**	2	82.6
5-Cl	C_6H_5	**16d**	4	48.0[b]
5-OTf	i-C_3H_7	**17a**	3	40.0
5-OTf	n-C_4H_9	**17b**	2.5	64.6
5-OTf	C_6H_5	**17c**	3.5	52.7

[a] Reactions were carried out in acetonitrile at 60 °C using 10 mol % $(CH_3CN)_2PdCl_2$. The reaction was complete when TLC showed disappearance of starting material. Yields are for isolated products. [b] Starting material also was isolated.

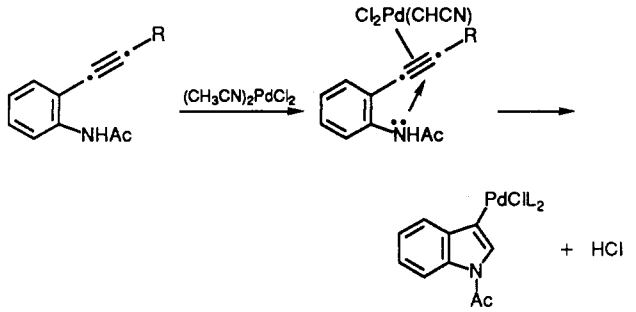
The cyclization of the 2-alkynylanilines (**7–12**) gave the disubstituted indoles (eq 8, Table IV). Substituents on the ethynyl group appear to have the greatest effect on the reaction rate. Only moderate yields of indoles **14d**, **15d–f**,



7–12 **13–18** (8)

and **16d** were obtained after 2.5–4 h, starting material being recovered in all cases. Aniline precursors to indoles **15d–f** containing silyl protecting groups as well as several

Scheme I



examples of phenylalkynylanilines, **8d** and **10d** (precursors to **14d** and **16d**) did not undergo efficient cyclization. In addition, alkynylanilines substituted in the 3-position cyclized slowly, giving low yields of indoles after 4 h.

The mechanism for this cyclization (Scheme I) undoubtedly requires nucleophilic attack by nitrogen on the complexed alkyne. Cleavage of the palladium carbon bond with the HCl produced gave the indole and regenerated the palladium(II) catalyst. Alternatively, an intermediate palladium(IV) dichlorohydridopalladium indole complex may be generated that can undergo reductive elimination, regenerating the palladium(II) catalyst.

Although palladium(IV) complexes have been suggested as intermediates in coupling reactions of electrophiles with main group organometallic reagents[13] and there was strong evidence for their existence, only relatively recently have certain Pd(IV) complexes been isolated.[14] Since no overall oxidation of the acetylenic aniline occurs in its cyclization to the indole, reduction of the palladium does not take place in the cyclization reaction of anilines to indoles.

(13) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 4981.
(14) (a) Byers, P. K.; Canty, A. J.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Chem. Commun.* **1986**, *23*, 1722. (b) Byers, P. K.; Canty, A. J.; Crespo, M.; Puddephatt, R. J.; Scott, J. D. *Organometallics* **1988**, *6*, 1363. (c) Byers, P. K.; Canty, A. J. *J. Chem. Soc., Chem. Commun.* **1988**, 639. (d) Catellani, M.; Chivsoli, G. P. *J. Organomet. Chem.* **1988**, *346*, C35. (e) Crespo, M.; Puddephatt, R. J. *Organometallics* **1988**, *6*, 2548.

Thus, a reoxidant for palladium is not required in this cyclization, making this reaction a convenient method of preparing 2-substituted indoles.

Because the palladium-catalyzed coupling reaction of organostannanes with aryl halides or triflates takes place under mild reaction conditions, in the presence of a wide variety of functionality on either coupling partners, a variety of functionalized ethynylanilines can be synthesized. In addition many different acetylenic tin reagents can be synthesized and purified by conventional methods, including column chromatography. The palladium-catalyzed cyclization also takes place under mild conditions, tolerating functionality that otherwise might not survive cyclization reactions carried out under alternate conditions such as strong acid or base.[4]

Experimental Section

^{1}H NMR spectra were recorded on an IBM WP 200 (200 MHz) or an IBM 270 (270 MHz) spectrometer with either tetramethylsilane (0.00 ppm) or $CDCl_3$ (7.24 ppm) as internal standards. Infrared spectra were obtained on a Beckman 4250 spectrometer. Melting points were determined with a Melt-Temp capillary melting point apparatus and are reported uncorrected. Toluene, dioxane, and acetonitrile were obtained from Mallinckrodt and used without further purification. Column chromatographic purifications were performed with Woelm 230–400 mesh silica gel. The catalysts, tetrakis(triphenylphosphine)-palladium(0)[15] and bis(acetonitrile)palladium dichloride,[16] and the organic compounds, *N*-acetyl-2-bromoaniline,[17] 2-bromo-3-((trifluoromethyl)sulfonyl)aniline[6] and *N*-acetyl-2-bromo-4-methylaniline,[12] were prepared according to published procedures. Organostannanes, including tributylpentyn-1-ylstannane,[19] tributyl(phenylethynyl)stannane,[20] tributyl((trimethylsilyl)-ethynyl)stannane,[20] tributylhexyn-1-ylstannane,[21] and tributyl-(3-methylbutyn-1-yl)stannane,[19] were prepared by known procedures. Elemental analyses were performed by Atlantic Microlab, Atlanta, GA. High-resolution mass spectra (HRMS) were obtained from the Midwest Center for Mass Spectrometry at the University of Nebraska.

Tributyl{4-[(*tert*-butyldimethylsilyl)oxy]butyn-1-yl}-stannane. To a mixture of 2.61 g (37.3 mmol) of 1-butyn-4-ol and 5.62 g (37.3 mmol) of *tert*-butyldimethylsilyl chloride in 35 mL of methylene chloride at 0 °C was added, dropwise over 10 min, 3.64 mL (45.0 mmol) of pyridine. After 30 min, the solution was allowed to warm to ambient temperature, and after 14 h, 200 mL of water and 100 mL of methylene chloride was added. The methylene chloride layer was dried over sodium sulfate. The methylene chloride was removed under reduced pressure, and the product was purified by column chromatography on silica (15:1 hexane/EtOAc) to yield 6.49 g (94.5%) of product.

To a solution of 1.88 g (10.2 mmol) of the silyl-protected butynol in 20 mL of THF at 0 °C was added 6.36 mL of 1.6 M (10.2 mmol) butyllithium. After 45 min, 2.76 mL (10.2 mmol) of chlorotributylstannane was added dropwise. The mixture was allowed to warm to ambient temperature and stir for 16 h. To the mixture was added 75 mL of methylene chloride, and the organic solution was washed twice with 75 mL of water. The organic layer was dried over sodium sulfate, and the solvent was removed under reduced pressure. Column chromatography on silica using hexane to elute the product gave 2.69 g (55.9%) of product: IR (neat) 2956, 2929, 2856, 2153, 1464, 1253, 1106, 837 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.70 (t, J = 7.3 Hz, 2 H), 2.44 (t, J = 7.3 Hz, 2 H), 1.52 (m, 6 H), 1.28 (m, 6 H), 0.89 (m, 24 H), 0.05 (s, 6 H). This compound was somewhat unstable and was prepared immediately before its use in the coupling reaction.

Tributyl{5-[(*tert*-butyldimethylsilyl)oxy]pentyn-1-yl}-stannane. To a solution of 11.85 g (85.3 mmol) of 3-bromopropanol and 13.5 g (89.5 mmol) of dimethyl-*tert*-butylsilyl chloride in 100 mL of methylene chloride at 0 °C was added 7.6 mL (93.8 mmol) and 30 mg of 4-(dimethylamino)pyridine. The mixture was allowed to come to ambient temperature and was stirred for 16 h. Water (50 mL) and 75 mL of ether were added, and the organic layer was washed with 10% aqueous HCl (2 × 50 mL) and 100 mL of water. The organic layer was dried over sodium sulfate. Removal of the solvent and distillation gave 20.4 g (94.6%) of product.

To a solution of 3.70 g (40.2 mmol) of lithium acetylide in 24 mL of DMSO at 0 °C was added dropwise (20 min) 8.86 g (35 mmol) of the silyl-protected bromo alcohol. The mixture was stirred overnight, and then ice was added. The mixture was extracted with ether (2 × 100 mL), and the combined organic layers were washed with saturated aqueous sodium chloride. The organic layer was dried over sodium sulfate and the solvent was removed in vacuo. The residue was chromatographed on silica gel (10:1 hexane/EtOAc) to yield 5.09 g (68.5%) of the silyl-protected 4-pentyn-1-ol. Anal. Calcd for $C_{11}H_{22}SiO$: C, 66.60; H, 11.18. Found: C, 66.42; H, 11.16.

To a solution of 1.10 g (5.97 mmol) of alkyne in 15 mL of THF at −78 °C was added 3.9 mL of 1.6 M (6.26 mmol) butyllithium. The mixture was allowed to stir for 2 h, and then 1.60 mL (5.97 mmol) of tributyltin chloride was added over 10 min. The mixture was allowed to come to ambient temperature and then stirred overnight. The addition of 150 mL of water and extraction with hexanes (2 × 100 mL) followed by washing the organic layer with 100 mL of saturated sodium chloride solution and 100 mL of water and drying the organic layer with sodium sulfate and removal of the solvent gave a yellow oil, which was purified by column chromatography on silica gel (8:1 hexane/EtOAc) to give 1.88 g (66.7%) of product: IR (neat) 2956, 2929, 2856, 2150, 1464, 1255, 1106, 846 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.68 (t, J = 6.1, 6.3 Hz, 2 H), 2.30 (t, J = 6.9, 7.0 Hz, 2 H), 1.69 (quin, 2 H), 1.50 (m, 6 H), 1.30 (m, 6 H), 0.83 (m, 24 H), 0.03 (s, 6 H). This compound was not stable enough to obtain a satisfactory elemental analysis, so it was prepared immediately before its use in the coupling reaction.

Tributyl[8-(trimethylsilyl)-1,7-octadiyn-1-yl]stannane. To a solution of 5.00 g (47.1 mmol) of 1,7-octadiyne in 50 mL of THF at −78 °C was added 14.7 mL of 1.6 M (23.5 mmol) butyllithium over 10 min. The mixture was allowed to stir for 20 min and then for 1 h at 0 °C. The solution was recooled to −78 °C, and 2.99 mL (23.5 mmol) of trimethylsilylchloride was added. The mixture was allowed to warm to ambient temperature and then stirred for 4 h. The addition of 150 mL of ether and 200 mL of water followed by drying of the organic layer over sodium sulfate, removing of the solvent, and purification of the residue by column chromatography (30:1 hexane/EtOAc) gave 5.42 g (64.5%) of product.

To a solution of 1.19 g (67.0 mmol) of monoprotected 1,7-octadiyne in 10 mL of THF at −78 °C was added 4.75 mL of 1.6 M (6.80 mmol) butyllithium, and the mixture was allowed to stir for 2 h. Tributylstannyl chloride (1.82 mL; 6.70 mmol) was added dropwise. The mixture was allowed to come to ambient temperature, and the mixture was stirred for 14 h. To this mixture was added 100 mL of water and 150 mL of hexane. The organic layer was dried over sodium sulfate, the solvent was removed under reduced pressure, and the residue was purified by column chromatography (20:1 hexane/EtOAc) to yield 2.96 g (94.6%) of product: IR (neat) 2956, 2928, 2871, 2854, 2176, 2151, 1464, 1249, 842 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.23 (m, 4 H), 1.58 (m, 4 H), 1.51 (m, 6 H), 1.29 (m, 6 H), 0.89 (m, 15 H), 0.12 (s, 9 H). This compound was not stable enough to obtain a satisfactory elemental analysis. Accordingly, it was prepared immediately before its use in the coupling reaction.

***N*-Acetyl-2-pentyn-1-ylaniline (2a).** A mixture of 1.001 g (4.68 mmol) of *N*-acetyl-2-bromoaniline, 2.005 g (5.614 mmol) tributylpentyn-1-ylstannane, and 0.162 g (0.140 mmol) of tetrakis(triphenylphosphine)palladium in toluene (50 mL) was heated at 100 °C for 2.5 h. The solvent was removed under reduced pressure. The resulting oil was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to yield **2a**, 0.724 g (76.9%), as a white crystalline solid: mp 72–73 °C; IR ($CHCl_3$) 3400, 2217,

(15) Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121.
(16) Doyle, J. R.; Slade, P. E.; Jonassen, H. B. *Inorg. Synth.* **1960**, *6*, 216.
(17) Loque, M. W.; Teng, K. *J. Org. Chem.* **1982**, *47*, 2549.
(18) Reference deleted on revision.
(19) Goure, W. F.; Wright, M. E.; Davis, P. D.; Labadie, S. S.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 6417.
(20) Loque, M. W.; Teng, K. *J. Org. Chem.* **1982**, *47*, 2549.
(21) Yamamoto, Y.; Nishi, S.; Yamada, J. *J. Am. Chem. Soc.* **1986**, *108*, 7116.

1680, 1565, 1500, 1430, 1351, 1290 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.35 (d, J = 8.3 Hz, 1 H), 7.92 (br s, 1 H), 7.33 (dd, J = 1.2, 7.6 Hz, 1 H), 7.26 (envelope, 1 H), 6.98 (t, J = 7.4, 7.6 Hz, 1 H), 2.47 (t, 2 H), 2.19 (s, 3 H), 1.66 (sext, 2 H), 1.07 (t, 3 H). Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51. Found: C, 77.39; H, 7.59.

***N*-Acetyl-2-(3-methylbutyn-1-yl)aniline (2b).** A mixture of 1.058 g (4.943 mmol) of *N*-acetyl-2-bromoaniline, 2.030 (5.684 mmol) of tributyl(3-methylbutyn-1-yl)stannane, and 0.171 g (0.148 mmol) of tetrakis(triphenylphosphine)palladium in toluene (50 mL) was heated at 100 °C for 2.5 h. The solvent was removed in vacuo. The resulting residue was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to give **2b**, 0.675 g (67.9%), as a white crystalline solid: mp 93–94 °C; IR ($CHCl_3$) 3403, 2219, 1695, 1580, 1522, 1450, 1368, 1320, 1306, 1266, 1155, 1038 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.34 (d, J = 8.2 Hz, 1 H), 7.92 (br s, 1 H), 7.28 (envelope, 2 H), 6.97 (dt, J = 1.0, 7.6 Hz, 1 H), 2.86 (sept, 1 H), 2.19 (s, 3 H), 1.30 (d, J = 6.7 Hz, 6 H). Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51. Found: C, 77.64; H, 7.54.

***N*-Acetyl-2-hexyn-1-ylaniline (2c).** A mixture of 0.846 g (3.95 mmol) of *N*-acetyl-2-bromoaniline, 1.61 g (4.35 mmol) of tributylhexyn-1-ylstannane, and 0.137 g (0.119 mmol) of tetrakis(triphenylphosphine)palladium in toluene (35 mL) was heated at 100 °C for 2 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (4:1 hexane/EtOAc) to give **2c**, 0.717 g (84.4%), as a white crystalline solid mp 46–47 °C; IR ($CHCl_3$) 3400, 2211, 1668, 1550, 1492, 1420, 1338, 1277, 1237, 1008 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.36 (d, J = 8.1 Hz, 1 H), 7.94 (br s, 1 H), 7.36 (dd, J = 1.1, 7.8 Hz), 7.28 (t, J = 7.8 Hz, 1 H), 6.99 (t, J = 7.5, 7.6 Hz, 1 H), 2.51 (t, 2 H), 2.21 (s, 3 H), 1.57 (m, 4 H), 0.98 (t, 3 H). Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96. Found: C, 77.93; H, 7.95.

***N*-Acetyl-2-(phenylethynyl)aniline (2d).** A mixture of 0.638 g (2.98 mmol) of *N*-acetyl-2-bromoaniline, 1.40 g (3.58 mmol) of tributyl(phenylethynyl)stannane, and 0.103 g (0.089 mmol) of tetrakis(triphenylphosphine)palladium in toluene (25 mL) was heated at 100 °C for 5 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (4:1 hexane/EtOAc) to give **2d**, 0.913 g (94.2%), as a white fibrous solid: mp 119–120 °C; IR ($CHCl_3$) 3400, 2193, 1685, 1568, 1509, 1480, 1440, 1309, 1296 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.41 (d, J = 8.4 Hz, 1 H), 7.98 (br s, 1 H), 7.53 (m, 3 H), 7.39 (m, 4 H), 7.08 (t, J = 7.4, 7.6 Hz, 1 H), 2.25 (s, 3 H). Anal. Calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57. Found: C, 81.51; H, 5.58.

***N*-Acetyl-2-[3-(tetrahydro-2*H*-pyranyloxy)propyn-1-yl]aniline (2e).** A mixture of 0.609 g (2.84 mmol) of *N*-acetyl-2-bromoaniline, 0.162 g (2.71 mmol) of tributyl[3-(tetrahydro-2*H*-pyranyloxy)propyn-1-yl]stannane and 0.099 g (0.085 mmol) of tetrakis(triphenylphosphine)palladium in toluene (22 mL) was heated at 110 °C for 6 h. The solvent was removed in vacuo, and the resulting oil was purified by column chromatography on silica gel (2:1 hexane/EtOAc) to give **2e**, 0.591 g (76.0%), as a white crystalline solid: mp 62.5–64.5 °C; IR ($CHCl_3$) 3404, 2213, 1697, 1570, 1516, 1446, 1367, 1300, 1112, 1016 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.37 (d, J = 8.3 Hz, 1 H), 7.99 (br s, 1 H), 7.36 (t, J = 7.3, 9.0 Hz, 1 H), 7.27 (envelope, 1 H), 7.00 (dt, J = 0.9, 7.4, 7.5 Hz), 4.90 (m, 1 H), 4.54 (s, 2 H), 3.89 (m, 1 H), 3.56 (m, 1 H), 2.21 (s, 3 H), 1.67 (m, 6 H); HRMS calcd for $C_{16}H_{19}NO_3$ 273.1365, found 273.1376.

***N*-Acetyl-2-[(trimethylsilyl)ethynyl]aniline (2f).** A mixture of 0.916 g (4.28 mmol) of *N*-acetyl-2-bromoaniline, 1.91 g (4.92 mmol) of tributyl[(trimethylsilyl)ethynyl]stannane, and 0.148 g (0.128 mmol) of tetrakis(triphenylphosphine)palladium in toluene (45 mL) was heated at 100 °C for 2.75 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (8:1 hexane/EtOAc) to yield **2f**, 0.939 g (94.8%), as an off-white crystalline solid: mp 94.5–95.5 °C; IR ($CHCl_3$) 3402, 2148, 1595, 1480, 1422, 1344, 1265, 1153, 1116, 1055, 997, 934 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.38 (d, J = 8.2 Hz, 1 H), 7.99 (br s, 1 H), 7.37 (d, J = 7.6 Hz, 1 H), 7.32 (t, J = 7.6, 7.4 Hz, 1 H), 7.01 (t, J = 7.6, 7.4 Hz, 1 H), 2.21 (s, 3 H), 0.30 (s, 9 H). Anal. Calcd for $C_{13}H_{17}NOSi$: C, 67.49; H, 7.41. Found: C, 67.33; H, 7.42.

***N*-Acetyl-2-(*cis*-4-methoxy-3-buten-1-ynyl)aniline (2g).** A mixture of 0.45 g (2.10 mmol) of *N*-acetyl-2-bromoaniline, 0.970 g (2.61 mmol) of tributyl(*cis*-1-methoxy-3-buten-1-yl)stannane, and 0.073 g (0.063 mmol) of tetrakis(triphenylphosphine)palladium in toluene (20 mL) was heated at 100 °C for 2.25 h. The solvent was removed under reduced pressure. Purification of the resulting oil by column chromatography on silica gel (5:2 hexane/EtOAc) yielded **2g**, 0.330 g (72.8%), as an off-white solid: mp 87.5–88.5 °C; IR ($CHCl_3$) 3379, 2190, 1695, 1632, 1579, 1525, 1455, 1444, 1310, 1304, 1262, 1099 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.41 (d, J = 8.2 Hz, 1 H), 8.27 (br s, 1 H), 7.34 (dd, J = 1.5, 7.6 Hz, 1 H), 7.28 (dt, J = 1.5, 7.3, 8.2 Hz, 1 H), 7.00 (dt, J = 1.2, 7.6 Hz, 1 H), 6.43 (d, J = 6.3 Hz, 1 H), 4.82 (d, J = 6.3 Hz, 1 H), 3.84 (s, 3 H), 2.23 (s, 3 H). Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09. Found: C, 72.30; H, 6.12.

***N*-Acetyl-2-{4-[(*tert*-butyldimethylsilyl)oxy]butyn-1-yl}aniline (2h).** A mixture of 0.508 g (2.37 mmol) of *N*-acetyl-2-bromoaniline, 1.348 g (2.85 mmol) of tributyl{4-[(*tert*-butyldimethylsilyl)oxy]butyn-1-yl}stannane and 0.082 g (0.071 mmol) of tetrakis(triphenylphosphine)palladium in toluene (30 mL) was heated at 100 °C for 1.75 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to give **2h**, 0.402 g (53.4%), as a white crystalline solid: mp 61.5–62 °C; IR ($CHCl_3$) 3391, 2221, 1690, 1575, 1511, 1440, 1299, 1251, 1093 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.34 (d, J = 8.3 Hz, 1 H), 7.92 (br s, 1 H), 7.33 (dd, J = 1.5, 7.6 Hz, 1 H), 7.25 (dt, 1 H), 6.97 (t, J = 7.6, 6.8 Hz, 1 H), 3.83 (t, J = 6.7 Hz, 2 H), 2.68 (t, J = 6.7 Hz, 2 H), 2.18 (s, 3 H), 0.89 (s, 9 H), 0.08 (s, 6 H). Anal. Calcd for $C_{18}H_{27}NO_2Si$: C, 68.09; H, 8.57. Found: C, 67.82; H, 8.51.

***N*-Acetyl-2-(3-methoxypropyn-1-yl)aniline (2i).** A mixture of 0.498 g (2.33 mmol) of *N*-acetyl-2-bromoaniline, 1.044 g (2.91 mmol) of tributyl(3-methoxypropyn-1-yl)stannane, 0.081 g (0.070 mmol) of tetrakis(triphenylphosphine)palladium in toluene (30 mL) was heated at 100 °C for 3.5 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (3:1 hexane/EtOAc) to give **2i**, 0.284 g (60.0%), as a white crystalline solid: mp 82.5–84 °C; IR ($CHCl_3$) 3400, 2210, 1694, 1577, 1442, 1300, 1085 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.36 (d, J = 8.3 Hz, 1 H), 7.84 (br s, 1 H), 7.41 (d, J = 7.7 Hz, 1 H), 7.32 (t, J = 7.7, 8.1 Hz, 1 H), 7.01 (t, J = 7.7 Hz, 1 H), 4.38 (s, 2 H), 3.46 (s, 3 H), 2.21 (s, 3 H). Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45. Found: C, 70.75; H, 6.49.

***N*-Acetyl-2-ethynylaniline (2j).** To a solution of 0.226 g (0.977 mmol) of *N*-acetyl-2-[(trimethylsilyl)ethynyl]aniline in 2 mL of methanol was added 0.014 g (0.071 mmol) of potassium carbonate, and the mixture was allowed to stir for 1.3 h at 23 °C. The solvent was removed under reduced pressure. The resulting solid was purified by column chromatography on silica gel (3:1 hexane/EtOAc) to yield **2j**,[22] 0.153 g (98.7%), as a colorless crystalline solid: mp 83–84 °C; IR ($CHCl_3$) 3408, 3304, 2089, 1695, 1581, 1517, 1443, 1364, 1302 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.38 (d, J = 8.4 Hz, 1 H), 7.88 (br s, 1 H), 7.43 (dd, J = 1.5, 7.7 Hz, 1 H), 7.34 (dt, J = 1.5, 7.1, 8.4 Hz, 1 H), 7.02 (dt, J = 1.0, 7.4, 7.7 Hz, 1 H), 3.48 (s, 1 H), 2.21 (s, 3 H). Anal. Calcd for $C_{10}H_9NO$: C, 75.45; H, 5.70. Found: C, 75.54; H, 5.71.

***N*-Acetyl-2-*n*-propylindole (3a).** To a solution of 0.173 g (0.860 mmol) of *N*-acetyl-2-pentyn-1-ylaniline and acetonitrile (6 mL) was added 0.022 g (0.086 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 1.5 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (4:1 hexane/EtOAc) to yield **3a**, 0.146 g (84.3%), as a white crystalline solid: mp 73–74 °C [lit.[23] mp 68–71 °C]; IR ($CHCl_3$) 1708, 1593, 1570, 1462, 1437, 1379, 1370, 1315, 1302 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.84 (d, J = 1.1, 6.6 Hz, 1 H), 7.48 (dd, J = 2.4, 6.6 Hz, 1 H), 7.25 (envelope, 2 H), 6.43 (s, 2 H), 2.99 (t, 2 H), 2.77 (s, 3 H), 1.75 (sext, 2 H), 1.05 (t, 3 H). Anal. Calcd for $C_{13}H_{15}NO$: C, 77.56; H, 7.51. Found: C, 77.47; H, 7.53.

***N*-Acetyl-2-isopropylindole (3b).** To a solution of 0.355 g (1.76 mmol) of *N*-acetyl-2-(3-methylbutyn-1-yl)aniline and acetonitrile (15 mL) was added 0.023 g (0.088 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 1.5 h. The solvent was removed in vacuo. The resulting oil was purified by column chromatography on silica gel (4:1 hexane/EtOAc) to yield **3b**, 0.323 g (91.0%), as a colorless oil:

(22) Bogoradovskii, E. T.; Zavgorodnii, V. S.; Petrov, A. *Zh. Obshch. Khim.* **1977**, 1548.
(23) Itahara, T. *J. Org. Chem.* **1985**, *50*, 5277.

IR (neat) 1708, 1563, 1452, 1370, 1295, 1191 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.34 (d, J = 8.2 Hz, 1 H), 7.91 (br s, 1 H), 7.28 (envelope, 2 H), 6.98 (dt, J = 1.0, 7.6 Hz, 1 H), 2.86 (sept, 1 H), 2.19 (s, 3 H), 1.30 (d, J = 6.7 Hz, 1 H); HRMS calcd for $C_{13}H_{15}NO$ 201.1154, found 201.1156.

***N*-Acetyl-2-*n*-butylindole (3c).** To a solution of 0.298 g (1.38 mmol) of *N*-acetyl-2-hexyn-1-ylaniline and acetonitrile (8 mL) was added 0.036 g (0.14 mmol) bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 1.5 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to yield **3c**, 0.277 g (93.0%), as a white crystalline solid: mp 55–55.5 °C; IR ($CHCl_3$) 1702, 1460, 1371, 1310 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.84 (dd, J = 1.1, 8.1 Hz, 1 H), 7.48 (dd, J = 2.5, 7.7 Hz, 1 H), 7.24 (envelope, 2 H), 6.43 (s, 1 H), 3.02 (t, 2 H), 2.78 (s, 3 H), 1.71 (quin, 2 H), 1.48 (sext, 2 H), 0.98 (t, 3 H). Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96. Found: C, 78.00; H, 8.02.

***N*-Acetyl-2-phenylindole (3d).** To a solution of 0.088 g (0.374 mmol) *N*-acetyl-2-(phenylethynyl)aniline in acetonitrile (5 mL) was added 0.013 g (0.037 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 2.5 h. The solvent was removed in vacuo. The resulting oil was purified by column chromatography on silica gel (4:1 hexane/EtOAc) to yield **3d**, 0.061 g (69.3%), as a colorless oil:[15] IR (neat) 1706, 1602, 1491, 1452, 1369, 1300, 1260, 1199, 1084, 1021 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.35 (d, J = 8.2 Hz, 1 H), 7.53 (dt, J = 1.4, 7.7, 8.2 Hz, 1 H), 7.42 (envelope, 7 H), 7.30 (dt, J = 1.2, 8.2, 8.3 Hz, 1 H), 6.61 (s, 1 H), 2.06 (s, 3 H). Anal. Calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57. Found: C, 81.48; H, 5.47.

2-Nitro-4-carbomethoxyphenyl Trifluoromethanesulfonate. A solution of 4.51 g (15.87 mmol) of 4-carbomethoxyphenyl trifluoromethanesulfonate[11] and 4 mL of sulfuric acid was cooled to 0 °C. A solution of concentrated nitric acid (1.7 mL) and sulfuric acid (4 mL) was added dropwise over 15 min. The reaction mixture was stirred overnight at 23 °C. After 14 h, the reaction was poured into ice water (25 mL) and extracted into diethyl ether (50 mL) and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to yield a yellow oil. Purification using column chromatography on silica gel yielded 4.57 g (87%) as a light yellow oil: IR (neat) 1740, 1614, 1547, 1434, 1345, 1290, 1249, 1216, 1133, 1112, 1072, 910, 860 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.79 (d, J = 2.0 Hz, 1 H), 8.39 (dd, J = 2.0, 8.6 Hz, 1 H), 7.56 (d, J = 8.6 Hz, 1 H), 3.99 (s, 3 H). Anal. Calcd for $C_9H_6F_3NO_7S$: C, 32.84; H, 1.84. Found: C, 32.90; H, 1.84.

2-Amino-4-carbomethoxyphenyl Trifluoromethanesulfonate. A solution of 5.0 g (15.1 mmol) of 2-nitro-4-carbomethoxyphenyl trifluoromethanesulfonate in ethanol (55 mL) and acetic acid (55 mL) was treated with iron powder and heated to reflux. After 2 h the reaction mixture was cooled to 23 °C and diluted with water (200 mL). Neutralization of the solution with potassium carbonate (s) was followed by extraction with dichloromethane (3 × 75 mL). The combined organic layers were dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure to give a white solid. The solid was recrystallized from dichloromethane and hexane, which yielded 3.81 g (83.8%) as a white solid: mp 85–86 °C; IR ($CHCl_3$) 3504, 3412, 1732, 1623, 1417, 1317, 1298, 1242, 1132 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53 (d, J = 2.1 Hz, 1 H), 7.43 (dd, J = 2.1, 8.5 Hz, 1 H), 7.23 (d, J = 8.5 Hz, 1 H), 4.06 (br s, 2 H), 3.90 (s, 3 H). Anal. Calcd for $C_9H_8F_3NO_5S$: C, 36.13; H, 2.70. Found: C, 36.13; H, 2.72.

***N*-Acetyl-5-carbomethoxy-2-[(trifluoromethyl)sulfonyl]aniline (4).** To a solution of 0.790 g (2.63 mmol) of 2-amino-4-carbomethoxyphenyl trifluoromethanesulfonate in dichloromethane (20 mL) were added 10 mL of pyridine and 0.274 g (2.68 mmol) of acetic anhydride, and the mixture was stirred at 23 °C for 20 h. The mixture was washed with 10% aqueous hydrogen chloride (2 × 50 mL) followed by water (75 mL). The organic layer was dried with anhydrous sodium sulfate. The solvent was removed in vacuo, and the resulting solid was purified by column chromatography on silica gel to yield 4, 0.642 g (71.3%), as a white crystalline solid: mp 108–109 °C; IR ($CHCl_3$) 3283, 1725, 1604, 1531, 1425, 1299, 1139, 1113 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.14 (d, J = 2.0 Hz, 1 H), 8.03 (dd, J = 2.0, 8.5 Hz, 1 H), 7.30 (d, J = 8.5 Hz, 1 H), 3.92 (s, 3 H), 2.35 (s, 3 H). Anal. Calcd for $C_{11}H_{10}F_3NO_6S$: C, 38.72; H, 2.95. Found: C, 38.73; H, 2.95.

4-Bromo-3-nitroanisole. A solution of 7.00 g (41.6 mmol) of 4-methoxy-2-nitroaniline in water (50 mL) and dioxane (25 mL) was heated until a homogeneous solution was obtained. To this solution was added dropwise 48% hydrogen bromide (23 mL). After all the reagent was added, the mixture was cooled to 0 °C, and an aqueous solution of sodium nitrite, 2.87 g (41.6 mmol), was added dropwise over 30 min. The reaction was allowed to stir at 23 °C for 36 h. The reaction was extracted with dichloromethane (3 × 75 mL), and the combined organic layers were dried with anhydrous sodium sulfate. The solvent was removed under reduced pressure to give a red oil. Purification by column chromatography on silica gel (4:1 hexane/EtOAc) yielded (91.7%) of a red-orange oil: IR (neat) 1734, 1604, 1570, 1537, 1479, 1441, 1354, 1306, 1046, 1021 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.59 (d, J = 8.8 Hz, 1 H), 7.36 (d, J = 3.0 Hz, 1 H), 6.98 (dd, J = 3.0, 8.8 Hz, 1 H), 3.85 (s, 3 H). Anal. Calcd for $C_7H_6BrNO_3$: C, 37.23; H, 2.61. Found: C, 37.21; H, 2.70.

***N*-Acetyl-2-bromo-5-methoxyaniline (5).** A mixture of 4.10 g (17.7 mmol) of 4-bromo-3-nitrosanisole, acetic acid (45 mL), ethanol (45 mL), and 4.04 g (72.4 mmol) of iron powder was heated to 100 °C for 2 h. The mixture was cooled to 23 °C and diluted with water (200 mL). The mixture was neutralized with solid potassium carbonate and extracted with dichloromethane (3 × 150 mL). The organic layers were combined and dried with anhydrous sodium sulfate. The solvent was removed under reduced pressure to give 3.22 g of 2-bromo-5-methoxyaniline, which was used without further purification. To a solution of 3.22 g (15.9 mmol) of 2-bromo-5-methoxyaniline in dichloromethane (25 mL) were added 1.30 mL (16.14 mmol) of pyridine and 1.53 mL (16.14 mmol) of acetic anhydride, and the mixture was stirred for 15 h. The mixture was extracted with 10% aqueous hydrogen chloride (2 × 40 mL) and washed with water (100 mL). The organic layer was dried with anhydrous sodium sulfate, and the solvent was removed under reduced pressure. Purification of the resulting oil by column chromatography on silica gel (3:1 hexane/EtOAc) yielded **5**, 3.16 g (81.2%), as a white crystalline solid: mp 115–116 °C; IR ($CHCl_3$) 3408, 1695, 1591, 1521, 1459, 1415, 1241 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.04 (d, J = 2.5 Hz, 1 H), 7.56 (br s, 1 H), 7.36 (d, J = 9.0 Hz, 1 H), 6.54 (dd, J = 2.5, 9.0 Hz, 1 H), 3.78 (s, 3 H), 2.22 (s, 3 H). Anal. Calcd for $C_9H_{10}BrNO_2$: C, 44.29; H, 4.13. Found: C, 44.39; H, 4.17.

***N*-Acetyl-2-bromo-4-chloroaniline.** To a solution of 2.13 g (10.3 mmol) of 2-bromo-4-chloroaniline in dichloromethane (20 mL) were added 1.0 mL (12 mmol) of pyridine and 1.1 mL (12 mmol) of acetic anhydride, and the mixture was stirred at 23 °C for 19 h. The mixture was washed with 10% aqueous hydrogen chloride (2 × 50 mL) followed by water (75 mL). The organic layer was dried with anhydrous sodium sulfate. The solvent was removed in vacuo, and the resulting solid was recrystallized from a mixture of dichloromethane and hexanes to yield 2.51 g (97.9%) as a white crystalline solid: mp 133–134 °C; IR ($CHCl_3$) 3408, 1704, 1686, 1582, 1565, 1500, 1372, 1288 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.29 (d, J = 8.9 Hz, 1 H), 7.51 (d, J = 2.4 Hz, 1 H), 7.27 (dd, J = 2.4, 8.9 Hz, 1 H), 2.22 (s, 3 H). Anal. Calcd for $C_8H_7BrClNO$: C, 38.67; H, 2.84. Found: C, 38.55; H, 2.86.

3-Bromo-4-nitrophenyl Trifluoromethanesulfonate. To a mixture of 2.30 g (10.55 mmol) of 3-bromo-4-nitrophenol in dichloromethane (25 mL) was added 0.94 mL (11.6 mmol) of pyridine. The reaction was cooled to 0 °C, and 1.95 mL (11.6 mmol) of trifluoromethanesulfonic anhydride was added dropwise to the reaction mixture. The mixture was stirred for 19 h at 23 °C. Dichloromethane (25 mL) was added, and the mixture was washed with water (100 mL), and the organic layer was dried with anhydrous sodium sulfate. The solvent was removed in vacuo, and the resulting oil was purified by column chromatography on silica gel (3:1 hexane/EtOAc) to give 2.66 g (72.1%) as a yellow oil: IR (neat) 3097, 1592, 1574, 1539, 1460, 1433, 1422, 1349, 1133, 1121, 1028 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.98 (d, J = 9.0 Hz, 1 H), 7.70 (d, J = 2.7 Hz, 1 H), 7.42 (dd, J = 2.7, 9.0 Hz, 1 H); HRMS calcd for $C_7H_3BrF_3NO_5S$ 348.8868, found 348.8868.

2-Bromo-4-[(trifluoromethyl)sulfonyl]aniline. To a mixture of 2.66 g (7.60 mmol) of 3-bromo-4-nitropehnyl trifluoromethanesulfonate in absolute ethanol (20 mL) and glacial acetic acid (20 mL) was added 1.74 g (31.15 mmol) of iron powder, and the mixture was heated to reflux for 2.25 h. The mixture was

allowed to cool to 23 °C and diluted with water (100 mL). Solid potassium carbonate was added until the solution was neutralized. The mixture was extracted with dichloromethane (100 mL) and dried with anhydrous sodium sulfate. The solvent was removed in vacuo, and the resulting oil was purified by column chromatography on silica gel (7:1 hexane/EtOAc) to give 2.32 g (95.4%) as a white crystalline solid: mp 73–74 °C; IR ($CHCl_3$) 3500, 3410, 1585, 1489, 1425, 1410, 1140, 1130 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (d, J = 2.8 Hz, 1 H), 7.04 (dd, J = 2.8, 8.9 Hz, 1 H), 6.75 (d, J = 8.9 Hz, 1 H), 4.25 (br s, 2 H). Anal. Calcd for $C_7H_5BrF_3NO_3S$: C, 26.27; H, 1.57. Found: C, 26.30; H, 1.60.

***N*-Acetyl-2-bromo-4-[(trifluoromethyl)sulfonyl]aniline (6).** To a solution of 1.027 g (3.21 mmol) of 2-bromo-4-[(trifluoromethyl)sulfonyl]aniline in dichloromethane (8 mL) were added 0.29 mL (3.53 mmol) of pyridine and 0.33 mL (3.53 mmol) of acetic anhydride, and the mixture was stirred at 23 °C for 20 h. The mixture was washed with 10% aqueous hydrogen chloride (2 × 50 mL) followed by water (75 mL). The organic layer was dried with anhydrous sodium sulfate. The solvent was removed in vacuo, and the resulting oil was purified by column chromatography on silica gel (3:1 hexane/EtOAc) to yield **6**, 1.140 g (98.1%), as a white crystalline solid: mp 86–87 °C; IR ($CHCl_3$) 3410, 1710, 1698, 1592, 1508, 1430, 1394, 1295, 1133 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.49 (d, J = 9.3 Hz, 1 H), 7.61 (br s, 1 H), 7.47 (d, J = 2.8 Hz, 1 H), 7.23 (dd, J = 2.8, 9.3 Hz, 1 H), 2.25 (s, 3 H). Anal. Calcd for $C_9H_7BrF_3NO_4S$: C, 29.85; H, 1.95. Found: C, 29.75; H, 1.97.

***N*-Acetyl-2-bromo-3-[(trifluoromethyl)sulfonyl]aniline.** To a solution of 1.275 g (3.98 mmol) of 2-bromo-3-[(trifluoromethyl)sulfonyl]aniline in dichloromethane (12 mL) were added 0.37 mL (4.58 mmol) of pyridine and 0.43 mL (4.58 mmol) of acetic acid anhydride, and the mixture was stirred at 23 °C for 36 h. Dichloromethane (50 mL) was added to the reaction mixture and was washed with 10% aqueous hydrogen chloride (2 × 50 mL) followed by water (75 mL). The organic layer was dried using anydrous sodium sulfate. The solvent was removed in vacuo, and the resulting oil was purified by column chromatography on silica gel (3:1 hexane/EtOAc) to yield 1.144 g (79.3%) as a white crystalline solid: mp 100.5–102.5 °C; IR ($CHCl_3$) 3405, 1705, 1592, 1577, 1510, 1457, 1419, 1130, 1028, 1007, 906 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.41 (d, J = 8.3 Hz, 1 H), 7.7 (br s, 1 H), 7.38 (t, J = 8.3 Hz, 1 H), 7.09 (d, J = 8.3 Hz, 1 H), 2.26 (s, 3 H). Anal. Calcd for $C_9H_7BrF_3NO_4S$: C, 29.85; H, 1.95. Found: C, 29.68; H, 1.96.

***N*-Acetyl-2-pentyn-1-yl-5-carbomethoxyaniline (7a).** A mixture of 0.358 g (1.05 mmol) of *N*-acetyl-2-[(trifluoromethyl)sulfonyl]-5-carbomethoxyaniline, 0.140 g (3.14 mmol) of lithium chloride, 0.448 g (1.26 mmol) of tributyl(pentyn-1-yl)-stannane, and 0.036 g (0.031 mmol) of tetrakis(triphenylphosphine)palladium in dioxane was heated at 100 °C for 3 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (3:1 hexane/EtOAc) to yield **7a**: 0.198 g (73.1%), as a white crystalline solid: mp 130–131 °C; IR (CHCl3) 3397, 2205, 1724, 1708, 1688, 1564, 1525 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.97 (d, J = 1.5 Hz, 1 H), 7.91 (br s, 1 H), 7.67 (dd, J = 1.5, 8.1 Hz, 1 H), 7.39 (d, J = 8.1 Hz, 1 H), 3.88 (s, 3 H), 2.50 (t, 2 H), 2.21 (s, 3 H), 1.67 (sext, 2 H), 1.08 (t, 3 H). Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61. Found: C, 69.24; H, 6.58.

***N*-Acetyl-2-(3-methylbutyn-1-yl)-5-carbomethoxyaniline (7b).** A mixture of 0.866 g (2.53 mmol) of *N*-acetyl-2-[(trifluoromethyl)sulfonyl]-5-carbomethoxyaniline, 1.085 g (3.04 mmol) of tributyl(3-methylbutyn-1-yl)stannane, 0.338 g (7.59 mmol) of lithium chloride, and 0.088 g (0.076 mmol) of tetrakis(triphenylphosphine)palladium in dioxane (25 mL) was heated at 100 °C for 1.75 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to give **7b**, 0.506 g (77.1%), as a white fibrous solid: mp 125–126 °C; IR ($CHCl_3$) 3395, 2207, 1720, 1700, 1569, 1523, 1457, 1434, 1416, 1362, 1319, 1290, 1255, 1114, 1097, 1078 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.96 (d, J = 1.5 Hz, 1 H), 7.90 (br s, 1 H), 7.68 (dd, J = 1.5, 8.1 Hz, 1 H), 7.39 (d, J = 8.1 Hz, 1 H), 3.89 (s, 3 H), 2.89 (sept, 1 H), 2.21 (s, 3 H), 1.31 (d, J = 6.9 Hz, 1 H). Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61. Found: C, 69.38; H, 6.64.

***N*-Acetyl-2-hexyn-1-yl-5-carbomethoxyaniline (7c).** A mixture of 0.201 g (0.587 mmol) of *N*-acetyl-2-[(trifluoromethyl)sulfonyl]-5-carbomethoxyaniline, 0.078 g (1.76 mmol) of lithium chloride, 0.273 g (0.734 mmol) of tributyl(hexyn-1-yl)-stannane, and 0.020 g (0.018 mmol) of tetrakis(triphenylphosphine)palladium in dioxane (15 mL) was heated at 100 °C for 3 h. After cooling to 23 °C, dichloromethane (35 mL) was added to the mixture and washed with water (2 × 40 mL). The organic layer was dried using sodium sulfate. The solvent was removed under reduced pressure. The resulting oil was purified by column chromatography on silica gel (8:1 hexane/EtOAc) to yield **7c**, 0.142 g (88.2%), as a white crystalline solid: mp 128.5–129.5 °C; IR ($CHCl_3$) 3399, 2218, 1725, 1710, 1695, 1568, 1526, 1460, 1433, 1419, 1302, 1290, 1258, 1112, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.96 (d, J = 1.5 Hz, 1 H), 7.89 (br s, 1 H), 7.67 (dd, J = 1.5, 8.1 Hz, 1 H), 7.39 (d, J = 8.1 Hz, 1 H), 3.88 (s, 3 H), 2.52 (s, 2 H), 2.21 (s, 3 H), 1.57 (m, 4 H), 0.96 (t, 3 H). Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01. Found: C, 70.08; H, 6.96.

***N*-Acetyl-2-(phenylethynyl)-5-carbomethoxyaniline (7d).** A mixture of 0.333 g (0.973 mmol) of *N*-acetyl-2-[(trifluoromethyl)sulfonyl]-5-carbomethoxyaniline, 0.130 g (2.92 mmol) of lithium chloride, 0.457 g (1.117 mmol) of tributyl(phenylethynyl)stannane, and 0.034 g (0.029 mmol) of tetrakis(triphenylphosphine)palladium in dioxane (20 mL) was heated at 100 °C for 2 h. The crude product was extracted into dichloromethane (75 mL) and was washed with water (2 × 50 mL). The organic layer was dried using sodium sulfate. The solvent was removed under reduced pressure. The resulting solid was recrystallized from dichloromethane and hexane to yield **7d**, 0.238 g (83.5%), as a white crystalline solid: mp 187.5–189.5 °C; IR ($CHCl_3$) 3403, 2185, 1719, 1698, 1567, 1523, 1485, 1456, 1431, 1414, 1282, 1252, 1108 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.03 (d, 1 H), 7.96 (br s, 1 H), 7.76 (dd, J = 1.4, 8.1 Hz, 1 H), 7.56 (envelope, 3 H), 7.43 (m, 3 H), 3.94 (s, 3 H), 2.27 (s, 3 H); HRMS calcd for $C_{18}H_{15}NO_3$ 293.1052, found 293.1064.

***N*-Acetyl-2-[(trimethylsilyl)ethynyl]-5-carbomethoxyaniline (7e).** A mixture of 0.478 g (1.40 mmol) of *N*-acetyl-2-[(trifluoromethyl)sulfonyl]-5-carbomethoxyaniline, 0.186 g (4.19 mmol) of lithium chloride, 0.622 g (1.61 mmol) of tributyl[(trimethylsilyl)ethynyl]stannane, and 0.048 g (0.042 mmol) of tetrakis(triphenylphosphine)palladium in dioxane (25 mL) was heated at 100 °C for 1 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (9:2 hexane/EtOAc) to yield **7e** 0.393 g (97.3%), as a white crystalline solid: mp 87–88 °C; IR ($CHCl_3$) 3399, 2138, 1720, 1700, 1569, 1526, 1457, 1434, 1419, 1363, 1289, 1255, 1110, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.98 (d, J = 1.1 Hz, 1 H), 7.4 (br s, 1 H), 7.68 (dd, J = 1.1, 8.0 Hz, 1 H), 7.44 (d, J = 8.0 Hz, 1 H), 3.89 (s, 3 H), 2.21 (s, 3 H), 0.29 (s, 9 H). Anal. Calcd for $C_{15}H_{19}NO_3Si$: C, 62.25; H, 6.62. Found: C, 62.19; H, 6.66.

***N*-Acetyl-2-pentyn-1-yl-5-methoxyaniline (8a).** A mixture of 0.515 g (2.11 mmol) of *N*-acetyl-2-bromo-5-methoxyaniline, 1.017 g (2.85 mmol) of tributylpentyn-1-ylstannane, and 0.073 g (0.063 mmol) of tetrakis(triphenylphosphine)palladium in toluene (30 mL) was heated at 100 °C for 6 h. The solvent was removed in vacuo. The resulting residue was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to give **8a**, 0.343 g (70.3%), as a white crystalline solid: mp 62–63 °C; IR ($CHCl_3$) 3389, 2199, 1690, 1612, 1568, 1525, 1464, 1421, 1363, 1304, 1160, 1118, 1099, 1028, 1102 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.07 (d, J = 2.7 Hz, 1 H), 7.97 (br s, 1 H), 7.26 (d, J = 8.6 Hz, 1 H), 6.55 (dd, J = 2.7, 8.6 Hz, 1 H), 3.81 (s, 3 H), 2.47 (t, 2 H), 2.21 (s, 3 H), 1.67 (sext, 2 H), 1.09 (t, 3 H). Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41. Found: C, 72.76; H, 7.44.

***N*-Acetyl-2-(3-methylbutyn-1-yl)-5-methoxyaniline (8b).** A mixture of 0.510 g (2.09 mmol) of *N*-acetyl-2-bromo-5-methoxyaniline, 1.102 g (3.09 mmol) of tributyl(3-methylbutyn-1-yl)stannane, and 0.096 g (0.083 mmol) of tetrakis(triphenylphosphine)palladium in toluene (25 mL) was heated at 100 °C for 3.5 h. The solvent was removed under reduced pressure. The resulting oil was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to give **8b**, 0.273 g (56.5%), as an off-white crystalline solid: mp 58.5–59.5 °C; IR ($CHCl_3$) 3397, 1692, 1616, 1569, 1532, 1468, 1423, 1363, 1303, 1161, 1116, 1083, 1031, 1001 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.05 (d, J = 2.5 Hz, 1 H), 7.94 (br s, 1 H), 7.23 (d, J = 8.5 Hz, 1 H), 6.53 (dd, J = 2.5, 8.5 Hz, 1 H), 3.79 (s, 3 H), 2.84 (sept, 1 H), 2.19 (s, 3 H), 1.29 (d, J = 6.8 Hz, 1 H).

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41. Found: C, 72.66; H, 7.42.

***N*-Acetyl-2-hexyn-1-yl-5-methoxyaniline (8c).** A mixture of 0.885 g (3.63 mmol) of *N*-acetyl-2-bromo-5-methoxyaniline, 1.615 g (4.35 mmol) of tributylhexyn-1-ylstannane, and 0.126 g (0.109 mmol) of tetrakis(triphenylphosphine)palladium in toluene (35 mL) was heated for 6 h at 110 °C. The solvent was removed in vacuo. The resulting oil was purified by column chromatography on silica gel (4:1 hexane/EtOAc) to yield **8c**, 0.547 g (61.5%), as a white crystalline solid: mp 47.5–49 °C; IR ($CHCl_3$) 3394, 2205, 1689, 1615, 1574, 1530, 1519, 1465, 1442, 1429, 1420, 1363, 1302, 1285, 1231, 1159, 1115, 1098, 1031, 1002 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.05 (d, J = 2.4 Hz, 1 H), 7.93 (br s, 1 H), 7.23 (d, J = 8.5 Hz, 1 H), 6.53 (dd, J = 2.4, 8.5 Hz, 1 H), 3.79 (s, 3 H), 2.47 (t, 2 H), 2.19 (s, 3 H), 1.57 (m, 4 H), 0.95 (t, 3 H). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81. Found: C, 73.37; H, 7.85.

***N*-Acetyl-2-(phenylethynyl)-5-methoxyaniline (8d).** A mixture of 0.546 g (2.24 mmol) of *N*-acetyl-2-bromo-5-methoxyaniline, 1.175 g (3.00 mmol) of tributyl(phenylethynyl)stannane, and 0.118 g (0.103 mmol) of tetrakis(triphenylphosphine)palladium in toluene (30 mL) was heated at 100 °C for 5 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (4:1 hexane/EtOAc) to yield **8d**, 0.449 g (75.7%), as a white crystalline solid: mp 119–120 °C; IR ($CHCl_3$) 3395, 2189, 1688, 1610, 1590, 1571, 1518, 1483, 1460, 1422, 1360, 1311, 1291, 1160, 1098, 1084, 1024, 1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.10 (d, J = 2.4 Hz, 1 H), 7.97 (br s, 1 H), 7.49 (m, 2 H), 7.37 (envelope, 4 H), 6.61 (dd, J = 2.4, 8.5 Hz, 1 H), 3.82 (s, 3 H), 2.23 (s, 3 H); HRMS calcd for $C_{17}H_{15}NO_2$ 265.1103, found 265.1106.

***N*-Acetyl-2-pentyn-1-yl-4-methylaniline (9a).** A mixture of 0.618 g (2.71 mmol) of *N*-acetyl-2-bromo-4-methylaniline, 1.21 g (3.39 mmol) of tributylpentyn-1-ylstannane, and 0.094 g (0.081 mmol) of tetrakis(triphenylphosphine)palladium in toluene (35 mL) was heated at 100 °C for 3.5 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (4:1 hexane/EtOAc) to give **9a** 0.377 g (64.7%), as a white crystalline solid: mp 89.5–90.5 °C; IR ($CHCl_3$) 3401, 2210, 1692, 1590, 1515, 1304 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.23 (d, J = 8.5 Hz, 1 H), 7.87 (br s, 1 H), 7.18 (s, 1 H), 7.08 (d, J = 8.5 Hz, 1 H), 2.48 (t, 2 H), 2.26 (s, 3 H), 2.19 (s, 3 H), 1.66 (sext, 2 H), 1.09 (t, 3 H). Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96. Found: C, 77.98; H, 8.00.

***N*-Acetyl-2-hexyn-1-yl-4-methylaniline (9b).** A mixture of 0.707 g (3.10 mmol) of *N*-acetyl-2-bromo-4-methylaniline, 1.38 g (3.72 mmol) of tributylhexyn-1-ylstannane, and 0.107 g (0.095 mmol) of tetrakis(triphenylphosphine)palladium in toluene (30 mL) was heated at 100 °C for 2 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to give **9b**, 0.574 g (80.7%), as a white crystalline solid: mp 85–86 °C; IR ($CHCl_3$) 3398, 2208, 1690, 1588, 1512, 1366, 1307 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.23 (d, J = 8.4 Hz, 1 H), 7.86 (br s, 1 H), 7.17 (s, 1 H), 7.08 (d, J = 8.4 Hz, 1 H), 2.50 (t, 2 H), 2.26 (s, 3 H), 2.19 (s, 3 H), 1.58 (m, 4 H), 0.98 (t, 3 H). Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35. Found: C, 78.42; H, 8.38.

***N*-Acetyl-2-(phenylethynyl)-4-methylaniline (9c).** A mixture of 0.761 g (3.34 mmol) of *N*-acetyl-2-bromo-4-methylaniline, 1.44 g (3.67 mmol) of tributyl(phenylethynyl)stannane, and 0.116 g (0.10 mmol) of tetrakis(triphenylphosphine)palladium in toluene (45 mL) was heated at 100 °C for 2 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to give **9c**, 0.743 g (89.3%), as a white crystalline solid: mp 128–129 °C; IR ($CHCl_3$) 3411, 2197, 1689, 1588, 1491, 1305 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.27 (d, J = 8.5 Hz, 1 H), 7.89 (br s, 1 H), 7.53 (m, 2 H), 7.39 (m, 3 H), 7.31 (d, J = 1.3 Hz, 1 H), 7.16 (dd, J = 1.3, 8.5 Hz, 1 H), 2.31 (s, 3 H), 2.23 (s, 3 H). Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06. Found: C, 81.64; H, 6.09.

***N*-Acetyl-2-{4-[(*tert*-butyldimethylsilyl)oxy]butyn-1-yl}-4-methylaniline (9d).** A mixture of 0.486 g (2.13 mmol) of *N*-acetyl-2-bromo-4-methylaniline, 1.26 g (2.66 mmol) of tributyl{4-[(*tert*-butyldimethylsilyl)oxy]butyn-1-yl}stannane, and 0.074 g (0.064 mmol) of tetrakis(triphenylphosphine)palladium in toluene (15 mL) was heated at 100 °C for 2 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to give **9d**, 0.305 g (43.2%), as a white crystalline solid: mp 117–118 °C; IR ($CHCl_3$) 3398, 1683, 1585, 1510, 1302 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.64 (d, J = 8.6 Hz, 1 H), 7.27 (envelope, 1 H), 7.06 (dd, J = 1.5, 8.6 Hz, 1 H), 6.40 (s, 1 H), 3.95 (t, 2 H), 3.24 (t, 2 H), 2.76 (s, 3 H), 2.43 (s, 3 H), 0.88 (s, 9 H), 0.02 (s, 6 H). Anal. Calcd for $C_{19}H_{29}NO_2Si$: C, 68.84; H, 8.82. Found: C, 68.90; H, 8.86.

***N*-Acetyl-2-{5-[(*tert*-butyldimethylsilyl)oxy]pentyn-1-yl}-4-methylaniline (9e).** A mixture of 0.635 g (2.78 mmol) of *N*-acetyl-2-bromo-4-methylaniline, 1.519 g (3.21 mmol) of tributyl{5-[(*tert*-butyldimethylsilyl)oxy]pentyn-1-yl}stannane, and 0.097 g (0.084 mmol) of tetrakis(triphenylphosphine)palladium in toluene (15 mL) was heated at 100 °C for 1.5 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to give **9e**, 0.687 g (71.4%), as a white crystalline solid: mp 80.5–81.5 °C; IR ($CHCl_3$) 3398, 2225, 1691, 1591, 1518, 1472, 1408, 1308, 1256, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.64 (d, J = 8.6 Hz, 1 H), 7.27 (envelope, 1 H), 7.06 (dd, J = 1.5, 8.6 Hz, 1 H), 6.40 (s, 1 H), 3.95 (t, 2 H), 3.24 (t, 2 H), 2.76 (s, 3 H), 2.43 (s, 3 H), 0.88 (s, 9 H), 0.02 (s, 6 H). Anal. Calcd for $C_{20}H_{31}NO_2Si$: C, 69.52; H, 9.04. Found: C, 69.26; H, 9.09.

***N*-Acetyl-2-[8-(trimethylsilyl)-1,7-octadiyn-1-yl)]-4-methylaniline (9f).** A mixture of 0.335 g (1.47 mmol) of *N*-acetyl-2-bromo-4-methylaniline, 1.037 g (2.22 mmol) of tributyl[8-(trimethylsilyl)-1,7-octadiyn-1-yl]stannane, and 0.060 g (0.052 mmol) of tetrakis(triphenylphosphine)palladium in toluene (12 mL) was heated at 100 °C for 4 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to give **9f**, 0.248 g (51.9%), as a white solid: mp 108–112 °C; IR ($CHCl_3$) 3398, 2172, 1691, 1590, 1517, 1458, 1438, 1429, 1368, 1308, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.21 (d, J = 8.6 Hz, 1 H), 7.82 (br s, 1 H), 7.15 (s, 1 H), 7.07 (d, J = 8.6 Hz, 1 H), 2.52 (t, 2 H), 2.29 (t, 2 H), 2.25 (s, 3 H), 2.19 (s, 3 H), 1.71 (m, 4 H), 0.12 (s, 9 H); HRMS calcd for $C_{20}H_{27}NOSi$ 325.1862, found 325.1868.

***N*-Acetyl-2-pentyn-1-yl-4-chloroaniline (10a).** A mixture of 0.818 g (3.29 mmol) of *N*-acetyl-2-bromo-4-chloroaniline, 1.470 g (4.11 mmol) of tributylpentyn-1-ylstannane, and 0.114 g (0.099 mmol) of tetrakis(triphenylphosphine)palladium in toluene (35 mL) was heated at 100 °C for 3.5 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to give **10a**, 0.630 g (81.2%), as a white crystalline solid: mp 106–107 °C; IR ($CHCl_3$) 3398, 2208, 1700, 1687, 1595, 1570, 1510, 1395, 1297 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.34 (d, J = 8.9 Hz, 1 H), 7.88 (br s, 1 H), 7.33 (d, J = 2.4 Hz, 1 H), 7.23 (dd, J = 2.4, 8.9 Hz, 1 H), 2.49 (t, 2 H), 2.21 (s, 3 H), 1.68 (sext, 2 H), 1.09 (t, 3 H). Anal. Calcd for $C_{13}H_{14}ClNO$: C, 66.24; H, 5.99. Found: C, 65.98; H, 5.94.

***N*-Acetyl-2-(3-methylbutyn-1-yl)-4-chloroaniline (10b).** A mixture of 0.961 g (3.87 mmol) of *N*-acetyl-2-bromo-4-chloroaniline, 1.588 g (4.45 mmol) of tributyl(3-methylbutyn-1-yl)-stannane, and 0.134 g (0.116 mmol) of tetrakis(triphenylphosphine)palladium in toluene (43 mL) was heated at 100 °C for 2 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to give **10b**, 0.697 g (76.4%), as a white crystalline solid: mp 121–122 °C; IR ($CHCl_3$) 3392, 2203, 1692, 1569, 1506, 1393, 1297 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.31 (d, J = 8.8 Hz, 1 H), 7.85 (br s, 1 H), 7.30 (d, J = 2.5 Hz, 1 H), 7.22 (dd, J = 2.5, 8.8 Hz, 1 H), 2.85 (hept, 1 H), 2.18 (s, 3 H), 1.29 (d, J = 6.09 Hz, 6 H). Anal. Calcd for $C_{13}H_{14}ClNO$: C, 66.24; H, 5.99. Found: C, 66.23; H, 6.00.

***N*-Acetyl-2-hexyn-1-yl-4-chloroaniline (10c).** A mixture of 1.083 g (4.36 mmol) of *N*-acetyl-2-bromo-4-chloroaniline, 1.860 g (5.01 mmol) of tributylhexyn-1-ylstannane, and 0.151 g (0.131 mmol) of tetrakis(triphenylphosphine)palladium in toluene (40 mL) was heated at 100 °C for 1.5 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (4:1 hexane/EtOAc) to give **10c**, 0.881 g (81.0%), as a white crystalline solid: mp 81–82 °C; IR ($CHCl_3$) 3396, 1690, 1570, 1509, 1396, 1299, 1292 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.32 (d, J = 8.9 Hz, 1 H), 7.86 (br s 1 H), 7.31 (d, J = 2.5 Hz, 1 H), 7.20 (dd, J = 2.5, 8.9 Hz, 1 H), 2.49 (t, 2 H), 2.19 (s, 3 H), 1.55 (m, 4 H), 0.97 (t, 3 H). Anal. Calcd for $C_{14}H_{16}ClNO$: C, 67.33; H, 6.46. Found: C, 67.41; H, 6.49.

N-Acetyl-2-(phenylethynyl)-4-chloroaniline (10d). A mixture of 0.900 g (3.162 mmol) of N-acetyl-2-bromo-4-chloroaniline, 1.629 g (4.16 mmol) of tributyl(phenylethynyl)stannane, and 0.125 g (0.109 mmol) of tetrakis(triphenylphosphine)palladium in toluene (30 mL) was heated at 100 °C for 1.5 h. The solvent was removed in vacuo, and the solid was recrystallized twice from a mixture of dichloromethane and hexanes to yield **10d**, 0.753 g (77.1%), as a white crystalline solid: mp 179–180.5 °C; IR ($CHCl_3$) 3392, 1698, 1690, 1570, 1500, 1484, 1395, 1296 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.37 (d, J = 8.9 Hz, 1 H), 7.90 (br s, 1 H), 7.51 (m, 2 H), 7.45 (d, J = 2.5, 1 H), 7.40 (m, 3 H), 7.28 (dd, J = 2.5, 8.9 Hz, 1 H), 2.23 (s, 3 H). Anal. Calcd for $C_{16}H_{12}ClNO$: C, 71.25; H, 4.48. Found: C, 71.15; H, 4.51.

N-Acetyl-2-(3-methylbutyn-1-yl)-4-[(trifluoromethyl)sulfonyl]aniline (11a). A mixture of 0.692 g (1.91 mmol) of N-acetyl-2-bromo-4-[(trifluoromethyl)sulfonyl]aniline, 0.819 g (2.29 mmol) of tributyl(3-methylbutyn-1-yl)stannane, and 0.066 g (0.057 mmol) of tetrakis(triphenylphosphine)palladium in toluene (15 mL) was heated at 100 °C for 2 h. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to give **11a**, 0.534 g (79.9%), as a white crystalline solid: mp 81–82 °C; IR ($CHCl_3$) 3395, 2222, 1699, 1520, 1422, 1142 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.47 (d, J = 9.2 Hz, 1 H), 7.92 (br s, 1 H), 7.23 (d, J = 2.8 Hz, 1 H), 7.15 (dd, J = 2.8, 9.2 Hz, 1 H), 2.87 (hept, 1 H), 2.21 (s, 3 H), 1.31 (d, J = 6.9 Hz, 6 H). Anal. Calcd for $C_{14}H_{14}F_3NO_4S$: C, 48.14; H, 4.04. Found: C, 48.05; H, 4.08.

N-Acetyl-2-hexyn-1-yl-4-[(trifluoromethyl)sulfonyl]aniline (11b). A mixture of 0.687 g (1.90 mmol) of N-acetyl-2-bromo-4-[(trifluoromethyl)sulfonyl]aniline, 0.845 g (2.28 mmol) of tributylhexyn-1-ylstannane, and 0.066 g (0.057 mmol) of tetrakis(triphenylphosphine)palladium in toluene (18 mL) was heated at 100 °C for 2 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to give **11b**, 0.578 g (83.9%), as a white crystalline solid: mp 73–74 °C; IR ($CHCl_3$) 3389, 2212, 1695, 1510, 1460, 1300, 1130, 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.49 (d, J = 9.3 Hz, 1 H), 7.94 (br s, 1 H), 7.27 (envelope, 1 H), 7.17 (dd, J = 2.8, 9.3 Hz, 1 H), 2.53 (t, 2 H), 2.23 (s, 3 H), 1.58 (m, 4 H), 0.98 (t, 3 H). Anal. Calcd for $C_{15}H_{16}F_3NO_4S$: C, 49.58; H, 4.44. Found: C, 49.82; H, 4.50.

N-Acetyl-2-(phenylethynyl)-4-[(trifluoromethyl)sulfonyl]aniline (11c). A mixture of 0.519 g (1.43 mmol) of N-acetyl-2-bromo-4-[(trifluoromethyl)sulfonyl]aniline, 0.645 g (1.65 mmol) of tributyl(phenylethynyl)stannane, and 0.050 g (0.043 mmol) of tetrakis(triphenylphosphine)palladium in toluene (12 mL) was heated at 100 °C for 3 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to give **11c**, 0.529 g (96.4%), as a white crystalline solid: mp 151–152.5 °C; IR ($CHCl_3$) 3402, 2189, 1702, 1578, 1510, 1485, 1460, 1420, 1292, 1134, 930 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.54 (d, J = 9.4 Hz, 1 H), 7.99 (br s, 1 H), 7.56 (m, 2 H), 7.50 (d, J = 2.8 Hz, 1 H), 7.44 (m, 3 H), 7.24 (envelope, 1 H), 2.27 (s, 3 H). Anal. Calcd for $C_{17}H_{12}F_3NO_4S$: C, 53.27; H, 3.16. Found: C, 52.98; H, 3.04.

N-Acetyl-2-hexyn-1-yl-3-[(trifluoromethyl)sulfonyl]aniline (12a). A mixture of 0.545 g (1.50 mmol) of N-acetyl-2-bromo-3-[(trifluoromethyl)sulfonyl]aniline, 0.642 g (1.73 mmol) of tributylhexyn-1-ylstannane, and 0.052 g (0.045 mmol) of tetrakis(triphenylphosphine)palladium in toluene (17 mL) was heated at 100 °C for 3 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (4:1 hexane/EtOAc) to give **12a**, 0.198 g (36.2%), as a white crystalline solid: mp 55.5–56.5 °C; IR ($CHCl_3$) 3389, 2203, 1700, 1569, 1511, 1456, 1418, 1295, 1131, 1010, 905 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.42 (d, J = 8.4 Hz, 1 H), 7.29 (br s, 1 H), 7.30 (t, J = 8.4 Hz, 1 H), 6.95 (d, J = 8.4 Hz, 1 H), 2.56 (t, 2 H), 2.22 (s, 3 H), 1.67 (m, 2 H), 1.51 (m, 2 H), 0.96 (t, 3 H). Anal. Calcd for $C_{15}H_{16}F_3NO_4S$: C, 49.58; H, 4.44. Found: C, 49.48; H, 4.45.

N-Acetyl-2-(phenylethynyl)-3-[(trifluoromethyl)sulfonyl]aniline (12b). A mixture of 0.658 g (1.82 mmol) of N-acetyl-2-bromo-3-[(trifluoromethyl)sulfonyl]aniline, 0.817 g (2.09 mmol) of tributyl(phenylethynyl)stannane, and 0.063 g (0.055 mmol) of tetrakis(triphenylphophine)palladium in toluene (25 mL) was heated at 100 °C for 3 h. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to give **12b**, 0.466 g (67.0%), as a white crystalline solid: mp 102–103 °C; IR ($CHCl_3$) 3398, 2198, 1709, 1697, 1572, 1515, 1485, 1460, 1419, 1437, 1131, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.46 (d, J = 8.5 Hz, 1 H), 7.98 (br s, 1 H), 7.58 (m, 2 H), 7.41 (m, 3 H), 7.38 (t, 1 H), 7.02 (d, J = 8.3 Hz, 1 H), 2.27 (s, 3 H). Anal. Calcd for $C_{17}H_{12}F_3NO_4S$: C, 53.27; H, 3.16. Found: C, 53.36; H, 3.21.

N-Acetyl-2-isopropyl-6-carbomethoxyindole (13a). To a solution of 0.107 g (0.413 mmol) of N-acetyl-2-(3-methylbutyn-1-yl)-5-carbomethoxyaniline and acetonitrile (4 mL) was added 11 mg (0.041 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 1.5 h. The solvent was removed in vacuo. The resulting oil was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **13a**, 0.088 g (82.2%), as a white crystalline solid: mp 67.5–68.5 °C; IR ($CHCl_3$) 1711, 1554, 1462, 1313, 1304, 1297, 1255, 1108 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.41 (d, J = 1.4 Hz, 1 H), 7.89 (dd, J = 1.4, 8.1 Hz, 1 H), 7.49 (d, J = 8.1 Hz, 1 H), 6.50 (s, 1 H), 3.92 (s, 3 H), 3.72 (hept, 1 H), 2.84 (s, 3 H), 1.30 (d, J = 6.8 Hz, 6 H). Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61. Found: C, 69.40; H, 6.61.

N-Acetyl-2-*n*-butyl-6-carbomethoxyindole (13b). To a solution of 0.091 g (0.333 mmol) of N-acetyl-2-hexyn-1-yl-5-carbomethoxyaniline and acetonitrile (3 ml) was added 9 mg (0.033 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 1.75 h. The solvent was removed in vacuo. The resulting oil was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **13b**, 0.065 g (71.4%), as a white crystalline solid: mp 91.5–92.5 °C; IR ($CHCl_3$) 1710, 1605, 1433, 1310, 1295 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.53 (d, J = 1.1 Hz, 1 H), 7.92 (s, 3 H), 7.49 (d, J = 8.1 Hz, 1 H), 6.46 (s, 1 H), 3.94 (s, 3 H), 3.04 (t, 2 H), 2.83 (s, 3 H), 1.71 (quint, 2 H), 1.47 (sext, 2 H), 0.98 (t, 3 H). Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01. Found: C, 70.27; H, 7.06.

N-Acetyl-2-phenyl-6-carbomethoxyindole (13c). To a solution of 0.158 g (0.539 mmol) of N-acetyl-2-(phenylethynyl)-5-carbomethoxyaniline and acetonitrile (6 ml) was added 0.014 g (0.054 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 1.5 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (3:1 hexane/EtOAc) to yield **13c**, 0.120 g (75.9%), as a white crystalline solid: mp 162–163 °C; IR ($CHCl_3$) 3011, 1710, 1599, 1426, 1417, 1359, 1301, 1269 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.00 (s, 1 H), 7.98 (dd, J = 1.1, 8.4 Hz, 1 H), 7.57 (d, J = 8.4 Hz, 1 H), 7.47 (s, 5 H), 6.64 (s, 1 H), 3.94 (s, 3 H), 2.09 (s, 3 H). Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15. Found: C, 73.48; H, 5.17.

N-Acetyl-2-*n*-propyl-6-methoxyindole (14a). To a solution of 0.112 g (0.484 mmol) of N-acetyl-2-pentyn-1-yl-5-methoxyaniline in acetonitrile (4 mL) was added 0.013 g (0.048 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 30 min. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **14a**, 0.084 g (75.0%), as a white crystalline solid: mp 74.5–75.5 °C; IR ($CHCl_3$) 1695, 1610, 1567, 1480, 1431, 1368, 1315, 1308, 1135 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.52 (d, J = 2.1 Hz, 1 H), 7.32 (d, J = 8.5 Hz, 1 H), 6.84 (dd, J = 2.1, 8.5 Hz, 1 H), 6.31 (s, 1 H), 3.85 (s, 3 H), 2.91 (t, 2 H), 2.70 (s, 3 H), 1.71 (sext, 2 H), 1.01 (t, 3 H). Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41. Found: C, 72.59; H, 7.45.

N-Acetyl-2-isopropyl-6-methoxyindole (14b). To a solution of 0.100 g (0.432 mmol) of N-acetyl-2-(3-methylbutyn-1-yl)-5-methoxyaniline and acetonitrile (4 ml) was added 0.011 g (0.043 mmol) bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 1 h. The solvent was removed under reduced pressure. The impure product was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to give **14b**, 0.078 g (78.0%), as a while crystalline solid: mp 61.5–62 °C; IR ($CHCl_3$) 1701, 1615, 1568, 1488, 1438, 1373, 1317, 1169 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.36 (envelope, 2 H), 6.83 (dd, J = 2.2, 8.5 Hz, 1 H), 6.37 (s, 1 H), 3.84 (s, 3 H), 3.62 (hept, 1 H), 2.74 (s, 3 H), 1.28 (d, J = 6.7 Hz, 6 H). Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41. Found: C, 72.89; H, 7.48.

N-Acetyl-2-*n*-butyl-6-methoxyindole (14c). To a solution of 0.112 g (0.457 mmol) of N-acetyl-2-hexyn-1-yl-5-methoxyaniline and acetonitrile (6 mL) was added 0.012 g (0.046 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 1.5 h. The solvent was removed under reduced

pressure. The impure product was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **14c**, 0.074 g (66.1%), as white crystalline needles mp 61–62 °C; IR ($CHCl_3$) 1703, 1614, 1571, 1486, 1440, 1431, 1371, 1318 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53 (d, J = 2.4 Hz, 1 H), 7.32 (d, J = 8.4 Hz, 1 H), 6.83 (dd, J = 2.4, 8.4 Hz, 1 H), 6.32 (s, 1 H), 3.85 (s, 3 H), 2.93 (t, 2 H), 2.70 (s, 3 H), 1.69 (m, 2 H), 1.44 (m, 2 H), 0.95 (t, 3 H). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81. Found: C, 73.50; H, 7.83.

***N*-Acetyl-2-phenyl-6-methoxyindole (14d).** To a solution of 0.107 g (0.403 mmol) of *N*-acetyl-2-(phenylethynyl)-5-methoxyaniline and acetonitrile (5 mL) was added 0.010 g (0.040 mmol) bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 3 h. The solvent was removed under reduced pressure. The impure product was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to give **14d**, 0.037 g (34.6%), as a white crystalline solid: mp 88–89 °C; IR ($CHCl_3$) 1691, 1600, 1477, 1426, 1358, 1300 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.96 (d, J = 2.3 Hz, 1 H), 7.42 (envelope, 6 H), 6.91 (dd, J = 2.3, 8.5 Hz, 1 H), 6.54 (s, 1 H), 3.88 (s, 3 H), 2.05 (s, 3 H). Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70. Found: C, 76.89; H, 5.74.

***N*-Acetyl-2-*n*-propyl-5-methylindole (15a).** To a solution of 0.151 g (0.701 mmol) of *N*-acetyl-2-(pentyn-1-yl)-4-methylaniline in acetonitrile (4 mL) was added 0.018 g (0.070 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 1 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **15a**, 0.123 g (81.5%), as a white crystalline solid: mp 92–93 °C; IR ($CHCl_3$) 1710, 1695, 1472, 1462, 1370, 1306 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.69 (d, J = 8.6 Hz, 1 H), 7.24 (envelope, 1 H), 7.05 (dd, J = 1.7, 8.6 Hz, 1 H), 6.34 (s, 1 H), 2.97 (t, 2 H), 2.74 (s, 3 H), 2.42 (s, 3 H), 1.73 (sext, 2 H), 1.03 (t, 3 H). Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96. Found: C, 78.00; H, 8.00.

***N*-Acetyl-2-*n*-butyl-5-methylindole (15b).** To a solution of 0.133 g (0.580 mmol) of *N*-acetyl-2-hexyn-1-yl-4-methylaniline in acetonitrile (4 mL) was added 0.015 g (0.058 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 30 min. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **15b**, 0.103 g (77.4%), as a white crystalline solid: mp 68.5–69.5 °C; IR ($CHCl_3$) 1692, 1471, 1462, 1364, 1302 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.70 (d, J = 8.6 Hz, 1 H), 7.26 (envelope, 1 H), 7.04 (dd, J = 1.5, 8.6 Hz, 1 H), 6.34 (s, 1 H), 2.99 (t, 2 H), 2.74 (s, 3 H), 2.42 (s, 3 H), 1.69 (hept, 2 H), 1.44 (sext, 2 H), 0.97 (t, 3 H). Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35. Found: C, 78.46; H, 8.36.

***N*-Acetyl-2-phenyl-5-methylindole (15c).** To a solution of 0.142 g (0.570 mmol) of *N*-acetyl-2-(phenylethynyl)-4-methylaniline in acetonitrile (4 mL) was added 0.015 g (0.057 mmol) of bis(acetonitrile)palladium dichloride and the mixture was heated at 80 °C for 1.25 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to yield **15c**, 0.114 g (80.3%), as a white crystalline solid: mp 71.5–72.5 °C; IR ($CHCl_3$) 1699, 1689, 1460, 1363, 1298, 1291 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.24 (d, J = 8.6 Hz, 1 H), 7.45 (m, 5 H), 7.35 (s, 1 H), 7.17 (d, J = 8.6 Hz, 1 H), 6.55 (s, 1 H), 2.46 (s, 3 H), 2.07 (s, 3 H). Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06. Found: 81.92; H, 6.10.

***N*-Acetyl-2-{2-[(*tert*-butyldimethylsilyl)oxy]ethyl}-5-methylindole (15d).** To a solution of 0.119 g (0.359 mmol) of *N*-acetyl-2-{4-[(*tert*-butyldimethylsilyl)oxy)]butyn-1-yl}-4-methylaniline in acetonitrile (4 mL) was added 9 mg (0.036 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 1.5 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to yield **15d**, 0.044 g (37.0%), as a colorless oil: IR 1705, 1472, 1370, 1305, 1099 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.62 (d, J = 8.5 Hz, 1 H), 7.25 (d, J = 1.6 Hz, 1 H), 7.04 (dd, J = 1.6, 8.5 Hz, 1 H), 6.37 (s, 1 H), 3.93 (t, 2 H), 3.22 (t, 2 H), 2.74 (s, 3 H), 2.40 (s, 3 H), 0.86 (s, 9 H), 0.00 (s, 6 H); HRMS calcd for $C_{19}H_{29}NO_2Si$ 331.1967, found 331.1970.

***N*-Acetyl-2-{3-[(*tert*-butyldimethylsilyl)oxy]propyl}-5-methylindole (15e).** To a solution of 0.128 g (0.37 mmol) of *N*-acetyl-2-{5-[(*tert*-butyldimethylsilyl)oxy]pentyn-1-yl}-4-methylaniline in acetonitrile (4 mL) was added 10 mg (0.037 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 2.5 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (6:1 hexane/EtOAc) to yield **15e**, 0.045 g (35.2%), as a slightly yellow oil: IR 1706, 1589, 1569, 1369, 1306, 1103 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.69 (d, J = 8.5 Hz, 1 H), 7.23 (envelope, 1 H), 7.03 (d, J = 8.5 Hz, 1 H), 6.33 (s, 1 H), 3.70 (t, 2 H), 3.04 (t, 2 H), 2.72 (s, 3 H), 2.40 (s, 3 H), 1.88 (quin, 2 H), 0.89 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H); HRMS calcd for $C_{20}H_{31}NO_2Si$ 345.2124, found 345.2120.

***N*-Acetyl-2-[6-(trimethylsilyl)hexyn-5-yl]-5-methylindole (15f).** To a solution of 0.050 g (0.154 mmol) of *N*-acetyl-2-[8-(trimethylsilyl)-1,7-octadiyn-1-yl]-4-methylaniline in acetonitrile (2 mL) was added 4 mg (0.015 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 5 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAce to yield **15f**, 0.020 g (40.0%), as a colorless oil: IR (neat) 2174, 1708, 1260, 1093, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.64 (d, J = 8.4 Hz, 1 H), 7.23 (envelope, 1 H), 7.03 (d, J = 8.4 Hz, 1 H), 6.34 (s, 1 H), 3.00 (t, 2 H), 2.73 (s, 3 H), 2.40 (s, 3 H), 2.27 (t, 2 H), 1.79 (sext, 2 H), 1.62 (sext, 2 H), 0.05 (s, 9 H); HRMS calcd for $C_{20}H_{27}NOSi$ 325.1862, found 325.1865.

***N*-Acetyl-2-*n*-propyl-5-chloroindole (16a).** To a solution of 0.115 g (0.49 mmol) of *N*-acetyl-2-pentyn-1-yl-4-chloroaniline in acetonitrile (7 mL) was added 0.013 g (0.049 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 2.75 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **16a**, 0.087 g (75.7%), as a white crystalline solid: mp 77–78 °C; IR ($CHCl_3$) 1707, 1582, 1444, 1368, 1300 cm^{-1}; ^1H NMR ($CDCl_3$) 7.80 (d, J = 8.9 Hz, 1 H), 7.41 d, J = 2.2 Hz, 1 H), 7.17 (dd, J = 2.2, 8.9 Hz, 1 H), 6.33 (s, 1 H), 2.94 (t, 2 H), 2.72 (s, 3 H), 1.72 (sext, 2 H), 1.02 (t, 3 H). Anal. Calcd for $C_{13}H_{14}ClNO$: C, 66.24; H, 5.99. Found: C, 66.00; H, 6.04.

***N*-Acetyl-2-*n*-butyl-5-chloroindole (16b).** To a solution of 0.115 g (0.46 mmol) of *N*-acetyl-2-hexyn-1-yl-4-chloroaniline and acetonitrile (6 mL) was added 0.012 g (0.046 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 2 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **16b**, 0.095 g (82.6%), as a white crystalline solid: mp 51–52.5 °C; IR ($CHCl_3$) 1710, 1702, 1586, 1445, 1370, 1303 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.81 (d, J = 9.0 Hz, 1 H), 7.43 (d, J = 2.1 Hz, 1 H), 7.19 (dd, J = 2.1, 9.0 Hz, 1 H), 6.36 (s, 1 H), 2.98 (t, 2 H), 2.74 (s, 3 H), 1.70 (sept, 2 H), 1.46 (sext, 2 H), 0.97 (t, 3 H). Anal. Calcd for $C_{14}H_{16}ClNO$: C, 67.33; H, 6.46. Found: C, 67.08; H, 6.41.

***N*-Acetyl-2-isopropyl-5-chloroindole (16c).** To a solution of 0.100 g (0.42 mmol) of *N*-acetyl-2-(3-methylbutyn-1-yl)-4-chloroaniline in acetonitrile (8 mL) was added 0.011 g (0.042 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 1.5 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **16c**, 0.080 g (80.0%), as an oil: IR ($CHCl_3$) 1708, 1598, 1580, 1460, 1362, 1296, 1270, 1188, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.65 (d, J = 8.8 Hz, 1 H), 7.42 (d, J = 2.1 Hz, 1 H), 7.16 (dd, J = 2.1, 8.8 Hz, 1 H), 6.39 (s, 1 H), 3.66 (hept, 1 H), 2.75 (s, 3 H), 1.29 (d, J = 6.7 Hz, 6 H); HRMS calcd for $C_{13}H_{14}ClNO$ 235.0764, found 235.0771.

***N*-Acetyl-2-phenyl-5-chloroindole (16d).** To a solution of 0.100 g (0.37 mmol) of *N*-acetyl-2-(phenylethynyl)-4-chloroaniline in acetonitrile (8 mL) was added 0.010 g (0.037 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 4 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to give **16d**, 0.048 g (48.0%), as a colorless oil: IR ($CHCl_3$) 1704, 1574, 1445, 1436, 1362, 1295 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.28 (d, J = 8.9 Hz, 1 H), 7.49 (d, J = 2.2 Hz, 1 H), 7.45 (s, 5 H), 7.27 (dd, J = 2.2, 8.9 Hz, 1 H), 6.53 (s, 1 H), 2.04 (s, 3 H); HRMS calcd for $C_{16}H_{12}ClNO$ = 269.0607, found 269.0609.

***N*-Acetyl-2-isopropyl-5-[(trifluoromethyl)sulfonyl]indole (17a).** To a solution of 0.170 g (0.49 mmol) of *N*-acetyl-2-(3-methylbutyn-1-yl)-4-[(trifluoromethyl)sulfonyl]aniline in acetonitrile (4 mL) was added 13 mg (0.049 mmol) of bis(aceto-

nitrile)palladium dichloride, and the mixture was heated at 80 °C for 3 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **17a**, 0.068 g (40.0%), as a white crystalline solid: mp 47–48 °C; IR ($CHCl_3$) 1714, 1609, 1596, 1460, 1421, 1374, 1306, 1282, 1141, 1107 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.81 (d, J = 9.1 Hz, 1 H), 7.37 (d, J = 2.6 Hz, 1 H), 7.11 (dd, J = 2.6, 9.1 Hz, 1 H), 6.49 (s, 1 H), 3.64 (sept, 1 H), 2.77 (s, 3 H), 1.31 (d, J = 6.7 Hz, 6 H). Anal. Calcd for $C_{14}H_{14}F_3NO_4S$: C, 48.14; H, 4.04. Found: C, 47.93; H, 3.97.

***N*-Acetyl-2-*n*-butyl-5-[(trifluoromethyl)sulfonyl]indole (17b).** To a solution of 0.144 g (0.396 mmol) of *N*-acetyl-2-hexyn-1-yl-4-[(trifluoromethyl)sulfonyl]aniline in acetonitrile (4 mL) was added 0.010 g (0.058 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 2.5 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **17b**, 0.093 g (64.6%), as a white crystalline solid: mp 69–70 °C; IR ($CHCl_3$) 1706, 1450, 1415, 1362, 1304, 1132, 1095, 940 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.98 (d, J = 9.2 Hz, 1 H), 7.35 (d, J = 2.6 Hz, 1 H), 7.11 (dd, J = 2.6, 9.2 Hz, 1 H), 6.43 (s, 1 H), 2.97 (t, 2 H), 2.73 (s, 3 H), 1.70 (quin, 2 H), 1.45 (sext, 2 H), 0.96 (t, 3 H). Anal. Calcd for $C_{15}H_{16}F_3NO_4S$: C, 49.58; H, 4.44. Found: C, 49.75; H, 4.46.

***N*-Acetyl-2-phenyl-5-[(trifluoromethyl)sulfonyl]indole (17c).** To a solution of 0.091 g (0.237 mmol) of *N*-acetyl-2-(phenylethynyl)-4-[(trifluoromethyl)sulfonyl]aniline in acetonitrile (3 mL) was added 6 mg (0.024 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 3.5 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **17c**, 0.048 g (52.7%), as a white crystalline solid: mp 87–87.5 °C; IR ($CHCl_3$) 1702, 1449, 1437, 1411, 1360, 1301, 1292, 1130, 1088, 939 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.43 (d, J = 8.9 Hz, 1 H), 7.48 (s, 5 H), 7.47 (d, J = 2.5 Hz, 1 H), 7.23 (dd, J = 2.5, 8.9 Hz, 1 H), 6.65 (s, 1 H), 2.06 (s, 3 H). Anal. Calcd for $C_{17}H_{12}F_3NO_4S$: C, 53.27; H, 3.16. Found: C, 53.37; H, 3.16.

***N*-Acetyl-2-*n*-butyl-4-[(trifluoromethyl)sulfonyl]indole (18a).** To a solution of 0.137 g (0.38 mmol) of *N*-acetyl-2-hexyn-1-yl-3-[(trifluoromethyl)sulfonyl]aniline in acetonitrile (3 mL) was added 10 mg (0.038 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 4 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **18a**, 0.031 g (22.6%), as an oil: IR (film) 1718, 1424, 1304, 1181, 1141 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.91 (d, J = 8.3 Hz, 1 H), 7.25 (t, J = 8.2, 8.3 Hz, 1 H), 7.18 (d, J = 8.2 Hz, 1 H), 6.50 (s, 1 H), 2.97 (t, 2 H), 2.75 (s, 3 H), 1.71 (quin, 2 H), 1.44 (sext, 2 H), 0.97 (t, 3 H); HRMS calcd for $C_{15}H_{16}F_3NO_4S$ 363.0752, found 363.0761.

***N*-Acetyl-2-phenyl-4-[(trifluoromethyl)sulfonyl]indole (18b).** To a solution of 0.141 g (0.37 mmol) of *N*-acetyl-2-(phenylethynyl)-3-[(trifluoromethyl)sulfonyl]aniline in acetonitrile (4 mL) was added 10 mg (0.037 mmol) of bis(acetonitrile)palladium dichloride, and the mixture was heated at 80 °C for 4 h. The solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel (5:1 hexane/EtOAc) to yield **18b**, 0.045 g (31.9%), as a white crystalline solid: mp 79.5–81 °C; IR ($CHCl_3$) 1712, 1458, 1422, 1370, 1304, 1246, 1141 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.36 (d, J = 8.3 Hz, 1 H), 7.48 (s, 5 H), 7.36 (t, J = 8.2, 8.3 Hz, 1 H), 7.22 (envelope, 1 H), 6.71 (s, 1 H), 2.07 (s, 3 H). Anal. Calcd for $C_{17}H_{12}F_3NO_4S$: C, 53.27; H, 3.16. Found: C, 53.16; H, 3.19.

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Registry No. 1, 614-76-6; **2a**, 90585-00-5; **2b**, 123027-90-7; **2c**, 116491-53-3; **2d**, 26385-33-1; **2e**, 123027-91-8; **2f**, 110598-59-9; **2g**, 123027-92-9; **2h**, 123027-93-0; **2i**, 123027-94-1; **2j**, 61403-29-0; **3a**, 90585-31-2; **3b**, 123051-57-0; **3c**, 116491-55-5; **3d**, 78388-91-7; **4**, 123027-98-5; **5**, 123027-99-6; **6**, 123028-02-4; **7a**, 123028-05-7; **7b**, 123028-06-8; **7c**, 123028-07-9; **7d**, 123028-08-0; **7e**, 123028-09-1; **8a**, 123028-10-4; **8b**, 123028-11-5; **8c**, 123028-12-6; **8d**, 123028-13-7; **9a**, 123028-14-8; **9b**, 123028-15-9; **9c**, 104683-00-3; **9d**, 123028-16-0; **9e**, 123028-17-1; **9f**, 123028-18-2; **10a**, 123028-19-3; **10b**, 123028-20-6; **10c**, 123028-21-7; **10d**, 123028-22-8; **11a**, 123028-23-9; **11b**, 123051-58-1; **11c**, 123028-24-0; **12a**, 123028-25-1; **12b**, 123028-26-2; **13a**, 123028-27-3; **13b**, 123028-28-4; **13c**, 123028-29-5; **14a**, 123028-30-8; **14b**, 123028-31-9; **14c**, 123051-59-2; **14d**, 123028-32-0; **15a**, 123028-33-1; **15b**, 123028-34-2; **15c**, 104683-04-7; **15d**, 123028-35-3; **15e**, 123028-36-4; **15f**, 123028-37-5; **16a**, 123028-38-6; **16b**, 123028-39-7; **16c**, 123028-40-0; **16d**, 123028-41-1; **17a**, 123028-42-2; **17b**, 123028-43-3; **17c**, 123028-44-4; **18a**, 123028-45-5; **18b**, 123028-46-6; $HC{\equiv}C(CH_2)_2OSi(Me)_2Bu$-t, 78592-82-2; $Bu_3SnC{\equiv}C(CH_2)_2OSi(Me)_2Bu$-t, 98155-22-7; $HC{\equiv}C(CH_2)_3OSi(Me)_2Bu$-t, 61362-77-4; $Br(CH_2)_3OSi(Me)_2Bu$-t, 89031-84-5; $Bu_3SnC{\equiv}C(CH_2)_3OSi(Me)_2Bu$-t, 123027-88-3; $HC{\equiv}C(CH_2)_4C{\equiv}CTMS$, 83182-85-8; $Bu_3SnC{\equiv}C(CH_2)_4C{\equiv}CTMS$, 123027-89-4; $Bu_3SnC{\equiv}C(CH_2)_3CH_3$, 86633-17-2; $Bu_3SnC{\equiv}CCH(CH_3)_2$, 58064-11-2; $Bu_3SnC{\equiv}C(CH_2)_3CH_3$, 35864-20-1; $Bu_3SnC{\equiv}CPh$, 3757-88-8; $Bu_3SnC{\equiv}CCH_2OTHP$, 109669-44-5; $Bu_3SnC{\equiv}CTMS$, 81353-38-0; *cis*-$Bu_3SnC{\equiv}CCH{=}CHOMe$, 123027-95-2; $Bu_3SnC{\equiv}CCH_2OMe$, 113794-24-4; $(CH_3CN)_2PolCl_2$, 14592-56-4; 1-butyn-4-ol, 927-74-2; 3-bromopropanol, 627-18-9; lithium acetaldehyde, 7447-41-8; 1,7-octadiyne, 871-84-1; 4-carbomethoxyphenyl trifluoromethanesulfonate, 17763-71-2; 2-nitro-4-carbomethoxyphenyl trifluoromethanesulfonate, 123027-96-3; 2-amino-4-carbomethoxyphenyl trifluoromethanesulfonate, 123027-97-4; 4-methoxy-2-nitroaniline, 96-96-8; 4-bromo-3-nitroanisole, 5344-78-5; 2-bromo-5-methoxyaniline, 59557-92-5; 2-bromo-4-chloroaniline, 873-38-1; *N*-acetyl-2-bromo-4-chloroaniline, 57045-85-9; 3-bromo-4-nitrophenol, 5470-65-5; 3-bromo-4-nitrophenyl trifluoromethanesulfonate, 123028-00-2; 2-bromo-4-[(trifluoromethyl)sulfonyl]aniline, 123028-01-3; 2-bromo-3-[(trifluoromethyl)sulfonyl]aniline, 123028-03-5; *N*-acetyl-2-bromo-3-[(trifluoromethyl]sulfonyl]-aniline, 123028-04-6; *N*-acetyl-2-bromo-4-methylaniline, 614-83-5.

Synthesis of (±)-2,3-Methanovaline and (±)-2,3-Methanoleucine

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The synthesis of racemic 2,3-methanovaline and 2,3-methanoleucine have been accomplished by dipolar addition of the appropriate diazocompounds to dehydroalanine derivatives followed by decomposition of the resulting pyrazolines. Both chemical and NMR evidence allowed assignment of configuration to the *E* and *Z* isomers of 2,3-methanoleucine.

The two aliphatic amino acids, valine and leucine, occupy an important place in peptide structure and function. They are often in conformation-controlling positions in peptide hormones such as angiotensin II and may appear at crucial enzymatic cleavage sites such as the Leu-Val site in human angiotensinogen, which affords angiotensin I. In our studies of the synthesis of conformationally constrained cyclopropane-containing amino acids, we felt it

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