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Platinum-Catalyzed, One-Pot Tandem Synthesis of Indoles and Isoquinolines via Sequential Rearrangement of Amides and Aminocyclization

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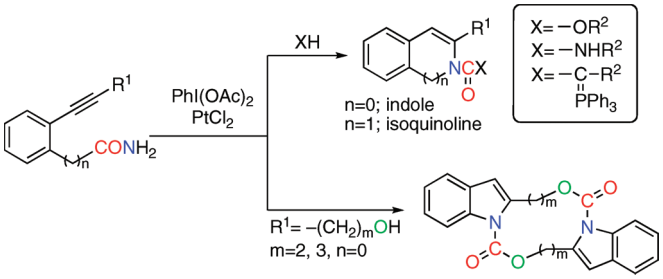

By using platinum(II) chloride as a Lewis acid catalyst, concise and efficient syntheses of indole carbamates, 1,2-dihydroisoquinoline carbamates, macrocyclic indole carbamates, indole ureas, and indole phosphoranes have been achieved via tandem Hofmann-type rearrangement of 2-alkynylbenzamides and 2-alkynylbenzylamides, nucleophilic addition of alcohols and amines to the isocyanate intermediates, and intramolecular aminocyclization of the thus-formed carbamates and ureas to 2-alkynyl functions. A variety of nucleophiles such as alcohols, amines, and stable Wittig reagents could be introduced to the highly electrophilic carbon of the isocyanate intermediates derived from amides. We observed enhancement of the reaction rates when the reactions were run under microwave irradiation.

Introduction

The development of tandem reactions for efficient construction of complex molecules is an important goal of organic synthesis from the viewpoint of operational simplicity and assembly efficiency. Since the indole and isoquinoline ring systems are key structural units for a variety of biologically important compounds, an efficient and expedient method to synthesize a wide variety of these classes of molecules would be highly desirable. Among available strategies, metal-catalyzed annulation processes have recently been proven to be powerful methods for the construction of these ring systems. Metal-catalyzed ring closure of 2-alkynylaniline and 2-alkynylbenzylamine derivatives **A** (Scheme 1) would be one of the most efficient approaches for the construction of benzo-fused *N*-containing heterocyclic compounds.[1,2] However, one drawback of the method is air instability of the amines. We became interested in using 2-alkynylbenzamide and 2-alkynylbenzylamide derivatives

(1) Indole synthesis: (a) Huang, N.-Y.; Liu, M.-G.; Ding, M.-W. *J. Org. Chem.* **2009**, *74*, 6874–6877. (b) Sakai, N.; Annaka, K.; Fujita, A.; Sato, A.; Konakahara, T. *J. Org. Chem.* **2008**, *73*, 4160–4165. (c) Ma, D.; Cai, Q. *Acc. Chem. Res.* **2008**, *41*, 1450–1460. (d) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410–3449. (e) Zhang, Y.; Donahue, J. P.; Li, C.-J. *Org. Lett.* **2007**, *9*, 627–630. (f) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*, 2875–2911. and references therein. (g) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079–3159. (h) Hiroya, K.; Itoh, S.; Sakamoto, T. *J. Org. Chem.* **2004**, *69*, 1126–1136. (i) Takeda, A.; Kamijo, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 5662–5663.

(2) Isoquinoline synthesis: (a) Enomoto, T.; Girard, A.-L.; Yasui, Y.; Takemoto, Y. *J. Org. Chem.* **2009**, *74*, 9158–9164. (b) Chen, Z.; Yang, X.; Wu, J. *Chem. Commun.* **2009**, 3469–3471. (c) Fischer, D.; Tomeba, H.; Pahadi, N. K.; Patil, N. T.; Huo, Z.; Yamamoto, Y. *J. Am. Chem. Soc.* **2008**, *130*, 15720–15725. (d) Obika, S.; Yasui, Y.; Yanada, R.; Takemoto, Y. *J. Org. Chem.* **2008**, *73*, 5206–5209. (e) Enomoto, T.; Obika, S.; Yasui, Y.; Takemoto, Y. *Synlett* **2008**, 1647–1650. (f) Gao, K.; Wu, J. *J. Org. Chem.* **2007**, *72*, 8611–8613. (g) Ding, Q.; Ye, Y.; Fan, R.; Wu, J. *J. Org. Chem.* **2007**, *72*, 5439–5442. (h) Su, S.; Porco, J. A., Jr. *Org. Lett.* **2007**, *9*, 4983–4986. (i) Ding, Q.; Wu, J. *Org. Lett.* **2007**, *9*, 4959–4962. (j) Obika, S.; Kono, H.; Yasui, Y.; Yanada, R.; Takemoto, Y. *J. Org. Chem.* **2007**, *72*, 4462–4468. (k) Yanada, R.; Obika, S.; Kono, H.; Takemoto, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 3822–3825. (l) Asao, N.; Yudha, S. S.; Nogami, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2005**, *44*, 5526–5528.

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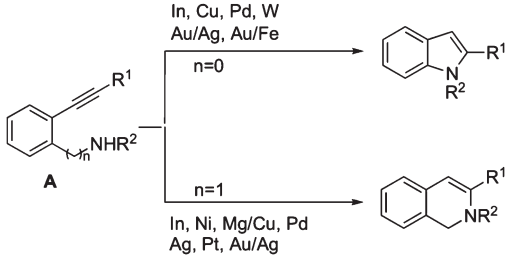
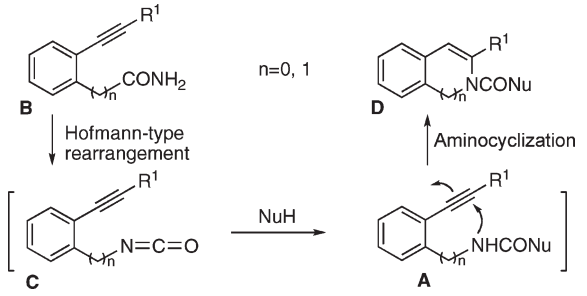
SCHEME 1. Metal-Catalyzed Synthesis of Indoles and Isoquinolines



SCHEME 2. Synthetic Strategy for the Constuction of Indoles and Isoquinolines



as substrates for the reaction since they can be converted to amine derivatives via a Hofmann-type rearrangement.

We have recently described in a communication the one-pot, platinum(II)-catalyzed tandem synthesis of indoles and isoquinolines starting from 2-alkynylbenzamides and 2-alkynylbenzylamides **B** (Scheme 2).[3] Therein, we described that isocyanate intermediates **C**[4,5] derived from a Hofmann-type rearrangement of amides **B** using hypervalent iodine reagents were superior substrates for the construction of heterocycles **D** through carbamate intermediates **A** obtained from the reaction with isocyanate intermediates **C** and alcohols; thus, the work showed that stable 2-alkynylamides **B** can be used as starting materials for the efficient one-pot synthesis of indoles and isoquinolines.

To further extend our method, we focused on reactions of different kinds of nucleophiles with isocyanate **C**. Herein, we present in greater detail our efforts to achieve platinum(II)-catalyzed one-pot concise tandem synthesis of indole carbamates, 1,2-dihydroisoquinoline carbamates, macrocyclic indole carbamates, indole ureas, and indole phosphoranes (Scheme 3).

Results and Discussion

Examination of Reaction Conditions. First, we examined the reaction conditions using 2-(1-hexynyl)benzamide **1a**. The results are shown in Table 1. Two basic procedures were examined: a stepwise procedure based on the formation of isocyanate **C** and its subsequent cyclization to **D** (entries 1 and 2) and a one-pot procedure (entries 3−10). The Hofmann-type rearrangement reaction of 2-(1-hexynyl)benzamide **1a** with $PhI(OAc)_2$ in 1,2-dichlorobenzene proceeded smoothly to give 2-(1-hexynyl)phenyl isocyanate **C** (n = 0, R^1 = Bu) within 2 h.[6,7] After completion of the Hofmann-type rearrangement was confirmed by thin-layer chromatography,[8] $PtCl_2$, ethanol, and triethylamine were added. Et_3N was used to neutralize the acetic acid formed during the reaction. This reaction did not proceed sufficiently, and a large amount of **3** remained (entry 1). Successful cyclization to indole **2a** with

SCHEME 3. Synthesis of Indole Carbamates, Ureas, and Phosphoranes

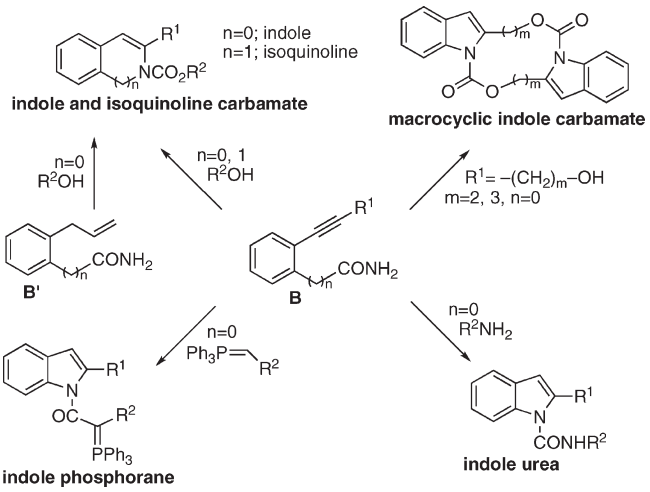
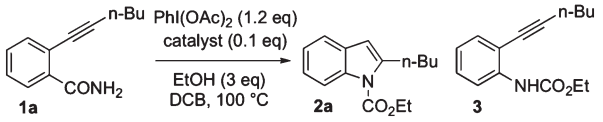


TABLE 1. Examination of Catalysts and Reaction Conditions



entry	catalyst	time (h)	yield (%) 2a	yield (%) 3
1[a]	$PtCl_2$, Et_3N (3 equiv)	2.0 + 3.0	9	64
2[a]	$PtCl_2$	2.0 + 0.5	82	0
3	$PtCl_2$	0.5	85	0
4[b]	$PtCl_2$	2.5	84	0
5	$PdCl_2$	2.5	78	0
6	$InBr_3$	3.0	0	92
7	$InBr_3$ (0.2 equiv)	41.0	85	0
8	$Pd(OAc)_2$	3.0	6	62
9	$CuCl_2$	3.0	0	84
10	$Cu(OTf)_2$	3.0	4	93

[a]Stepwise procedure. [b]At 70 °C.

(3) Okamoto, N.; Miwa, Y.; Minami, H.; Takeda, K.; Yanada, R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9693–9696.

(4) Indole synthesis with 2-alkynylaryl isocyanates: (a) Kamijo, S.; Yamamoto, Y. *J. Org. Chem.* **2003**, *68*, 4764–4771. (b) Kamijo, S.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2002**, *41*, 3230–3233.

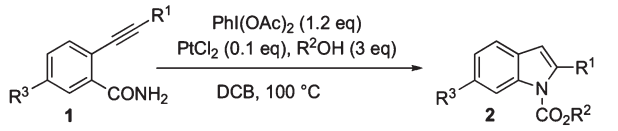
(5) Alkylideneoxindole synthesis with 2-alkynylaryl isocyanates: (a) Miura, T.; Toyoshima, T.; Takahashi, Y.; Murakami, M. *Org. Lett.* **2009**, *11*, 2141–2143. (b) Miura, T.; Toyoshima, T.; Takahashi, Y.; Murakami, M. *Org. Lett.* **2008**, *10*, 4887–4889. (c) Miura, T.; Takahashi, Y.; Murakami, M. *Org. Lett.* **2007**, *9*, 5075–5077. (d) Kamijo, S.; Sasaki, Y.; Kanazawa, C.; Schüsseler, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2005**, *44*, 7718–7721.

(6) Isocyanates prepared with hypervalent iodine reagents: (a) Liu, W.; Buck, M.; Chen, N.; Shang, M.; Taylor, N. J.; Asoud, J.; Wu, X.; Hasinoff, B. B.; Dmitrienko, G. I. *Org. Lett.* **2007**, *9*, 2915–2918. (b) Moriarty, R. M.; Chany, C. J., II; Vaid, R. K.; Prakash, O.; Tuladhar, S. M. *J. Org. Chem.* **1993**, *58*, 2478–2482.

(7) Isocyanates prepared with triphosgene: (a) Fustero, S.; Chiva, G.; Piera, J.; Sanz-Cervera, J. F.; Volonterio, A.; Zanda, M.; Ramirez de Arellano, C. *J. Org. Chem.* **2009**, *74*, 3122–3132. (b) Alaoui, A. E.; Schmidt, F.; Monneret, C.; Florent, J.-C. *J. Org. Chem.* **2006**, *71*, 9628–9636.

(8) Isocyanate was used without further purification because of its instability.

TABLE 2. Tandem Indole Formation from 2-Alkynylbenzamide with Alcohol as Nucleophile



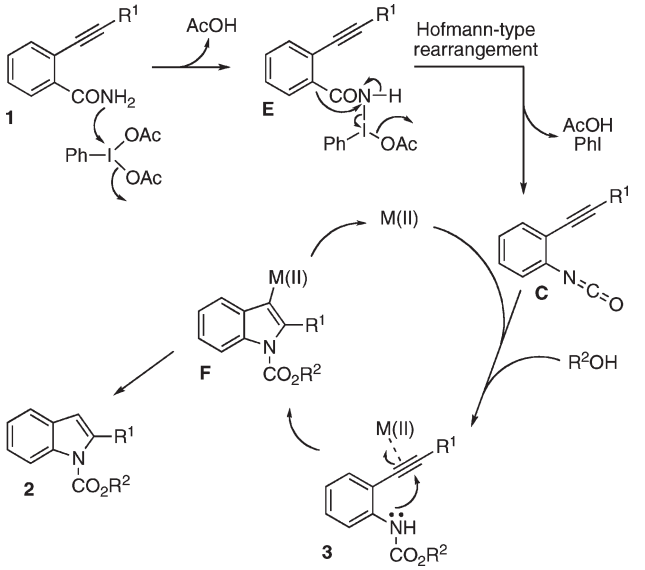
						$PtCl_2$		$PdCl_2$	
entry	**1**	R^1	R^2	R^3	**2**	time (h)	yield (%)	time (h)	yield (%)
1	**1b**	*n*-Bu	Et	F	**2b**	2.0	84	2.7	61
2	**1c**	*n*-Bu	Et	NO_2	**2c**	2.0	91	5.5	48
3	**1d**	*n*-Bu	Et	OMe	**2d**	2.0	82	1.8	63
4	**1e**	Ph	Et	H	**2e**	2.5	84	6.0	36
5	**1f**	*p*-Tol	Et	H	**2f**	1.0	66	1.7	62
6	**1g**	$-(CH_2)_3OTs$	Et	H	**2g**	2.0	100	1.8	78
7	**1h**	H	Et	H	**2h**	6.0	33	6.0	dec
8	**1i**	TMS	Et	H	**2i**	3.0	0[a]	4.0	0[b]
9	**1a**	*n*-Bu	Bn	H	**2j**	1.0	90	1.3	86
10	**1a**	*n*-Bu	*t*-Bu	H	**2k**	3.0	34	1.8	48
11[c]	**1e**	Ph	Et	H	**2e**	20 min	83		–
12[d]	**1e**	Ph	Et	H	**2e**	2.0	97		–

[a]Desilylated product **2h** was obtained in 66% yield. [b]Carbamate **3** (R^1 = TMS, R^2 = Et) was produced in 45% yield. [c]Under microwave irradiation at 100 °C. [d]Under microwave irradiation in EtOH at 60 °C.

0.1 equiv of $PtCl_2$ proceeded under an acidic reaction conditions (entry 2). To simplify the method, a one-pot reaction was developed. When a solution of **1a** in DCB in the presence of $PhI(OAc)_2$, $PtCl_2$, and ethanol was heated at 100 °C for 30 min, **2a** was obtained in 85% yield (entry 3). $PdCl_2$ and $InBr_3$ (0.2 equiv) showed catalytic activity similar to that of $PtCl_2$ but required longer reaction times (entry 3 versus entries 5 and 7). Only carbamate **3** was produced when 0.1 equiv of $InBr_3$ was used in a shorter reaction time (entry 6). The use of $Pd(OAc)_2$, $CuCl_2$, and $Cu(OTf)_2$, which have been used in previous studies for intramolecular hydroamination of 2-alkynylaniline derivatives,[1,2] gave unsatisfactory results (entries 8–10).

Tandem Reactions with Alcohols As Nucleophiles. Having in hand the optimized conditions for the cyclization step, we next examined the scope of this tandem reaction for various 2-alkynylbenzamides **1a**–**1i** using $PtCl_2$ and $PdCl_2$ as catalysts (Table 2). In comparison with the reaction catalyzed by $PdCl_2$, the reaction with $PtCl_2$ proceeded smoothly and gave the corresponding indoles in better yields except for entry 10. Reaction efficiency was not affected by the substitution pattern on the aromatic ring in the presence of either electron-withdrawing groups or electron-donating groups. The yields of the indole products **2** were within the range of 82–91% (entries 1–3). Alkynylbenzamides **1**, bearing aromatic or aliphatic substituents on the acetylene terminus, gave the corresponding indoles **2** in good to excellent yields (entries 4–6). Unfortunately, terminal alkyne **1h** was not suitable for this reaction, resulting in 33% yield of **2h** (entry 7). This result may be due to the known dimerization of terminal acetylenes with $PhI(OAc)_2$.[9] The reaction of trimethylsilyl derivative **1i** resulted in desilylation to furnish **2h** in 66% yield (entry 8). Using benzyl alcohol as the nucleophile, *N*-Cbz-protected indole was obtained in good yield (entry 9), although the use of *tert*-butyl alcohol resulted in only 34% yield of **2k**, probably due to the steric hindrance of the bulky nucleophile (entry 10). We previously reported microwave-promoted tandem one-pot synthesis of isoquinolines.[10] In expectation of shorter reaction time, microwave irradiation was applied for this tandem indole synthesis. The reaction of **1e**, $PhI(OAc)_2$, $PtCl_2$, and EtOH in DCB under microwave irradiation was completed within 20 min at 100 °C to give the desired indole **2e** (entry 11). The reaction in EtOH under microwave irradiation at 60 °C also gave **2e** in high yield (entry 12).

SCHEME 4. Plausible Mechanism for Indole Formation



A plausible mechanism for the formation of indoles **2** is depicted in Scheme 4. Reaction of the 2-alkynylbenzamides **1** with $PhI(OAc)_2$ probably leads to the formation of the *N*-(phenyliodonio)intermediates **E**. Hofmann-type rearrangement generates isocyanate intermediates **C**, which then undergo electrophilic addition to alcohols to afford carbamates **3**. Intramolecular nucleophilic addition of the resulting carbamate nitrogen to π-coordinated activated alkyne with Pt(II) or Pd(II) affords the desired indoles **2** through intermediate **F**.

We applied our one-pot tandem reaction to the synthesis of 2,3-disubstituted indoles. Sakamoto reported the synthesis of 2,3-disubstituted indoles from 2-ethynylphenylcarbamates and alkenes using Pd(II)-catalyzed cyclization.[11] After carbamate formation derived from amide **1a**, $PdCl_2$, $CuCl_2$, methyl acrylate, and TBAF were added. The solution was stirred for 18 h at 60 °C. Unfortunately, the desired 2,3-disubstituted indole **4** was obtained only in 26% yield accompanied by 2-substituted indole **2a** in 65% yield (Scheme 5). The reason why the predominant formation of **2a** is unclear.

To further extend our tandem Hofmann-type rearrangement and cyclization strategy, the procedure was applied to the construction of dihydroisoquinolines **6** from 2-alkynylbenzylamides **5**, which are one-carbon homologues of 2-alkynylbenzamides **1**.

(9) (a) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523–2584. (b) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123–1178.

(10) Okamoto, N.; Sakurai, K.; Ishikura, M.; Takeda, K.; Yanada, R. *Tetrahedron Lett.* **2009**, *50*, 4167–4169.

(11) Yasuhara, A.; Takeda, Y.; Suzuki, N.; Sakamoto, T. *Chem. Pharm. Bull.* **2002**, *50*, 235–238.

SCHEME 5. Attempted 2,3-Disubstituted Indole Synthesis

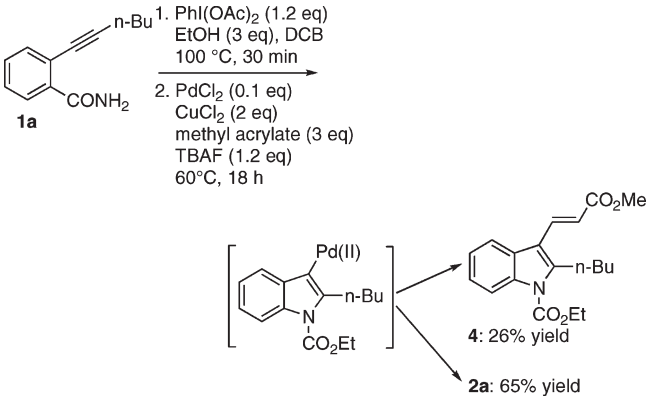
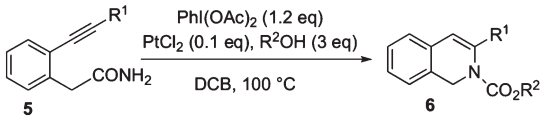


TABLE 3. Tandem Dihydroisoquinoline Formation from 2-Alkynylbenzylamide

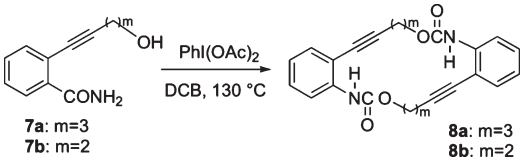


entry	5	R^1	R^2	time (h)	6	yield (%)
1	**5a**	Ph	Et	1	**6a**	86
2	**5a**	Ph	Me	1	**6b**	92
3	**5a**	Ph	Bn	1	**6c**	92
4	**5b**	*p*-Tol	Et	1	**6d**	82
5	**5b**	*p*-Tol	Bn	1	**6e**	82
6	**5c**	*n*-Bu	Et	3	**6f**	66
7	**5c**	*n*-Bu	Bn	1	**6g**	73

The reactions of **5** with different alcohols proceeded smoothly under the same reaction conditions to furnish the desired isoquinolines **6** in high yields (Table 3, entries 1−7). The structures of **6** were confirmed by X-ray crystallographic analysis of compound **6c**.[12] Cyclization occurred via a 6-*endo* mode to produce **6** as the sole product; 5-*exo*-cyclized products were not obtained at all. The indoles and isoquinolines synthesized contain enecarbamate frameworks, which are attractive synthetic intermediates owing to their applicability to synthetic transformations.[13]

We became interested in determining whether 2-alkynylbenzamides bearing a ω-(hydroxy)alkyl group **7a** and **7b** would undergo intermolecular or intramolecular carbamate formation. The tandem reaction was examined at 130 °C with various concentrations of the reactant **7** (Table 4). Eighteen- and twenty-membered ring compounds, bis(yne carbamate) **8**, were obtained in 35−62% yields. The optimal concentration for the production of **8** was found to be between 0.01 and 0.05 M (entries 2, 3, and 7); the structure of **8a** was confirmed by X-ray crystallography.[12] It was found that the reaction using **7** bearing a ω-(hydroxy)alkyl group proceeded with only intermolecular reaction to give dimerized carbamates **8** without intramolecular carbamate formation.

TABLE 4. Macrocyclic Bis(yne carbamate) Synthesis



entry	7	conc. (M)	time (h)	8	yield (%)
1	**7a**	0.005	5	**8a**	39
2	**7a**	0.01	5	**8a**	62
3	**7a**	0.05	2	**8a**	62
4	**7a**	0.1	1	**8a**	48
5	**7a**	0.5	1	**8a**	35
6	**7b**	0.005	5	**8b**	39
7	**7b**	0.01	5	**8b**	62
8	**7b**	0.05	3	**8b**	38

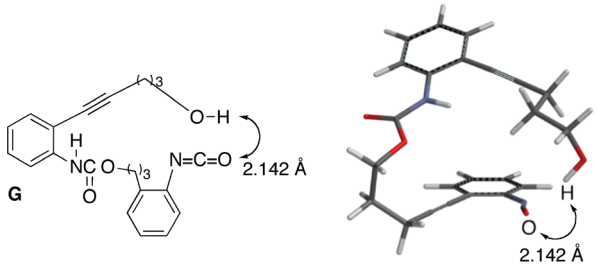
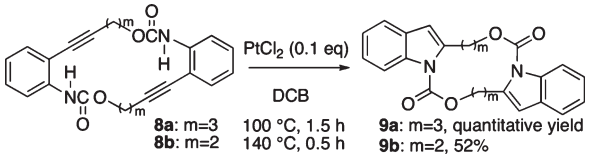


FIGURE 1. B3LYP/6-31G* geometry of intermediate **G**.

SCHEME 6. Macrocyclic Bis(indole) Synthesis from Macrocyclic Bis(yne carbamate)



The facile formation of the dimers led us to search for a stable ground-state conformation of monocarbamate intermediate **G**, a product from the bimolecular coupling process of compound **7a**, by quantum chemical calculations. Geometry optimizations were carried out at the B3LYP level with the 6-31G* basis set (Figure 1). The hydrogen atom of the hydroxyl group was placed near the oxygen atom of the isocyanate group of intermediate **G** (O→H distance: 2.142 Å), providing an easy access to bis(yne carbamate) **8a**.[14]

We then confirmed that bis(yne carbamate) **8a** and **8b** were converted into bis(indole) **9a** and **9b** by Pt(II)-catalyzed transannular hydroaminations (Scheme 6).[15]

(12) CCDC 745937 (**6c**), CCDC 745938 (**8a**), CCDC 745939 (**9a**), and CCDC 770817 (**9f**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(13) (a) Gross, U.; Nieger, M.; Bräse, S. *Org. Lett.* **2009**, *11*, 4740–4742. (b) Deng, H.; Yang, X.; Tong, Z.; Li, Z.; Zhai, H. *Org. Lett.* **2008**, *10*, 1791–1793. (c) Guin, J.; Fröhlich, R.; Studer, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 779–782. (d) Sivaguru, J.; Solomon, M. R.; Poon, T.; Jockusch, S.; Bosio, S. G.; Adam, W.; Turro, N. J. *Acc. Chem. Res.* **2008**, *41*, 387–400. (e) Su, S.; Porco, J. A., Jr. *Org. Lett.* **2007**, *9*, 4983–4986. (f) Harrison, T. J.; Patrick, B. O.; Dake, G. R. *Org. Lett.* **2007**, *9*, 367–370. (g) De Faria, A. R.; Salvador, E. L.; Correia, C. R. D. *J. Org. Chem.* **2002**, *67*, 3651–3661. (h) Severino, E. A.; Correia, C. R. D. *Org. Lett.* **2000**, *2*, 3039–3042.

(14) Calculations were performed on the Spartan 06: Spartan 06 (Ver. 1.0.1 for Mac), Wavefunction, Inc, Irvine, CA.

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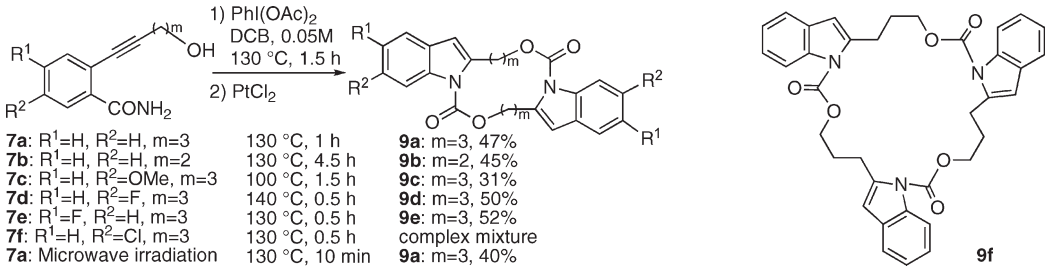
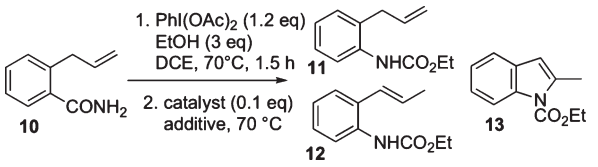
SCHEME 7. Macrocyclic Bis(indole) Synthesis



Finally, we applied the stepwise procedure to tandem macrocyclic bis(indole) synthesis. Treatment of a 0.05 M solution of amides **7** with $PhI(OAc)_2$ at 130 °C for 1.5 h, followed by cyclization with $PtCl_2$ at 100−140 °C for 0.5−4.5 h, afforded the desired indoles **9** via macrocyclic bis(yne carbamate) intermediates **8**. The yields of **9a**−**e** were moderate due to the formation of a complex mixture (Scheme 7). For example, trimeric indole **9f** was obtained in 8% yield from **7a**. The structures of compounds **9a** and **9f** were also confirmed by X-ray crystallography.[12] Under microwave irradiation conditions, the tandem one-pot formation of macrocyclic indole **9a** from **7a** at 130 °C was also completed within 30 min (first step) and within 10 min (second step) in 40% yield. These macrocyclic compounds[16] have been the subject of recent interest because of their potential biological activities.[17]

We expected that the same reaction would occur for 2-allylbenzamide **10** in the presence of an oxidant.[18] $AuClPPh_3/AgOTf$- or $PtCl_2$-catalyzed reaction in 1,2-dichloroethane (DCE) afforded only carbamate **11** (Table 5, entries 1 and 2). In the case of a longer reaction time with $PtCl_2$, only isomerization of the double bond of carbamate **11** occurred to give a mixture of **11** and **12** (entry 3). This isomerization was accelerated by $PdCl_2$ (entry 4). When 1 equiv of $CuCl_2$ was added in order to reoxidize Pd(0), indole **13** was obtained in 46% yield (entry 5). With an increase in the amount of $CuCl_2$, the reaction was completed within 2 h, but the yield of **13** remained moderate (53%) (entry 6).[19] We have demonstrated the synthesis of ethyl 2-methyl-1*H*-indole-1-carboxylate **13** via tandem Hofmann-type rearrangement of 2-allylbenzamide **10**, carbamate formation, and continuous oxidative amino cyclization.

TABLE 5. Tandem Indole Formation from 2-Allylbenzamide



entry	catalyst	additive (equiv)	time (h)	yield (%)
1	$AuClPPh_3/AgOTf$		2.5	**11** (82)
2	$PtCl_2$		1.0	**11** (86)
3	$PtCl_2$		5.5	**11** (84) + **12** (16)
4	$PdCl_2$		4.0	**12** (94)
5	$PdCl_2$	$CuCl_2$ (1)	5.0	**13** (46)
6	$PdCl_2$	$CuCl_2$ (2)	2.0	**13** (53)

Tandem Reactions with Amines As Nucleophiles. Next, we investigated the synthesis of indole *N*-carboxyamide derivatives using amines as nucleophiles toward isocyanates.[20] Indole *N*-carboxyamides are found in biologically active compounds such as 5-hydroxytryptamine (5-HT_3) receptor antagonists[21] and endothelin-A (ET-A) receptor antagonists.[22] $PtCl_2$ and $PdCl_2$ as catalysts for the aminocyclization were examined, and the results are shown in Table 6. Although alcohols were added together with 2-alkynylbenzamide and the catalyst, amines were added after isocyanate formation to avoid the amine being oxidized by $PhI(OAc)_2$. The reaction catalyzed by $PtCl_2$ gave better yields of desired products than that catalyzed by $PdCl_2$. However, a longer reaction time than the time for reaction using alcohols was required. It was assumed that the decrease of catalytic activity was caused by excess amine. When aniline was used as the nucleophile, 2-butyl-1*H*-indole was obtained together with the desired indole **14a** (entry 1). The formation of 1*H*-indole was suppressed by addition of CuBr, leading to a better yield, although the reason is unclear (entry 2). Benzylamine, allylamine, *S*-methyl-L-cysteine methyl ester, 2-phenylethylamine, and cyclohexylamine also reacted with the isocyanate intermediate to give indole *N*-carboxyamides **14b**−**f** in moderate to good yields (entries 3−7). The reaction

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(17) (a) Dakas, P.-Y.; Jogireddy, R.; Valot, G.; Barluenga, S.; Winssinger, N. *Chem.—Eur. J.* **2009**, *15*, 11490–11497. (b) Avolio, S.; Robertson, K.; Hernando, J. I. M.; DiMuzio, J.; Summa, V. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 2295–2298. (c) Abell, A. D.; Jones, M. A.; Coxon, J. M.; Morton, J. D.; Aitken, S. G.; McNabb, S. B.; Lee, H. Y.-Y.; Mehrtens, J. M.; Alexander, N. A.; Stuart, B. G.; Neffe, A. T.; Bickerstaffe, R. *Angew. Chem., Int. Ed.* **2009**, *48*, 1455–1458. (d) Venkatraman, S.; Velazquez, F.; Wu, W.; Blackman, M.; Chen, K. X.; Bogen, S.; Nair, L.; Tong, X.; Chase, R.; Hart, A.; Agrawal, S.; Pichardo, J.; Prongay, A.; Cheng, K.-C.; Girijavallabhan, V.; Piwinski, J.; Shih, N.-Y.; Njoroge, F. G. *J. Med. Chem.* **2009**, *52*, 336–346. (e) Shen, G.; Wang, M.; Welch, T. R.; Blagg, B. S. J. *J. Org. Chem.* **2006**, *71*, 7618–7631. (f) Albrecht, B. K.; Williams, R. M. *Org. Lett.* **2003**, *5*, 197–200.

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(19) Chemler reported the intramolecular aminohalogenation of olefins catalyzed by palladium(II). These reactions used 3−4 equiv of copper(II) halides under K_2CO_3 basic conditions to give halogenated indoles: Manzoni, M. R.; Zabawa, T. P.; Kasi, D.; Chemler, S. R. *Organometallics* **2004**, *23*, 5618–5621.

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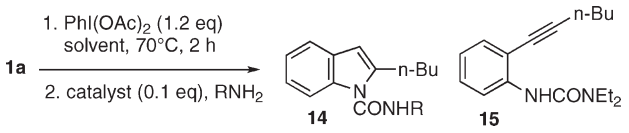
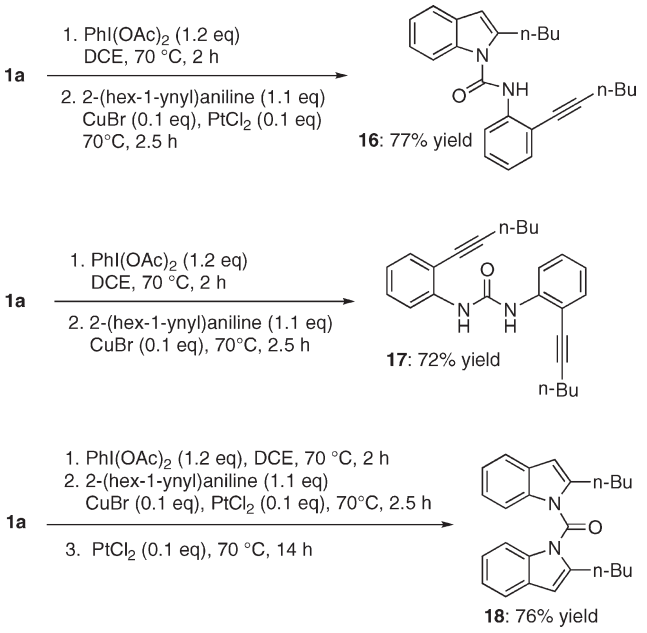
TABLE 6. Tandem Indole *N*-Carboxyamide Formation from 2-(1-Hexynyl)benzamide



entry	catalyst	RNH_2	RNH_2 (eq.)	solvent	temp (°C)	time (day)	yield (%) of **14**
1	$PtCl_2$	aniline	1.2	DCB	70	2.0	75 (**14a**)[a]
2[b]	$PtCl_2$	aniline	1.2	DCB	70	1.3	82 (**14a**)
3	$PtCl_2$	benzylamine	3.0	DCB	100	4.0	91 (**14b**)
4	$PtCl_2$	allylamine	3.0	DCB	100	7.0	63 (**14c**)
5	$PtCl_2$	*S*-methyl-L-cysteine methyl ester	1.2	DCB	100	5.0	98 (**14d**)
6	$PtCl_2$	2-phenylethylamine	3.0	DCB	100	1.6	80 (**14e**)
7	$PtCl_2$	cyclohexylamine	3.0	DCE	100	4.0	87 (**14f**)
8	$PtCl_2$	diethylamine	3.0	DCB	100	2.7	0[c]
9[b]	$PtCl_2$	2-iodoaniline	1.2	DCB	70	15.0 h	72 (**14g**)
10[b]	$PtCl_2$	2-toluidine	1.2	DCE	70	3.0 h	73 (**14h**)
11[b]	$PtCl_2$	4-aminobenzonitrile	1.2	DCE	70	2.5 h	75 (**14i**)
12[d]	$PtCl_2$	benzylamine	3.0	DCB	100	5.0 h	84 (**14b**)
13	$PdCl_2$	aniline	3.0	DCB	100	0.3	44 (**14a**)[e]
14	$PdCl_2$	benzylamine	3.0	DCB	100	3.0	71 (**14b**)
15	$PdCl_2$	allylamine	3.0	DCB	100	1.0	60 (**14c**)

[a]2-Butyl-1*H*-indole was obtained in 15% yield. [b]CuBr (0.1 equiv) was used as additive. [c]1,1-Diethyl-3-(2-(hex-1-ynyl)phenyl)urea **15** was obtained in 92% yield. [d]Under microwave irradiation. [e]2-Butyl-1*H*-indole was obtained in 25% yield.

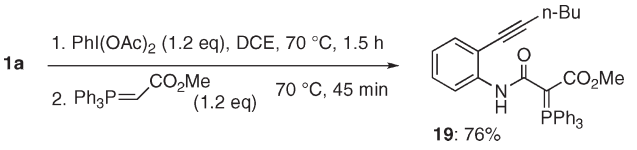
SCHEME 8



with diethylamine did not proceed to give only 1,1-diethyl-3-(2-(hex-1-ynyl)phenyl)urea intermediate **15** in 92% yield (entry 8). It should be noted that the reactions with 2-iodoaniline, 2-toluidine, and 4-aminobenzonitrile which have *ortho* or *para* substituents were completed in considerably shorter reaction times than that with other amines (entries 9−11). We observed enhancement of the rate when the reaction was run under microwave irradiation as well as in the case of the reaction with alcohol as the nucleophile (entry 3 versus entry 12).

The same tendency was observed when 2-alkynylaniline was used. The formation of monoindole **16** was complete in 2.5 h (Scheme 8). In the absence of $PtCl_2$, indole formation did not occur, and symmetrical 1,3-bis(ethynylphenyl)urea **17** was obtained. This urea **17** could be used for the synthesis of

SCHEME 9. Synthesis of Carbamoyl Ylide



G-quadruplex ligands by using copper(I)-catalyzed "click" chemistry.[23] Although the second step of the indole formation was very slow and required an additional 0.1 equivalent of $PtCl_2$, bis-indole **18** was obtained in 76% yield (Scheme 9).

Tandem Reactions with Phosphonium Ylides As Nucleophiles. Finally we tried the reaction using stabilized phosphonium ylides as carbon nucleophiles. Since AcOH was formed in the Hofmann-type rearrangement step, anionic nucleophiles such as enolate and organometallic reagents (RLi, RMgX) could not be used. Therefore, we focused on stabilized phosphonium ylide that could be used without base. It has been reported that stabilized phosphonium ylides react with phenyl isocyanate to form the carbamoyl stabilized ylides.[24] After formation of the isocyanate intermediate was complete, phosphonium ylide was added and the reaction mixture was stirred at 70 °C to give carbamoyl stabilized ylide **19** in 76% yield (Scheme 9). Next we also tried the tandem reaction. 2-(1-Hexynyl)benzamide **1a** could be converted into indole ylides **20a**−**20d** in 72−89% yields by a one-pot tandem procedure, in which $PtCl_2$ catalyst was used (Table 7, entries 1−4). The reaction with (triphenylphosphoranylidene)acetaldehyde gave only a complex mixture (entry 5). Indole ylide **20a** could be converted into the corresponding β-keto ester with Al/Hg[25] or subjected to ozonolysis to give α,β-diketo ester.[26]

(23) Drewe, W. C.; Neidle, S. *Chem. Commun.* **2008**, 5295–5297.
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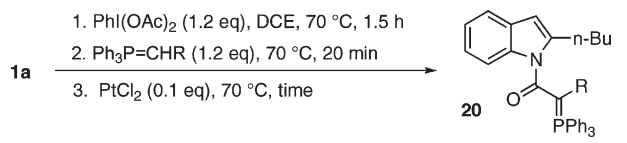
(25) Benetti, S.; Romagnoli, R.; Risi, C. D.; Spalluto, G.; Zanirato, V. *Chem. Rev.* **1995**, *95*, 1065–1114.
(26) Rubin, M. B.; Gleiter, R. *Chem. Rev.* **2000**, *100*, 1121–1164.

TABLE 7. Tandem Indole Ylide Formation from 2-(1-Hexynyl)-benzamide



entry	R	time (day)	yield (%)
1	CO_2Me	0.6	89 (**20a**)
2	COPh	0.9	80 (**20b**)
3	COMe	1.8	77 (**20c**)
4	CN	3.5	72 (**20d**)
5	CHO	2.0	0

Conclusions

In summary, we have developed a novel, concise, Pt(II)-catalyzed, one-pot tandem synthesis of indoles and isoquinolines via nucleophilic addition to isocyanates intermediates derived from Hofmann-type rearrangement of amides with a hypervalent iodine reagent and intramolecular aminocyclization. A variety of alcohols, amines, and stable Wittig reagents as nucleophiles to the isocyanates gave carbamates, ureas, and carbamoyl-stabilized ylides. Furthermore, C_2-symmetrical macrocyclic bis(yne carbamate) was efficiently synthesized by cyclodimerization of 2-(ω-hydroxy-1-alkynyl)benzamides. This reaction discovery led to transannular cyclization to provide macrocyclic bis(indole) in moderate yields. We also noticed a significant enhancement of the reaction rates of these tandem one-pot reactions under microwave irradiation.

Experimental Section

General Procedure for the Preparation of Indole Carbamate. To a solution of 2-alkynylbenzamide (0.05 mmol), $PhI(OAc)_2$ (0.06 mmol), and $PtCl_2$ (0.005 mmol) in 1,2-dichlorobenzene (0.5 mL) was added the alcohol (0.15 mmol), and the mixture was stirred at 100 °C. The reaction mixture was directly chromatographed on silica gel to afford the indole carbamate **2**.

Ethyl 2-Butyl-6-fluoro-1*H*-indole-1-carboxylate (2b). The reaction mixture was chromatographed on silica gel [AcOEt−hexane (1:20)] to afford **2b** as a white solid: mp 49−51 °C (colorless plate from $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.83 (1H, dd, J = 11.0, 2.1 Hz), 7.34 (1H, dd, J = 8.2, 5.5 Hz), 6.95 (1H, td, J = 9.1, 2.1 Hz), 6.32 (1H, s), 4.50 (2H, q, J = 7.2 Hz), 2.98 (2H, t, J = 7.6 Hz), 1.69−1.64 (2H, m), 1.49 (3H, t, J = 7.2 Hz), 1.47−1.41 (2H, m), 0.96 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 159.5, 151.8, 142.9, 136.7, 125.7, 120.0, 110.9, 107.0, 103.4, 63.2, 31.0, 29.7, 22.6, 14.3, 14.0; IR ($CHCl_3$, cm^{-1}) 3036, 3009, 2961, 2931, 1734, 1599, 1483, 1439, 1379, 1331, 1269, 1194, 1074, 854, 810; MS (EI) m/z = 263 (M^+); HRMS (EI) m/z calcd for $C_{15}H_{18}FNO_2$ 263.1322, found 263.1317.

Ethyl 2-Butyl-6-nitro-1*H*-indole-1-carboxylate (2c). The reaction mixture was chromatographed on silica gel [AcOEt−hexane (1:20)] to afford **2c** as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 9.02 (1H, s), 8.11 (1H, d, J = 8.2 Hz), 7.50 (1H, d, J = 8.2 Hz), 6.47 (1H, s), 4.58 (2H, q, J = 7.2 Hz), 3.07 (2H, t, J = 7.9 Hz), 1.74−1.69 (2H, m), 1.55 (3H, t, J = 7.2 Hz), 1.50−1.44 (2H, m), 0.99 (3H, t, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 151.2, 148.7, 144.2, 135.2, 134.6, 119.5, 118.5, 112.2, 107.3, 63.9, 30.7, 29.9, 22.6, 14.3, 13.9; IR ($CHCl_3$, cm^{-1}) 2959, 1744, 1518, 1339, 1319, 1196, 1099, 837, 808; MS (EI) m/z = 290 (M^+); HRMS (EI) m/z calcd for $C_{15}H_{18}N_2O_4$ 290.1267, found 290.1272.

Ethyl 2-(3-Tosyloxy)propyl)-1*H*-indole-1-carboxylate (2g). The reaction mixture was chromatographed on silica gel [AcOEt−hexane (1:3)] to afford **2g** as a white solid: mp 71−72 °C (colorless needles from $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.06 (1H, d, J = 8.2 Hz), 7.79 (2H, d, J = 8.2 Hz), 7.41 (1H, d, J = 6.9 Hz), 7.32 (2H, d, J = 8.2 Hz), 7.26−7.19 (2H, m), 6.23 (1H, s), 4.48 (2H, q, J = 7.2 Hz), 4.11 (2H, t, J = 6.2 Hz), 3.06 (2H, t, J = 7.2 Hz), 2.44 (3H, s), 2.08−2.04 (2H, m), 1.48 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 151.8, 144.8, 139.8, 136.5, 133.0, 129.8, 129.2, 127.9, 123.7, 123.0, 119.9, 115.7, 108.6, 69.6, 63.2, 28.1, 25.8, 21.7, 14.3; IR ($CHCl_3$, cm^{-1}) 3008, 1730, 1456, 1379, 1360, 1325, 1190, 1175, 1096, 928, 810, 692; MS (EI) m/z = 401 (M^+); HRMS (EI) m/z calcd for $C_{21}H_{23}NO_5S$ 401.1297, found 401.1297.

Benzyl 2-Butyl-1*H*-indole-1-carboxylate (2j). The reaction mixture was chromatographed on silica gel [AcOEt−hexane (1:20)] to afford **2j** as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 8.08 (1H, d, J = 8.9 Hz), 7.49 (2H, d, J = 6.2 Hz), 7.44−7.36 (4H, m), 7.21−7.17 (2H, m), 6.35 (1H, s), 5.45 (2H, s), 2.97 (2H, t, J = 7.6 Hz), 1.65−1.60 (2H, m), 1.39−1.33 (2H, m), 0.91 (3H, t, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 151.9, 142.6, 136.5, 135.0, 129.6, 128.8, 128.7, 128.7, 123.4, 122.9, 119.7, 115.7, 107.6, 68.7, 31.0, 29.8, 22.5, 14.0; IR ($CHCl_3$, cm^{-1}) 3034, 2959, 2932, 1732, 1570, 1456, 1392, 1325, 1258, 1196, 1119, 1078, 689; MS (EI) m/z = 307 (M^+); HRMS (EI) m/z calcd for $C_{20}H_{21}NO_2$ 307.1572, found 307.1571.

(*E*)-Ethyl 2-Butyl-3-(3-methoxy-3-oxoprop-1-enyl)-1*H*-indole-1-carboxylate (4). A solution of 2-alkynylbenzamide **1a** (0.05 mmol), $PhI(OAc)_2$ (0.06 mmol), and ethanol (0.15 mmol) in 1,2-dichlorobenzene (0.5 mL) was stirred at 100 °C for 1 h, and then $PdCl_2$ (0.005 mmol), $CuCl_2$ (0.1 mmol), TBAF (1 M solution in THF, 0.06 mmol), and methyl acrylate (0.15 mmol) was added, and the mixture was stirred at 60 °C for 18 h. The reaction mixture was directly chromatographed on silica gel [AcOEt−hexane (1:30)] to afford the indole **4** as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 8.16−8.14 (1H, m), 7.93 (1H, d, J = 16.2 Hz), 7.84−7.83 (1H, m), 7.34−7.31 (2H, m), 6.57 (1H, d, J = 16.2 Hz), 4.55 (2H, q, J = 7.1 Hz), 3.84 (3H, s), 3.20 (2H, t, J = 7.9 Hz), 1.65−1.41 (7H, m), 0.95 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 168.2, 151.5, 145.4, 136.4, 136.3, 127.2, 124.5, 123.8, 119.7, 117.0, 115.8, 114.9, 63.6, 51.6, 32.4, 26.6, 22.7, 14.3, 13.9; IR ($CHCl_3$, cm^{-1}) 3036, 3009, 2959, 1736, 1628, 1545, 1477, 1456, 1435, 1398, 1373, 1342, 1323, 1281, 1238, 1194, 1175, 1163, 1144, 1123, 1015, 976, 810; MS (EI) m/z = 329 (M^+); HRMS (EI) m/z calcd for $C_{19}H_{23}NO_4$ 329.1627, found 329.1631.

General Procedure for the Preparation of Dihydroisoquinoline Carbamate. To a solution of 2-alkynylbenzylamide **5** (0.05 mmol), $PhI(OAc)_2$ (0.06 mmol), and $PtCl_2$ (0.005 mmol) in 1,2-dichlorobenzene (0.5 mL) was added alcohol (0.15 mmol), and the mixture was stirred at 100 °C. The reaction mixture was directly chromatographed on silica gel to afford the dihydroisoquinoline **6**.

Ethyl 3-Phenylisoquinoline-2(1*H*)-carboxylate (6a). The reaction mixture was chromatographed on silica gel [AcOEt−hexane (1:10)] to afford **6a** as a yellow viscous oil: mp 114−115 °C (colorless plate from $CHCl_3$−hexane); ^{1}H NMR ($CDCl_3$) δ 7.49 (2H, d, J = 6.9 Hz), 7.37−7.20 (7H, m), 6.53 (1H, s), 4.92 (2H, s), 3.89 (2H, br), 0.74 (3H, br); ^{13}C NMR ($CDCl_3$) δ 154.4, 140.2, 138.2, 132.5, 131.9, 128.2, 127.9, 127.7, 127.4, 126.0, 125.2, 125.1, 115.8, 61.8, 48.0, 13.8; IR ($CHCl_3$, cm^{-1}) 3034, 3009, 1699, 1622, 1402, 1379, 1342, 1236, 1198, 1167, 1020, 980; MS (EI) m/z = 279 (M^+); HRMS (EI) m/z calcd for $C_{18}H_{17}NO_2$ 279.1259, found 279.1265.

Methyl 3-Phenylisoquinoline-2(1*H*)-carboxylate (6b). The reaction mixture was chromatographed on silica gel [AcOEt−hexane (1:10)] to afford **6b** as a pale yellow solid: mp 113−116 °C (pale yellow plate from $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.50 (2H, d, J = 7.6 Hz), 7.38 (2H, t, J = 7.6 Hz), 7.33−7.20 (5H, m), 6.58

(1H, s), 4.91 (2H, s), 3.46 (3H, br); ^{13}C NMR ($CDCl_3$) δ 155.0, 140.0, 137.6, 132.5, 132.0, 128.3, 128.0, 127.7, 125.8, 125.3, 125.0, 116.2, 52.8, 48.2; IR ($CHCl_3$, cm^{-1}) 1703, 1449, 1360, 1198, 808, 687, 673; MS (EI) m/z = 265 (M^+); HRMS (EI) m/z calcd for $C_{17}H_{15}NO_2$ 265.1103, found: 265.1111.

Benzyl 3-Phenylisoquinoline-2(1*H*)-carboxylate (6c). The reaction mixture was chromatographed on silica gel [AcOEt−hexane (1:10)] to afford **6c** as a yellow viscous oil: mp 143−144 °C (colorless plate from $CHCl_3$−hexane); ^{1}H NMR ($CDCl_3$) δ 7.50 (2H, d, J = 7.6 Hz), 7.36−7.13 (11H, m), 6.55 (2H, br), 4.95 (2H, s), 4.90 (2H, br); ^{13}C NMR ($CDCl_3$) δ 154.3, 139.9, 138.0, 135.4, 132.5, 132.0, 128.5, 128.1, 128.0, 127.7, 127.6, 127.5, 126.1, 125.3, 125.1, 116.3, 67.8, 48.2; IR ($CHCl_3$, cm^{-1}) 3034, 1701, 1622, 1454, 1396, 1344, 1260, 1236, 1161, 1123, 968, 808; MS (EI) m/z = 341 (M^+); HRMS (EI) m/z calcd for $C_{23}H_{19}NO_2$ 341.1416, found 341.1408.

Ethyl 3-*p*-Tolylisoquinoline-2(1*H*)-carboxylate (6d). The reaction mixture was chromatographed on silica gel [AcOEt−hexane (1:10)] to afford **6d** as a yellow viscous oil: mp 124−125 °C (colorless prism from $CHCl_3$−hexane); ^{1}H NMR ($CDCl_3$) δ 7.39 (2H, d, J = 8.2 Hz), 7.27−7.19 (4H, m), 7.17 (2H, d, J = 7.6 Hz), 6.50 (1H, s), 4.90 (2H, s), 3.91 (2H, br), 2.37 (3H, s), 0.79 (3H, br); ^{13}C NMR ($CDCl_3$) δ 154.4, 140.3, 137.8, 135.2, 132.7, 131.9, 128.9, 127.6, 127.2, 125.9, 125.1, 125.0, 115.2, 61.8, 48.1, 21.3, 13.9; IR ($CHCl_3$, cm^{-1}) 1697, 1454, 1400, 1377, 1342, 1260, 1117, 689; MS (EI) m/z = 293 (M^+); HRMS (EI) m/z calcd for $C_{19}H_{19}NO_2$ 293.1416, found 293.1416.

Benzyl 3-*p*-Tolylisoquinoline-2(1*H*)-carboxylate (6e). The reaction mixture was chromatographed on silica gel [AcOEt−hexane (1:20)] to afford **6e** as a yellow viscous oil: ^{1}H NMR ($CDCl_3$) δ 7.39−7.14 (11H, m), 6.62 (1H, br), 6.52 (1H, s), 4.92 (4H, br), 2.38 (3H, s); ^{13}C NMR ($CDCl_3$) δ 137.9, 132.6, 129.1, 128.0, 127.7, 127.6, 127.3, 126.0, 125.1, 125.0, 115.5, 67.7, 48.2, 21.3; IR ($CHCl_3$, cm^{-1}) 3034, 1701, 1620, 1512, 1485, 1454, 1441, 1396, 1344, 1310, 1260, 1198, 1161, 966; MS (EI) m/z = 355 (M^+); HRMS (EI) m/z calcd for $C_{24}H_{21}NO_2$ 355.1572, found 355.1579.

Ethyl 3-Butylisoquinoline-2(1*H*)-carboxylate (6f). The reaction mixture was chromatographed on silica gel [AcOEt−hexane (1:20)] to afford **6f** as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 7.20 (1H, td, J = 7.4, 1.6 Hz), 7.16−7.12 (2H, m), 7.05 (1H, d, J = 6.9 Hz), 6.08 (1H, s), 4.71 (2H, s), 4.18 (2H, q, J = 7.1 Hz), 2.68 (2H, t, J = 7.6 Hz), 1.54−1.50 (2H, m), 1.41−1.37 (2H, m), 1.28 (3H, t, J = 7.2 Hz), 0.93 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 153.8, 142.3, 132.5, 131.3, 127.6, 126.6, 124.8, 124.1, 114.9, 61.9, 48.0, 34.1, 30.7, 22.4, 14.5, 13.9; IR ($CHCl_3$, cm^{-1}) 1697, 1632, 1464, 1456, 1443, 1402, 1379, 1342, 1186, 1117, 662; MS (EI) m/z = 259 (M^+); HRMS (EI) m/z calcd for $C_{16}H_{21}NO_2$ 259.1572, found 259.1572.

Benzyl 3-Butylisoquinoline-2(1*H*)-carboxylate (6g). The reaction mixture was chromatographed on silica gel [AcOEt−hexane (1:20)] to afford **6g** as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 7.36−7.31 (5H, m), 7.22−7.11 (3H, m), 7.04 (1H, d, J = 6.9 Hz), 6.08 (1H, s), 5.16 (2H, s), 4.73 (2H, s), 2.63 (2H, br), 1.47−1.43 (2H, m), 1.30 (2H, br), 0.87 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 153.6, 142.2, 136.0, 132.4, 131.3, 128.5, 128.3, 128.2, 127.6, 126.7, 124.8, 124.2, 115.2, 67.8, 48.2, 34.0, 30.7, 22.3, 13.9; IR ($CHCl_3$, cm^{-1}) 3009, 2959, 2930, 1697, 1634, 1456, 1398, 1344, 1281, 1238, 1184, 1117, 810; MS (EI) m/z = 321 (M^+); HRMS (EI) m/z calcd for $C_{21}H_{23}NO_2$ 321.1729, found: 321.1727.

Bis-yne Carbamate (8a). A solution of 2-alkynylbenzylamide (10 mg, 0.05 mmol) and $PhI(OAc)_2$ (16 mg, 0.05 mmol) in 1,2-dichlorobenzene (5 mL) was stirred at 130 °C for 5 h. 1,2-Dichlorobenzene was removed by vacuum distillation, and the residue was purified by column chromatography on silica gel [hexane−$CHCl_3$ (1:10)] to afford **8a** (6.2 mg, 62%) as a white solid: mp 217 °C (colorless prism from $CHCl_3$−hexane); ^{1}H NMR ($CDCl_3$) δ 8.14 (1H, d, J = 8.2 Hz), 7.65 (1H, s), 7.34 (1H, dd, J = 7.6, 1.4 Hz), 7.30 (1H, t, J = 7.9 Hz), 6.97 (1H, t, J = 7.6 Hz), 4.46 (2H, t, J = 5.5 Hz), 2.71 (2H, t, J = 6.5 Hz), 2.05−2.00 (2H, m); ^{13}C NMR ($CDCl_3$) δ 153.0, 139.5, 131.0, 129.3, 122.4, 117.2, 111.6, 95.6, 77.3, 63.0, 26.8, 15.6; IR ($CHCl_3$, cm^{-1}) 1732, 1601, 1582, 1522, 1454, 1308, 1236, 1198, 771, 746, 727; MS (EI) m/z = 402 (M^+); HRMS (EI) m/z calcd for $C_{24}H_{22}N_2O_4$ 402.1580, found 402.1580. Crystals for X-ray diffraction analysis were obtained by recrystallization from $CHCl_3$−hexane.

Bis-yne Carbamate (8b). A solution of **7b** (9.5 mg, 0.05 mmol) and $PhI(OAc)_2$ (16 mg, 0.05 mmol) in 1,2-dichlorobenzene (1 mL) was stirred at 130 °C for 3 h. The reaction mixture was directly chromatographed on silica gel [AcOEt−hexane−$CHCl_3$ (1:20:20)] to afford **8b** (3.6 mg, 38%) as a white solid: mp 208−209 °C (colorless prisms from $CHCl_3$−hexane); ^{1}H NMR ($CDCl_3$) δ 8.25 (1H, d, J = 8.2 Hz), 7.79 (1H, s), 7.35 (1H, dd, J = 7.6, 1.4 Hz), 7.33−7.30 (1H, m), 6.98 (1H, t, J = 7.6 Hz), 4.42 (2H, t, J = 5.5 Hz), 2.91 (2H, t, J = 5.2 Hz); ^{13}C NMR ($CDCl_3$) δ 152.7, 139.3, 131.2, 129.4, 122.5, 117.0, 111.2, 94.1, 77.0, 63.4, 20.6; IR ($CHCl_3$, cm^{-1}) 3389, 3036, 3009, 2965, 2928, 2359, 2342, 1734, 1582, 1533, 1518, 1458, 1339, 1308, 1242, 1067, 1042, 810; MS (EI) m/z = 374 (M^+); HRMS (EI) m/z calcd for $C_{22}H_{18}N_2O_4$ 374.1267, found 374.1263.

Bis-indole (9a). A solution of 2-alkynylbenzylamide (10 mg, 0.05 mmol) and $PhI(OAc)_2$ (16 mg, 0.05 mmol) in 1,2-dichlorobenzene (1 mL) was stirred at 130 °C. After the solution was stirred for 1 h, $PtCl_2$ (1.3 mg, 0.005 mmol) was added, and the mixure was stirred for 1 h at 130 °C. The reaction mixture was directly chromatographed on silica gel [AcOEt−hexane−$CHCl_3$ (1:20:20)] to afford **9a** (4.7 mg, 47%) as a white solid: mp 238−239 °C (colorless plates from $CHCl_3$−hexane); ^{1}H NMR ($CDCl_3$) δ 8.39 (1H, d, J = 8.2 Hz), 7.48 (1H, d, J = 7.6 Hz), 7.31 (1H, td, J = 7.6, 1.4 Hz), 7.24 (1H, t, J = 7.6 Hz), 6.45 (1H, s), 4.53 (2H, dd, J = 5.2 Hz), 3.27−3.24 (2H, m), 2.23−2.18 (2H, m); ^{13}C NMR ($CDCl_3$) δ 151.8, 139.6, 137.6, 129.3, 124.2, 123.3, 119.8, 116.0, 109.6, 67.8, 30.5, 29.2; IR ($CHCl_3$, cm^{-1}) 3036, 3009, 1728, 1595, 1572, 1456, 1429, 1398, 1368, 1325, 1258, 1238, 1121, 1098, 1034, 812; MS (EI) m/z = 402 (M^+); HRMS (EI) m/z calcd for $C_{24}H_{22}N_2O_4$ 402.1580, found 402.1584.

Bis-indole (9b). A solution of 2-alkynylbenzylamide (9.5 mg, 0.05 mmol) and $PhI(OAc)_2$ (16 mg, 0.05 mmol) in 1,2-dichlorobenzene (1 mL) was stirred at 130 °C. After the solution was stirred for 1.5 h, $PtCl_2$ (1.3 mg, 0.005 mmol) was added, and the mixure was stirred for 4.5 h at 130 °C. The reaction mixture was directly chromatographed on silica gel [AcOEt−hexane−$CHCl_3$ (1:20:20)] to afford **9b** (4.2 mg, 45%) as a white solid: mp 216−217 °C (colorless plate from $CHCl_3$−hexane); ^{1}H NMR ($CDCl_3$) δ 8.08 (1H, d, J = 8.1 Hz), 7.47 (1H, d, J = 7.6 Hz), 7.23 (1H, td, J = 8.1, 1.4 Hz), 7.19 (1H, td, J = 7.6, 1.4 Hz), 6.51 (1H, s), 4.78 (2H, br), 3.55 (2H, br); ^{13}C NMR ($CDCl_3$) δ 151.1, 137.6, 137.3, 128.8, 124.3, 123.1, 120.0, 115.3, 110.3, 67.6, 29.3; IR ($CHCl_3$, cm^{-1}) 3688, 3034, 1736, 1601, 1566, 1456, 1427, 1395, 1329, 1196, 1121, 1098, 1013, 810; MS (EI) m/z = 374 (M^+); HRMS (EI) m/z calcd for $C_{22}H_{18}N_2O_4$ 374.1267, found 374.1258.

Bis-indole (9c). A solution of **7c** (19 mg, 0.08 mmol) and $PhI(OAc)_2$ (26 mg, 0.08 mmol) in 1,2-dichlorobenzene (1.6 mL) was stirred at 130 °C. After the solution was stirred for 1 h, $PtCl_2$ (2.1 mg, 0.008 mmol) was added, and the mixure was stirred for 1 h at 130 °C. The reaction mixture was directly chromatographed on silica gel [AcOEt−hexane−$CHCl_3$ (1:20:20)] to afford **9c** (5.7 mg, 31%) as a white solid: ^{1}H NMR ($CDCl_3$) δ 8.00 (1H, d, J = 2.1 Hz), 7.34 (1H, d, J = 8.2 Hz), 6.88 (1H, dd, J = 8.2, 2.1 Hz), 6.37 (1H, s), 4.52 (2H, t, J = 5.2 Hz), 3.89 (3H, s), 3.23 (2H, dd, J = 10.7, 6.5 Hz), 2.22−2.17 (2H, m); ^{13}C NMR ($CDCl_3$) δ 157.6, 152.0, 138.5, 138.3, 122.9, 120.1, 112.5, 109.3, 100.4, 67.8, 55.7, 30.6, 29.2; IR ($CHCl_3$, cm^{-1}) 2963, 1724, 1614,

1574, 1489, 1441, 1400, 1368, 1323, 1277, 1196, 1238, 1167, 1098, 1034, 918, 810; MS (EI) m/z = 462 (M^+); HRMS (EI) m/z calcd for $C_{26}H_{26}N_2O_6$ 462.1791, found 462.1784.

Bis-indole (9d). A solution of **7d** (19 mg, 0.08 mmol) and $PhI(OAc)_2$ (26 mg, 0.08 mmol) in 1,2-dichlorobenzene (1.6 mL) was stirred at 130 °C. After the solution was stirred for 1 h, $PtCl_2$ (2.1 mg, 0.008 mmol) was added, and the mixure was stirred for 1 h at 130 °C. The reaction mixture was directly chromatographed on silica gel [AcOEt−$CHCl_3$ (1:20)] to afford **9d** (8.8 mg, 50%) as a white solid: ^{1}H NMR ($CDCl_3$) δ 8.13 (1H, dd, J = 10.7, 2.4 Hz), 7.38 (1H, dd, J = 8.2, 5.5 Hz), 7.00 (1H, td, J = 8.9, 2.7 Hz), 6.43 (1H, s), 4.54 (2H, t, J = 5.2 Hz), 3.26−3.23 (2H, m), 2.26−2.17 (2H, m); ^{13}C NMR ($CDCl_3$) δ 160.0, 151.6, 139.9, 125.4, 120.3, 120.2, 111.5, 111.3, 109.1, 103.7, 103.5, 99.9, 67.9, 30.4, 29.1; IR ($CHCl_3$, cm^{-1}) 3690, 1730, 1601, 1483, 1439, 1398, 1368, 1325, 1267, 1238, 1196, 1115, 1094, 926; MS (EI) m/z = 438 (M^+); HRMS (EI) m/z calcd for $C_{24}H_{20}F_2N_2O_4$ 438.1391, found 438.1391.

Bis-indole (9e). A solution of **7e** (11 mg, 0.05 mmol) and $PhI(OAc)_2$ (16 mg, 0.05 mmol) in 1,2-dichlorobenzene (1 mL) was stirred at 130 °C. After the solution was stirred for 1 h, $PtCl_2$ (1.3 mg, 0.005 mmol) was added, and the mixure was stirred for 1 h at 130 °C. The reaction mixture was directly chromatographed on silica gel [AcOEt−$CHCl_3$ (1:20)] to afford **9e** (5.7 mg, 52%) as a white solid: ^{1}H NMR ($CDCl_3$) δ 8.33 (1H, dd, J = 9.6, 4.8 Hz), 7.13 (1H, dd, J = 8.9, 2.7 Hz), 7.02 (1H, td, J = 9.1, 2.5 Hz), 6.42 (1H, s), 4.54 (2H, t, J = 5.2 Hz), 3.27−3.24 (2H, m), 2.22 (2H, q, J = 9.2 Hz); ^{13}C NMR ($CDCl_3$) δ 158.8, 151.6, 141.2, 133.8, 130.2, 130.1, 117.00, 116.95, 111.8, 111.6, 109.3, 109.3, 105.3, 67.9, 30.3, 29.2; IR ($CHCl_3$, cm^{-1}) 3690, 1728, 1601, 1474, 1449, 1400, 1368, 1327, 1238, 1196, 1117, 1032, 810; MS (EI) m/z = 438 (M^+); HRMS (EI) m/z calcd for $C_{24}H_{20}F_2N_2O_4$ 438.1391, found 438.1394.

Trimeric indole (9f): white solid; mp 242 °C (white plates from hexane−$CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.14 (1H, d, J = 8.2 Hz), 7.41 (1H, d, J = 7.6 Hz), 7.26−7.18 (2H, m), 6.39 (1H, s), 4.57 (2H, t, J = 6.5 Hz), 3.19 (2H, t, J = 7.6 Hz), 2.28−2.23 (2H, m); ^{13}C NMR ($CDCl_3$) δ 151.9, 140.1, 136.8, 129.2, 123.9, 123.1, 119.9, 115.7, 108.3, 66.7, 28.3, 26.9; IR ($CHCl_3$, cm^{-1}) 2926, 1730, 1456, 1400, 1325, 1198, 1119, 1094, 685; MS (EI) m/z = 603 (M^+); HRMS (EI) m/z calcd for $C_{36}H_{33}N_3O_6$ 603.2369, found 603.2374.

General Procedure for the Preparation of Indole Urea. A solution of 2-alkynylbenzamide (0.05 mmol) and $PhI(OAc)_2$ (0.06 mmol) in 1,2-dichlorobenzene (0.5 mL) was stirred at 70 °C for 2 h. Then amine and $PtCl_2$ (0.005 mmol) were added, and the reaction mixture was stirred at the temperature listed in Table 6. The reaction mixture was directly chromatographed on silica gel to afford the indole urea.

2-Butyl-*N*-phenyl-1*H*-indole-1-carboxamide (14a): white solid; mp 110−111 °C (white needles from $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.64 (1H, d, J = 7.6 Hz), 7.57 (2H, d, J = 7.6 Hz), 7.55 (1H, d, J = 6.9 Hz), 7.46 (1H, br), 7.42 (2H, t, J = 7.9 Hz), 7.24−7.18 (3H, m), 6.41 (1H, s), 3.01 (2H, t, J = 7.9 Hz), 1.75−1.70 (2H, m), 1.47−1.41 (2H, m), 0.95 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 149.5, 142.2, 137.1, 135.4, 129.4, 124.9, 122.8, 122.1, 120.6, 119.7, 111.4, 105.0, 31.0, 28.0, 22.5, 14.0; IR ($CHCl_3$, cm^{-1}) 3032, 3011, 2959, 2932, 2874, 1717, 1599, 1524, 1456, 1441, 1381, 1314, 1298, 1234, 1198, 808, 687; MS (EI) m/z = 292 (M^+); HRMS (EI) m/z calcd for $C_{19}H_{20}N_2O$ 292.1576, found 292.1582.

***N*-Benzyl-2-butyl-1*H*-indole-1-carboxamide (14b):** white solid; mp 88−89 °C (white needles from hexane−EtOAc); ^{1}H NMR ($CDCl_3$) δ 7.55 (1H, d, J = 8.9 Hz), 7.49 (1H, dd, J = 6.5, 2.4 Hz), 7.41−7.37 (4H, m), 7.34−7.31 (1H, m), 7.16−7.11 (2H, m), 6.34 (1H, s), 5.96 (1H, br), 4.67 (2H, d, J = 6.2 Hz), 2.96 (2H, t, J = 7.9 Hz), 1.69−1.64 (2H, m), 1.44−1.38 (2H, m), 0.93 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 152.3, 142.0, 137.5, 135.4, 129.3, 129.0, 128.0, 122.5, 121.7, 120.3, 111.5, 104.5, 45.2, 31.0, 28.1, 22.5, 14.0; IR ($CHCl_3$, cm^{-1}) 3034, 3008, 2959, 2932, 2872, 1705, 1510, 1454, 1381, 1300, 1196, 779, 719; MS (EI) m/z = 306 (M^+); HRMS (EI) m/z calcd for $C_{20}H_{22}N_2O$ 306.1732, found 306.1740.

***N*-Allyl-2-butyl-1*H*-indole-1-carboxamide (14c):** yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.61 (1H, d, J = 8.2 Hz), 7.51 (1H, d, J = 6.9 Hz), 7.21−7.14 (2H, m), 6.35 (1H, s), 6.03−5.97 (1H, m), 5.74 (1H, br), 5.35−5.32 (1H, m), 5.27−5.25 (1H, m), 4.13 (2H, t, J = 5.8 Hz), 2.96 (2H, t, J = 7.6 Hz), 1.72−1.67 (2H, m), 1.46−1.40 (2H, m), 0.95 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 152.2, 142.1, 135.4, 133.5, 129.3, 122.4, 121.7, 120.4, 117.5, 111.5, 104.4, 43.5, 31.0, 28.1, 22.5, 14.0; IR ($CHCl_3$, cm^{-1}) 3445, 3389, 3009, 2961, 2930, 2874, 2862, 2359, 2340, 1709, 1670, 1607, 1585, 1518, 1454, 1381, 1300, 1238, 1175, 1105, 1074, 991, 810, 687; MS (EI) m/z = 256 (M^+); HRMS (EI) m/z calcd for $C_{16}H_{20}N_2O$ 256.1576, found 256.1572.

(*R*)-Methyl 2-(2-butyl-1*H*-indole-1-carboxamido)-3-(methylthio)-propanoate (14d): orange oil; ^{1}H NMR ($CDCl_3$) δ 7.89 (1H, d, J = 8.2 Hz), 7.51 (1H, d, J = 7.6 Hz), 7.26−7.23 (1H, m), 7.18 (1H, t, J = 6.9 Hz), 6.57 (1H, d, J = 7.6 Hz), 6.37 (1H, s), 4.98 (1H, td, J = 6.0, 4.6 Hz), 3.84 (3H, s), 3.20 (1H, dd, J = 14.4, 4.6 Hz), 3.10 (1H, dd, J = 14.4, 6.0 Hz), 2.98 (2H, t, J = 7.6 Hz), 2.15 (3H, s), 1.72−1.67 (2H, m), 1.46−1.40 (2H, m), 0.95 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 171.2, 151.8, 142.0, 135.6, 129.3, 122.9, 122.0, 120.3, 112.2, 105.2, 52.9, 36.5, 31.0, 28.2, 22.5, 16.2, 14.0; IR ($CHCl_3$, cm^{-1}) 3420, 3034, 3009, 2957, 2930, 2872, 1746, 1701, 1601, 1506, 1456, 1439, 1379, 1346, 1298, 1236, 1196, 1182, 1134, 1020, 833, 754; MS (EI) m/z = 348 (M^+); HRMS (EI) m/z calcd for $C_{18}H_{24}N_2O_3S$ 348.1508, found 348.1504.

2-Butyl-*N*-phenethyl-1*H*-indole-1-carboxamide (14e): pale yellow solid; ^{1}H NMR ($CDCl_3$) δ 7.46 (1H, d, J = 8.2 Hz), 7.36−7.33 (2H, m), 7.28−7.25 (3H, m), 7.22 (1H, d, J = 8.2 Hz), 7.10 (1H, t, J = 7.6 Hz), 7.05 (1H, t, J = 7.6 Hz), 6.30 (1H, s), 5.64 (1H, br), 3.79 (2H, q, J = 6.4 Hz), 3.02 (2H, t, J = 6.9 Hz), 2.89 (2H, t, J = 7.6 Hz), 1.68−1.63 (2H, m), 1.43−1.37 (2H, m), 0.94 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 152.2, 141.9, 138.3, 135.3, 129.1, 128.9, 128.8, 126.9, 122.23, 121.5, 120.12, 111.5, 104.3, 42.0, 35.3, 30.9, 28.0, 22.5, 14.0; IR ($CHCl_3$, cm^{-1}) 3435, 3036, 2959, 2932, 1705, 1508, 1454, 1381, 1302, 1238, 1194, 1128, 810, 691; MS (EI) m/z = 320 (M^+); HRMS (EI) m/z calcd for $C_{21}H_{24}N_2O$ 320.1889;, found 320.1881.

2-Butyl-*N*-cyclohexyl-1H-indole-1-carboxamide (14f): white solid; ^{1}H NMR ($CDCl_3$) δ 7.57 (1H, d, J = 8.2 Hz), 7.50 (1H, d, J = 7.6 Hz), 7.18 (1H, t, J = 7.6 Hz), 7.14 (1H, d, J = 7.2 Hz), 6.33 (1H, s), 5.57 (1H, d, J = 7.6 Hz), 3.95−3.90 (1H, m), 2.95 (2H, t, J = 7.6 Hz), 2.15−2.13 (2H, m), 1.81−1.77 (2H, m), 1.70−1.65 (3H, m), 1.49−1.39 (4H, m), 1.35−1.21 (3H, m), 0.94 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 151.3, 141.9, 135.4, 129.2, 122.3, 121.5, 120.3, 111.3, 104.0, 50.0, 33.2, 31.1, 28.0, 25.4, 24.8, 22.5, 13.9; IR ($CHCl_3$, cm^{-1}) 3426, 3007, 2934, 2859, 1703, 1506, 1454, 1381, 1321, 1294, 1192, 1152, 1128; MS (EI) m/z = 298 (M^+); HRMS (EI) m/z calcd for $C_{19}H_{26}N_2O$ 298.2045, found 298.2038.

2-Butyl-*N*-(2-iodophenyl)-1*H*-indole-1-carboxamide (14g): white solid; mp 104−108 °C (white needles from hexane−EtOAc); ^{1}H NMR ($CDCl_3$) δ 8.29 (1H, dd, J = 8.2, 1.4 Hz), 7.92 (1H, br), 7.86 (2H, t, J = 8.2 Hz), 7.55 (1H, d, J = 7.6 Hz), 7.45−7.42 (1H, m), 7.27−7.20 (2H, m), 6.92 (1H, td, J = 7.6, 1.4 Hz), 6.44 (1H, s), 3.04 (2H, t, J = 7.6 Hz), 1.77−1.72 (2H, m), 1.48−1.42 (2H, m), 0.96 (3H, t, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 149.6, 142.1, 139.3, 137.9, 135.4, 129.5, 129.4, 126.3, 122.9, 122.3, 121.4, 120.5, 112.3, 105.6, 89.5, 30.9, 28.3, 22.5, 14.0; IR ($CHCl_3$, cm^{-1}) 3032, 1714, 1585, 1518, 1454, 1431, 1234, 1198, 808, 799, 768, 743; MS (EI) m/z = 418 (M^+); HRMS (EI) m/z calcd for $C_{19}H_{19}IN_2O$ 418.0542, found 418.0533.

2-Butyl-*N*-*o*-tolyl-1*H*-indole-1-carboxamide (14h): pale yellow solid; ^{1}H NMR ($CDCl_3$) δ 7.87 (1H, d, J = 7.6 Hz), 7.74 (1H, d, J = 8.2 Hz), 7.55 (1H, d, J = 6.9 Hz), 7.32−7.15 (6H, m), 6.42 (1H, s), 3.02 (2H, t, J = 7.9 Hz), 2.34 (3H, s), 1.76−1.71 (2H, m), 1.47−1.41 (2H, m), 0.95 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 149.9, 142.3, 135.4, 135.1, 130.9, 129.4, 129.1, 127.1, 125.6, 122.7, 122.5, 122.0, 120.6, 111.4, 105.0, 31.0, 28.1, 22.5, 18.1, 13.9; IR ($CHCl_3$, cm^{-1}) 3009, 2959, 2932, 2872, 1717, 1589, 1521, 1489, 1454, 1381, 1304, 1250, 1186, 1123, 764, 691; MS (EI) m/z = 306 (M^+); HRMS (EI) m/z calcd for $C_{20}H_{22}N_2O$ 306.1732, found 306.1739.

2-Butyl-*N*-(4-cyanophenyl)-1*H*-indole-1-carboxamide (14i): pale yellow solid; ^{1}H NMR ($CDCl_3$) δ 7.77 (1H, s), 7.70−7.66 (4H, m), 7.56 (2H, dd, J = 15.8, 7.6 Hz), 7.26−7.20 (2H, m), 6.42 (1H, s), 2.98 (2H, t, J = 7.6 Hz), 1.73−1.68 (2H, m), 1.47−1.41 (2H, m), 0.95 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 149.2, 142.2, 141.3, 135.2, 133.5, 129.6, 123.1, 122.5, 120.8, 119.3, 118.6, 111.5, 107.6, 105.8, 30.8, 28.0, 22.5, 13.9; IR ($CHCl_3$, cm^{-1}) 3410, 3036, 2961, 2932, 2874, 2228, 1721, 1609, 1589, 1564, 1520, 1514, 1456, 1408, 1377, 1317, 1300, 1240, 1194, 1179, 1119, 1074, 839, 687; MS (EI) m/z = 317 (M^+); HRMS (EI) m/z calcd for $C_{20}H_{19}IN_3O$ 317.1528, found 317.1536.

1,1-Diethyl-3-(2-(hex-1-ynyl)phenyl)urea (15): pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 8.26 (1H, d, J = 8.2 Hz), 7.41 (1H, br), 7.33 (1H, d, J = 7.6 Hz), 7.25 (1H, t, J = 8.2 Hz), 6.89 (1H, t, J = 7.6 Hz), 3.41 (4H, q, J = 7.3 Hz), 2.47 (2H, t, J = 7.2 Hz), 1.63−1.59 (2H, m), 1.51−1.45 (2H, m), 1.26 (6H, t, J = 7.2 Hz), 0.95 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 154.1, 140.6, 131.3, 128.9, 121.3, 117.9, 111.6, 96.9, 76.5, 41.7, 30.9, 22.1, 19.3, 13.8, 13.6; IR ($CHCl_3$, cm^{-1}) 3412, 3007, 2967, 2934, 2874, 1659, 1580, 1524, 1520, 1489, 1447, 1400, 1383, 1364, 1304, 1261, 1163, 1098, 1080, 810, 671; MS (EI) m/z = 272 (M^+); HRMS (EI) m/z calcd for $C_{17}H_{24}N_2O$ 272.1889, found 272.1880.

2-Butyl-*N*-(2-(hex-1-ynyl)phenyl)-1*H*-indole-1-carboxamide (16): yellow oil; ^{1}H NMR ($CDCl_3$) δ 8.55 (1H, s), 8.45 (1H, d, J = 8.2 Hz), 7.86 (1H, d, J = 7.6 Hz), 7.54 (1H, d, J = 6.9 Hz), 7.43 (1H, dd, J = 7.6, 1.4 Hz), 7.37 (1H, t, J = 7.9 Hz), 7.22−7.17 (2H, m), 7.08 (1H, t, J = 7.6 Hz), 6.42 (1H, s), 3.06 (2H, t, J = 7.9 Hz), 2.30 (2H, t, J = 7.2 Hz), 1.77−1.72 (2H, m), 1.49−1.36 (4H, m), 1.29−1.23 (2H, m), 0.96 (3H, t, J = 7.2 Hz), 0.78 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 149.2, 142.4, 138.4, 135.3, 131.8, 129.4, 129.1, 123.6, 122.7, 122.1, 120.4, 118.3, 112.9, 111.8, 105.2, 98.7, 75.7, 30.9, 30.4, 28.2, 22.5, 22.0, 19.3, 14.0, 13.4; IR ($CHCl_3$, cm^{-1}) 3370, 3036, 3009, 2961, 2832, 2874, 2862, 2398, 1712, 1580, 1520, 1449, 1379, 1238, 1196, 1123, 928; MS (EI) m/z = 372 (M^+); HRMS (EI) m/z calcd for $C_{25}H_{28}N_2O$ 372.2202, found 372.2199.

1,3-Bis(2-(hex-1-ynyl)phenyl)urea (17): white solid; mp 162−165 °C (white needle from hexane−EtOAc); ^{1}H NMR ($CDCl_3$) δ 8.05 (1H, d, J = 8.2 Hz), 7.38 (1H, d, J = 7.6 Hz), 7.30 (1H, t, J = 7.9 Hz), 7.24 (1H, br), 7.00 (1H, t, J = 7.6 Hz), 2.39 (2H, t, J = 7.2 Hz), 1.58−1.53 (2H, m), 1.48−1.42 (2H, m), 0.94 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 152.0, 139.1, 132.0, 128.9, 123.0, 119.5, 113.8, 97.7, 76.1, 30.8, 22.1, 19.3, 13.6; IR ($CHCl_3$, cm^{-1}) 3391, 3007, 3961, 2934, 2874, 2862, 1690, 1605, 1580, 1518, 1317, 1300, 1194, 1105, 1042, 945; MS (EI) m/z = 372 (M^+); HRMS (EI) m/z calcd for $C_{25}H_{28}N_2O$ 372.2202, found 372.2200.

Bis(2-butyl-1*H*-indol-1-yl)methanone (18): yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.49 (1H, d, J = 7.6 Hz), 7.13 (1H, t, J = 7.6 Hz), 6.99 (1H, t, J = 7.9 Hz), 6.70 (1H, d, J = 8.2 Hz), 6.52 (1H, s), 2.81−2.69 (2H, m), 1.68−1.63 (2H, m), 1.37−1.33 (2H, m), 0.87 (3H, t, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 149.1, 141.8, 136.3, 129.3, 123.6, 122.9, 120.1, 112.6, 107.9, 31.0, 27.5, 22.4, 13.7; IR ($CHCl_3$, cm^{-1}) 3078, 2961, 2932, 2874, 2862, 1707, 1568, 1520, 1454, 1379, 1335, 1302, 1196, 810; MS (EI) m/z = 372 (M^+); HRMS (EI) m/z calcd for $C_{25}H_{28}N_2O$ 372.2202, found 372.2200.

Carbamoyl Ylide (19). A solution of 2-alkynylbenzamide **1a** (0.08 mmol) and $PhI(OAc)_2$ (0.096 mmol) in 1,2-dichloroethane (0.4 mL) was stirred at 70 °C for 1 h. Then, methyl (triphenylphosphoranylidene)acetate (0.06 mmol) was added, and the reaction mixture was stirred at 70 °C for 45 min. The reaction mixture was directly chromatographed on silica gel [AcOEt−hexane (1:3)] to afford **19** as a orange oil: ^{1}H NMR ($CDCl_3$) δ 11.39 (1H, s), 8.26 (1H, d, J = 8.9 Hz), 7.72 (6H, dd, J = 12.4, 7.6 Hz), 7.52 (3H, t, J = 7.2 Hz), 7.45 (6H, td, J = 7.6, 3.2 Hz), 7.32 (1H, d, J = 7.6 Hz), 7.05 (1H, t, J = 7.9 Hz), 6.80 (1H, t, J = 7.6 Hz), 3.10 (3H, s), 2.61 (2H, t, J = 7.2 Hz), 1.74−1.69 (2H, m), 1.54−1.48 (2H, m), 0.95 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 169.64, 169.55, 168.38, 168.32, 142.2, 133.40, 133.3, 131.59, 131.57, 131.4, 128.5, 128.4, 128.1, 127.7, 127.0, 120.8, 119.1, 112.4, 97.1, 76.9, 57.8, 57.0, 49.2, 30.8, 22.2, 19.6, 13.8; IR ($CHCl_3$, cm^{-1}) 3009, 1634, 1595, 1568, 1518, 1441, 1325, 1198, 1107; MS (EI) m/z = 533 (M^+); HRMS (EI) m/z calcd for $C_{34}H_{32}NO_3P$ 533.2120, found 533.2124.

Indole Ylide (20a). A solution of 2-alkynylbenzamide **1a** (0.08 mmol) and $PhI(OAc)_2$ (0.096 mmol) in 1,2-dichloroethane (0.4 mL) was stirred at 70 °C for 1 h, and then methyl (triphenylphosphoranylidene)acetate (0.06 mmol) was added. After the solution was stirred for 20 min, $PtCl_2$ (0.008 mmol) was added, and the reaction mixture was stirred at 70 °C for additional 13 h. The reaction mixture was directly chromatographed on silica gel [AcOEt−hexane (1:3)] to afford **20a** as a orange oil: orange oil; ^{1}H NMR ($CDCl_3$) δ 7.87 (1H, d, J = 8.2 Hz), 7.82 (6H, dd, J = 12.7, 7.2 Hz), 7.59−7.49 (9H, m), 7.45 (1H, d, J = 7.6 Hz), 7.11 (1H, t, J = 7.6 Hz), 7.05 (1H, t, J = 7.2 Hz), 6.29 (1H, s), 3.07−3.02 (1H, m), 3.02 (3H, s), 2.94−2.89 (1H, m), 1.70−1.63 (2H, m), 1.37−1.43 (2H, m), 0.92 (3H, t, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$) δ 167.6, 167.5, 167.1, 167.0, 142.1, 137.2, 133.6, 133.5, 132.20, 132.18, 128.8, 128.7, 125.6, 125.0, 64.4, 63.6, 50.2, 30.9, 27.9, 22.5, 14.0; IR ($CHCl_3$, cm^{-1}) 3009, 1682, 1599, 1574, 1454, 1437, 1379, 1323, 1105; MS (EI) m/z = 533 (M^+); HRMS (EI) m/z calcd for $C_{34}H_{32}NO_3P$ 533.2120, found 533.2125.

Indole ylide (20b): brown solid; ^{1}H NMR ($CDCl_3$) δ 7.88 (1H, d, J = 8.2 Hz), 7.82−7.79 (6H, m), 7.58 (3H, t, J = 7.6 Hz), 7.52−7.49 (6H, m), 7.13−7.05 (4H, m), 6.95 (2H, q, J = 7.3 Hz), 6.81 (2H, t, J = 6.9 Hz), 5.81 (1H, s), 2.99−2.94 (1H, m), 2.81−2.75 (1H, m), 1.64−1.54 (2H, m), 1.45−1.39 (2H, m), 0.95 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 192.8, 192.8, 167.2, 167.1, 141.6, 141.5, 141.4, 136.8, 133.8, 133.7, 132.2, 132.2, 128.9, 128.9, 128.9, 128.8, 126.6, 126.3, 125.8, 125.2, 121.5, 120.7, 119.0, 113.4, 103.4, 79.0, 78.3, 30.3, 28.8, 22.7, 14.1; IR ($CHCl_3$, cm^{-1}) 3063, 3007, 2959, 2932, 2872, 1624, 1584, 1551, 1539, 1483, 1454, 1439, 1319, 1238, 1194, 1163, 1105, 999, 908, 856, 810; MS (EI) m/z = 579 (M^+); HRMS (EI) m/z calcd for $C_{39}H_{34}NO_2P$ 579.2327, found 579.2330.

Indole ylide (20c): brown solid; ^{1}H NMR ($CDCl_3$) δ 8.07 (1H, d, J = 7.6 Hz), 7.73 (6H, dd, J = 12.4, 7.6 Hz), 7.56−7.45 (10H, m), 7.16−7.10 (2H, m), 6.35 (1H, s), 3.04−2.89 (2H, m), 1.72−1.61 (2H, m), 1.58 (3H, s), 1.47−1.39 (2H, m), 0.93 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 193.1, 193.0, 166.2, 166.1, 141.9, 137.0, 133.4, 133.3, 132.0, 131.9, 129.0, 128.8, 128.7, 126.0, 125.3, 122.1, 121.2, 119.8, 112.6, 104.4, 83.0, 82.3, 30.7, 28.2, 26.5, 26.4, 22.6, 14.0; IR ($CHCl_3$, cm^{-1}) 3032, 3010, 2961, 2932, 2872, 1624, 1547, 1483, 1452, 1437, 1368, 1317, 1198, 1107, 1026, 928, 808; MS (EI) m/z = 517 (M^+); HRMS (EI) m/z calcd for $C_{34}H_{32}NO_2P$ 517.2171, found 517.2174.

Indole ylide (20d): brown solid; ^{1}H NMR ($CDCl_3$) δ 7.79−7.76 (7H, m), 7.67 (3H, dd, J = 8.2, 6.9 Hz), 7.57 (6H, td, J = 7.9, 3.2 Hz), 7.47 (1H, d, J = 7.6 Hz), 7.21 (1H, t, J = 7.2 Hz), 7.10 (1H, t, J = 6.9 Hz), 6.33 (1H, s), 2.95 (2H, t, J = 7.6 Hz), 1.69−1.64 (2H, m), 1.42−1.36 (2H, m), 0.92 (3H, t, J = 7.2 Hz);

^{13}C NMR ($CDCl_3$) δ 168.9, 168.8, 141.6, 135.9, 133.8, 133.7, 133.5, 133.5, 129.4, 129.3, 128.8, 122.9, 122.2, 121.8, 120.8, 120.1, 120.0, 119.7, 112.5, 104.1, 45.5, 44.6, 31.3, 27.7, 22.6, 13.9; IR ($CHCl_3$, cm^{-1}) 3063, 3007, 2959, 2932, 2872, 2183, 1610, 1582, 1485, 1454, 1439, 1379, 1329, 1194, 1109, 908; MS (EI) m/z = 500 (M^+); HRMS (EI) m/z calcd for $C_{33}H_{29}N_2OP$ 500.2018, found 500.2017.

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Supporting Information Available: Experimental procedure for general reaction and spectral data for all new compounds. Crystallographic data for **6c**, **8a**, **9a**, and **9f**. This material is available free of charge via the Internet at http://pubs.acs.org.