Full Paper

Applied Organometallic Chemistry

Received: 13 January 2013 Revised: 24 February 2013 Accepted: 9 March 2013 Published online in Wiley Online Library: 30 May 2013

(wileyonlinelibrary.com) DOI 10.1002/aoc.2990

CuI/amino acid-catalyzed coupling and cyclization of β-bromo-α,β-unsaturated amides with terminal alkynes leading to (3*Z*)-3-alkylidenepyrrol-1-ones

Jong Ik Son, Chan Sik Cho* and Heung-Jin Choi

β-Bromo-α,β-unsaturated amides are coupled and cyclized with terminal alkynes in DMF at 110 °C in the presence of a catalytic amount of CuI and amino acid along with a base to give the corresponding (3*Z*)-3-alkylidenepyrrol-1-ones in moderate to good yields. Copyright © 2013 John Wiley & Sons, Ltd.

Keywords: (3*Z*)-3-alkylidenepyrrol-1-one; amino acid; β-bromo-α,β-unsaturated amide; terminal alkyne; coupling and cyclization

Introduction

Palladium- and CuI-catalyzed sp-carbon-sp^2-carbon bond formation by the cross-coupling of terminal alkynes with aryl and vinyl halides is known as the Sonogashira coupling reaction.[1–3] Many elegant catalytic systems which facilitate Sonogashira coupling under milder conditions have been developed by the tuning of phosphine ligand combined with palladium[4–7] or the addition of promoter.[8–10] Recently, Ma and co-workers also reported that CuI combined with amino acid effectively catalyzes cross-coupling reaction of aryl halides with terminal alkynes in the absence of palladium and phosphine.[11,12] The Sonogashira coupling protocol has been widely used as a powerful synthetic tool for the formation of conjugated acetylenic compounds, which frequently play an important role as an intermediate for the design of pharmaceuticals and organic materials.[3] Furthermore, the coupling reaction followed by intramolecular cyclization has also been used for the construction of various heterocyclic compounds.[3] In connection with this report, several groups have reported that 2-halobenzamides are coupled and cyclized with terminal alkynes under usual palladium catalyst systems to give (3*Z*)-3-alkylideneisoindolin-1-ones (Scheme 1).[13–15] For another synthetic method for 3-alkyl(aryl)ideneisoindolin-1-ones see County *et al.*[16] Such a similar coupling followed by cyclization was also exemplified by the reaction of 2-bromobenzamides and terminal alkynes in the presence of CuI and L-proline.[17] On the other hand, during the course of our ongoing studies on palladium-catalyzed cyclization reactions using β-bromo-α,β-unsaturated aldehydes and their derivatives, which are readily prepared from α-methylene containing ketones under bromination conditions of Vilsmeier–Haack reaction and subsequent transformation,[18,19] we have disclosed several new synthetic methods for the synthesis of carbo- and heterocyclic compounds.[20–51]Under these circumstances, this report describes CuI/amino acid-catalyzed coupling and cyclization of β-bromo-α,β-unsaturated amides with terminal alkynes leading to (3*Z*)-3-alkylidenepyrrol-1-ones.

Results and Discussion

The substrates (**4**) were prepared by three steps from the corresponding ketones (**1**) as shown in Scheme 2. Treatment of **1** under bromination conditions of Vilsmeier–Haack reaction affords β-bromo-α,β-unsaturated aldehydes **2**.[18,19] β-Bromo-α,β-unsaturated carboxylic acids (**3**) synthesized by oxidation of **2**[52] were converted into amides (**4**) by treatment with oxalyl chloride and DMF, followed by addition of primary amines and Et_3N.[53]

The initial study attempted to achieve direct three-component cyclization toward (3*Z*)-3-alkylidenepyrrol-1-ones. Treatment of 2-bromocyclohex-1-enecarboxylic acid (**3a**) with 1.5 equiv. of aniline (**5**) and 2 equiv. of phenylacetylene (**6a**) in dioxane at 110 °C for 40 h in the presence of 10% Pd/C (10 mol%) and CuI (20 mol %) afforded regio- and stereoselective 5-*exo-dig* cyclized product, (3*Z*)-3-benzylidene-2,3,4,5,6,7-hexahydro-2-phenylisoindol-1-one (**7a**)[17] and (3*Z*)-4,5,6,7-tetrahydro-3-benzylideneisobenzofuran-1(3*H*)-one (**8**) [49] in 2% and 34% yields, respectively (Scheme 3). This result excludes three-component cyclization because of higher reaction rate for direct coupling and cyclization of **3a** with **6a**, leading to **8**. Thus, in order to produce an allowable yield of **7a**, we attempted similar coupling and cyclization of 2-bromo-*N*-phenylcyclohex-1-enecarboxamide (**4a)** and **6a** as a model substrate (Table 1). Performing the reaction of **4a** with 1.5 equiv. of **6a** under Pd/C/PPh_3/CuI/Bu_3N or $PdCl_2(PPh_3)_2$/CuI/Bu_3N did not produce **7a** at all (entries 1 and 2). However, surprisingly, when **4a** was subjected to reaction with **6a** in the presence of a catalytic

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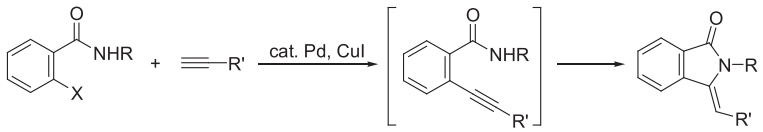
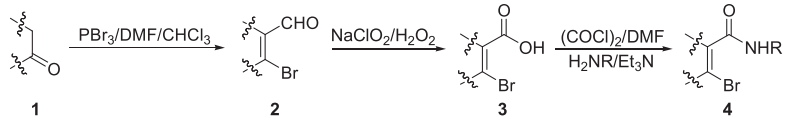
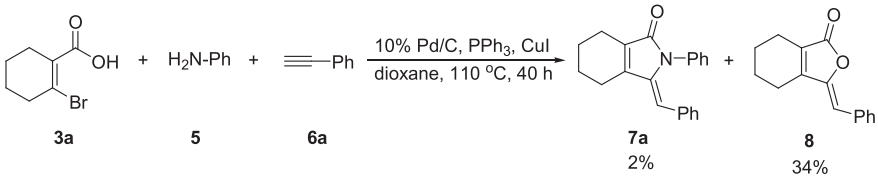
Applied Organometallic Chemistry



Scheme 1. Pd/CuI-catalyzed synthesis of (3*Z*)-3-alkylideneisoindolin-1-ones.

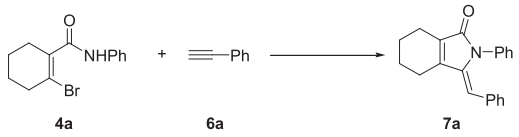


Scheme 2. Synthesis of β-bromo-α,β-unsaturated amides.



Scheme 3. Palladium-catalyzed three-component cyclization.

Table 1. Optimization of conditions for the reaction of **4a** with **6a**[a]



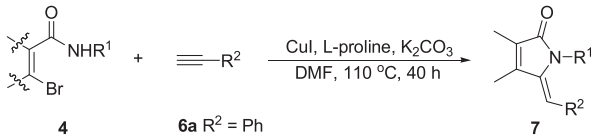
Entry	Catalyst	Base	Solvent	Time (h)	Yield (%)
1[b]	10% Pd/C, CuI, PPh_3	Bu_3N[c]	dioxane	20	0
2[b]	$PdCl_2(PPh_3)_2$, CuI	Bu_3N[c]	DMF	20	0
3	CuI, L-proline	K_2CO_3	DMF	40	56
4	CuI, L-phenylalanine	K_2CO_3	DMF	40	38
5	CuI, glycine	K_2CO_3	DMF	40	41
6	CuI, cysteine	K_2CO_3	DMF	40	3
7	CuI, *N*,*N*-dimethylglycine	K_2CO_3	DMF	40	35
8	CuI, L-proline	K_2CO_3	Propanol	40	30
9	CuI, L-proline	K_2CO_3	Toluene	40	36
10	CuI, L-proline	K_2CO_3	Dioxane	40	2

[a]Reaction conditions: **4a** (0.3 mmol), **6a** (0.45 mmol), CuI (0.03), amino acid (0.09 mmol), base (0.6 mmol), solvent (3 ml), 110 °C.
[b]0.015 mmol palladium catalyst was used.
[c]1.5 mmol.

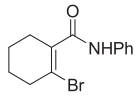
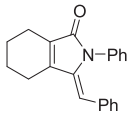
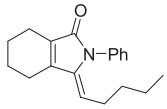
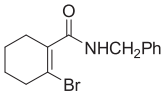
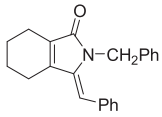
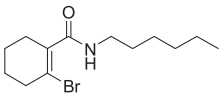
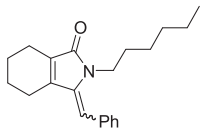
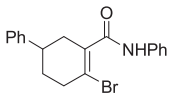
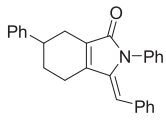
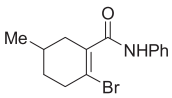
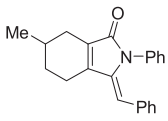
amount of CuI and L-proline, **7a** was obtained in 56% isolated yield with 75% conversion of **4a** (entry 3). The reaction proceeded using other amino acids such as L-phenylalanine, glycine and *N*,*N*-dimethylglycine, but the yield of **7a** was generally lower than that by the use of L-proline (entries 4–7). Among solvents examined under the employed conditions, DMF was shown to be the solvent of choice (entries 3, 8–10). As a result, the best yield of **7a** was accomplished by the standard set of reaction conditions shown in entry 3 of Table 1.

After the reaction conditions had been optimized, various β-bromo-α,β-unsaturated amides (**4**) were subjected to the reaction with terminal alkynes (**6**) in order to investigate the reaction scope, and several representative results are summarized in Table 2. The coupling and cyclization of amide **4a** with alkyl alkyne **6b** also proceeded to give the corresponding alkylidenehydroisoindolin-1-one (**7b**). However, the product yield was lower than when **4a** was subjected to the reaction with **6a**. From the reaction between *N*-benzyl-substituted amide **4b** and

Table 2. Palladium-catalyzed coupling and cyclization of β-bromo-α,β-unsaturated amides with alkynes.[a]



6a R^2 = Ph
6b R^2 = butyl

β-Bromo-α,β-unsaturated amides 4	1-Alkynes 6	Alkylidenepyrrolones 7	Yield[b] (%)
			
4a	6a	7a	53
			
	6b	7b	38
			
4b	6a	7c	62
			
4c	6a	7d	47[c]
			
4d	6a	7e	43
			
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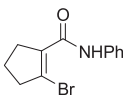
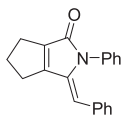
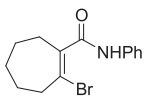
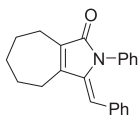
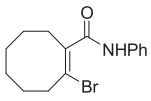
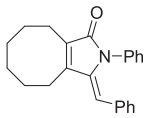
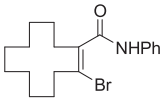
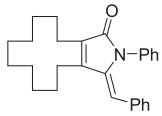
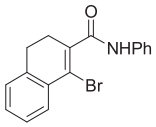
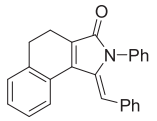
			
4f	6a	7 g	30
			
4 g		7 h	

Applied Organometallic Chemistry

Table 2. (Continued).

	6a		68
4 h	6a	7i	59
	6a		37
4i	6a	7j	
	6a		0
4j	6a	7 k	

[a]Reaction conditions: **4** (0.3 mmol), **6** (0.45 mmol), CuI (0.03 mmol), L-proline (0.09 mmol), K_2CO_3 (0.6 mmol), DMF (3 ml), 110 °C, 40 h.
[b]Dialkyne homo-coupling products (<15%) were formed.
[c](*Z*)-isomer/(*E*)-isomer = 7.5.

6a, the corresponding alkylidenehydroisoindolin-1-one (**7c**) was also produced in similar yield. The reaction of *N*-alkyl-substituted amide **4c** with **6a** also took place to give coupled and cyclized product **7d** in 47% yield as a mixture of (*E*)- and (*Z*)-isomers [(*Z*)-isomer/(*E*)-isomer = 7.5]. The configuration and molar ratio of isomers was confirmed by comparing the chemical shift and peak areas of vinyl proton signals in ^{1}H NMR. It is known that the chemical shifts of (*Z*)-isomers of analogues of **7d**, 3-methyleneisoindolin-1-ones are shifted downfield from those of (*E*)-isomers.[17] Methyl- and phenyl-substituted six-membered β-bromo-α,β-unsaturated amides (**4d** and **4e**) were also coupled and cyclized with **5a** to give the corresponding alkylidenehydroisoindolin-1-ones (**7e** and **7f**). With β-bromo-α,β-unsaturated amides (**4f–i**) having various ring sizes, the coupled and cyclized products (**7 g–j**) were formed in the range of 30–68% yield without any identifiable side product, and the product yield was considerably affected by the ring size of **4f–i**. Lower reaction rate and yield were observed with **4f** and **4i**. On the other hand, the reaction of benzo-fused β-bromo-α,β-unsaturated amide **4j** with **6a** did not proceed toward coupled and cyclized product **7 k** under the employed conditions, a small amount of homo-coupled 1,4-diphenyl-1,3-diyne being formed as an identifiable product.

Conclusion

In summary, it has been shown that β-bromo-α,β-unsaturated amides, which are readily prepared from α-methylene-containing ketones by three steps, undergo coupling and cyclization with terminal alkynes in the presence of CuI and L-proline along with K_2CO_3 to give (3*Z*)-3-alkylidenepyrrol-1-ones. The present reaction provides a promising route for the synthesis of valuable heterocycles from readily available starting ketones. Further study of synthetic applications to heterocycles using this ketone as starting compound and CuI/amino acids catalytic system is currently under investigation.

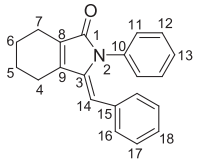
Experimental

^{1}H and ^{13}C NMR (400 and 100 MHz) spectra were recorded on a Bruker Avance Digital 400 spectrometer using tetramethylsilane as an internal standard. Melting points were determined on a Stanford Research Inc. MPA100 automated melting point apparatus. High-resolution mass spectrometry (HRMS) was performed at the Korea Basic Science Institute (Daegu). The isolation of pure products was carried out via thin-layer (silica gel 60 GF_{254}, Merck) chromatography. The starting β-bromo-α,β-unsaturated amides were synthesized via three steps from the corresponding ketones according to literature procedures.[18,19,52,53] Commercially available organic and inorganic compounds were used without further purification.

General Experimental Procedure for CuI/Amino Acid-Catalyzed Coupling and Cyclization of β-Bromo-α,β-Unsaturated Amides with Terminal Alkynes

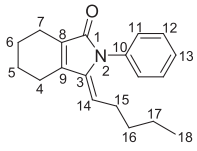
A mixture of β-bromo-α,β-unsaturated amide **4** (0.3 mmol), terminal alkyne **6** (0.45 mmol), CuI (0.006 g, 0.03 mmol), amino acid (0.09 mmol) and base (0.6 mmol) in solvent (3 ml) was placed in a 5 ml screw-capped vial (Wheaton) and the reaction mixture was allowed to react at 110 °C for 40 h. The reaction mixture was filtered through a short silica gel column (ethyl acetate–hexane

mixture) to eliminate inorganic salts. Removal of the solvent left a crude mixture, which was separated by thin-layer chromatography (silica gel, ethyl acetate–hexane mixture) to give (3*Z*)-3-alkylidenepyrrol-1-ones **7**. All new products prepared by the above procedure were characterized spectroscopically as shown below.



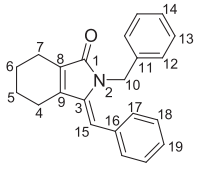
(3Z)-3-Benzylidene-2,3,4,5,6,7-hexahydro-2-phenylisoindol-1-one (***7a***)

Solid; m.p. 154–155 °C. ^{1}H NMR (400 MHz, DMSO-d$_6$) δ 1.74–1.80 (m, 4H, 2C*H*$_2$), 2.56 (s, 2H, C*H*$_2$), 2.59 (s, 2H, C*H*$_2$), 6.42 (s, 1H, vinylic C*H*), 6.86–6.98 (m, 7H, 7C*H*), 7.01–7.10 (m, 3H, 3C*H*). ^{13}C NMR (100 MHz, DMSO-d$_6$) δ 20.03 (C5), 20.94 (C6), 21.55 (C7), 21.72 (C4), 109.91 (C14), 125.95 (C13), 126.70 (C11), 126.75 (C18), 127.10 (C16), 127.96 (C17), 128.48 (C8), 129.21 (C12), 133.45 (C10), 136.30 (C15), 137.54 (C3), 147.23 (C9), 170.35 (C1), assignments to C5 and C6 are interchangeable, assignments to C4 and C7 are interchangeable, assignments to C11,12,16 and 17 are interchangeable, assignments to C13 and C18 are interchangeable. HRMS (EI). Anal. Calcd for $C_{21}H_{19}NO$ ($M^{+\cdot}$): 301.1467. Found: 301.1467. Anal. Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.55; H, 6.30; N, 4.62.



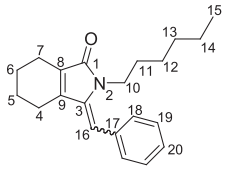
(3Z)-2,3,4,5,6,7-Hexahydro-3-pentylidene-2-phenylisoindol-1-one (**7b**)

Solid; m.p. 126–128 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.72 (t, J_{HH} = 7.3 Hz, 3H, C*H*$_3$), 1.02–1.11 (m, 2H, C*H*$_2$), 1.15–1.23 (m, 2H, C*H*$_2$), 1.58–1.64 (m, 2H, C*H*$_2$), 1.72–1.83 (m, 4H, 2C*H*$_2$), 2.33–2.36 (m, 2H, C*H*$_2$), 2.40–2.43 (m, 2H, C*H*$_2$), 5.08 (t, J_{HH} = 8.0 Hz, 1H, vinyl C*H*), 7.23–7.26 (m, 2H, 2C*H*), 7.32–7.36 (m, 1H, C*H*), 7.39–7.43 (m, 2H, 2C*H*). ^{13}C NMR (100 MHz, CDCl$_3$) δ 13.88 (C18), 20.49 (C17), 21.43 (C6), 22.31 (C5), 22.38 (C15), 22.46 (C7), 26.52 (C4), 31.94 (C16), 112.54 (C14), 127.82 (C13), 128.80 (C11), 129.00 (C8), 129.14 (C12), 137.82 (C10), 139.10 (C3), 145.40 (C9), 171.29 (C1), assignments to C5, C6 and C17 are interchangeable, assignments to C7 and C15 are interchangeable, assignments to C11 and C12 are interchangeable. HRMS (EI). Anal. Calcd for $C_{19}H_{23}NO$ ($M^{+\cdot}$): 281.1780. Found: 281.1778. Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.02; H, 8.10; N, 4.90.



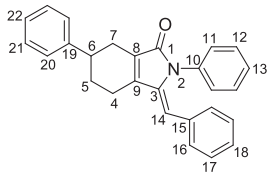
(3Z)-2-Benzyl-3-benzylidene-2,3,4,5,6,7-hexahydroisoindol-1-one (**7c**)

Solid; m.p. 115–116 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.75–1.85 (m, 4H, 2C*H*$_2$), 2.38–2.46 (m, 4H, 2C*H*$_2$), 4.71 (s, 2H, benzyl C*H*$_2$), 6.10 (s, 1H, vinyl C*H*), 6.50–6.53 (m, 2H, 2C*H*), 7.01–7.09 (m, 5H, 5C*H*), 7.20–7.27 (m, 3H, 3C*H*). ^{13}C NMR (100 MHz, CDCl$_3$) δ 20.54 (C6), 21.46 (C5), 22.17 (C7), 22.42 (C4), 44.66 (C10), 109.55 (C15), 126.71 (C12 and C17), 127.52 (C14), 128.04 (C13), 128.07 (C19), 129.73 (C18), 130.35 (C8), 135.01 (C16), 137.78 (C11), 138.74 (C3), 146.26 (C9), 172.65 (C1), assignments to C4 and C7 are interchangeable, assignments to C5 and C6 are interchangeable, assignments to C12, C13, C17 and C18 are interchangeable, assignments to C14 and C19 are interchangeable. HRMS (EI). Anal. Calcd for $C_{22}H_{21}NO$ ($M^{+\cdot}$): 315.1623. Found: 315.1620. Anal. Calcd for $C_{22}H_{21}NO$: C, 83.78; H, 6.71; N, 4.44. Found: C, 83.70; H, 6.60; N, 4.42.



(3Z)-3-Benzylidene-2-hexyl-2,3,4,5,6,7-hexahydroisoindol-1-one (**7d**)

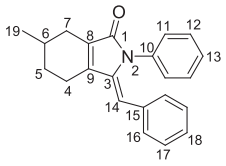
As a mixture of (*E*)- and (*Z*)-isomers. ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.87–0.91 (m, 3H, C*H*$_3$), 1.30–1.38 (m, 6H, 3C*H*$_2$), 1.46–1.52 (m, 2H, C*H*$_2$), 1.59–1.68 (m, 4H, 2C*H*$_2$), 1.90-1.94 (m, 2H, C*H*$_2$), 2.30–2.33 (m, 2H, C*H*$_2$), 3.42 (t, J_{HH} = 7.8 Hz, ≒ 0.24H, NC*H*$_2$, *E*-isomer), 3.67 (t, J_{HH} = 7.5 Hz, ≒ 1.76 H, NC*H*$_2$, *Z*-isomer), 6.16 (s, ≒ 0.12H, vinyl C*H*, *E*-isomer), 6.40 (s, ≒ 0.88H, vinyl C*H*, *Z*-isomer), 7.26–7.37 (m, 5H, 5C*H*). ^{13}C NMR (100 MHz, CDCl$_3$) δ 14.28 (C15), 20.95 (C14), 21.67 (C6), 22.81 (C5), 22.93 (C7), 25.52 (C12), 26.90 (C11), 29.10 (C4), 31.81 (C13), 39.29 (C10), 111.22 (C16), 127.67 (C20), 128.26 (C18), 129.89 (C19), 133.87 (C8), 135.54 (C17), 140.06 (C3), 141.80 (C9), 169.67 (C1), assignments to C4, C11 and C13 are interchangeable, assignments to C5–C7 and C14 are interchangeable. HRMS (EI). Anal. Calcd for $C_{21}H_{27}NO$ ($M^{+\cdot}$): 309.2093. Found: 309.2094. Anal. Calcd for $C_{21}H_{27}NO$: C, 81.51; H, 8.79; N, 4.53. Found: C, 81.48; H, 8.70; N, 4.43.



(3Z)-3-Benzylidene-2,3,4,5,6,7-hexahydro-2,6-diphenylisoindol-1-one (**7e**)

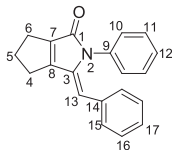
Solid; m.p. 168–170 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.95–2.05 (m, 1H, 1/2C*H*$_2$), 2.23–2.28 (m, 1H, 1/2C*H*$_2$), 2.45–2.53 (m, 1H, 1/2C*H*$_2$), 2.64–2.74 (m, 1H, 1/2C*H*$_2$), 2.78–2.86 (m, 2H, C*H*$_2$), 2.96–3.04 (m, 1H, C*H*), 6.27 (s, 1H, vinyl C*H*), 6.84–6.86 (m, 2H, 2C*H*), 6.89–6.94 (m, 2H, 2C*H*), 6.95–7.08 (m, 6H, 6C*H*), 7.22–7.27 (m, 1H, C*H*), 7.29–7.31 (m, 2H, 2C*H*), 7.34–7.38 (m, 2H, 2C*H*). ^{13}C NMR (100 MHz, CDCl$_3$) δ 22.20 (C4), 28.33 (C5), 30.00 (C7), 40.14 (C6), 110.35 (C14), 126.26 (C13), 126.69 (C22), 126.95 (C11), 127.02 (C18), 127.09 (C16), 127.41 (C20), 128.28 (C17), 128.79 (C21), 129.46 (C12), 129.75 (C8), 133.77 (C10), 136.44 (C15), 138.15 (C19), 145.57 (C3), 146.56 (C9), 171.03 (C1), assignments to C13, C18 and C22 are interchangeable, assignments to C11, C12,

C16, C17, C20 and C21 are interchangeable. HRMS (EI). Anal. Calcd for $C_{27}H_{23}NO$ ($M^{+\cdot}$): 377.1780. Found: 377.1781. Anal. Calcd for $C_{27}H_{23}NO$: C, 85.91; H, 6.14; N, 3.71. Found: C, 85.70; H, 6.09; N, 3.70.



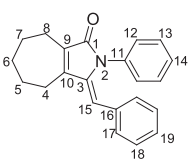
(3Z)-3-Benzylidene-2,3,4,5,6,7-hexahydro-6-methyl-2-phenylisoindol-1-one (**7f**)

Solid; m.p. 160–162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (d, J_{HH} = 6.3 Hz, 3H, CH_3), 1.42–1.52 (m, 1H, 1/2CH_2), 1.82–2.01 (m, 3H, CH_2 and CH), 2.49–2.58 (m, 2H, CH_2), 2.65–2.72 (m, 1H, 1/2CH_2), 6.23 (s, 1H, vinyl CH), 6.82–6.84 (m, 2H, 2CH), 6.88–6.92 (m, 2H, 2CH), 6.95–7.08 (m, 6H, 6CH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.48 (C19), 21.56 (C4), 28.76 (C6), 28.78 (C5), 30.70 (C7), 109.90 (C14), 126.17 (C13), 126.89 (C18), 126.96 (C11), 127.37 (C16), 128.23 (C17), 129.42 (C12), 129.80 (C8), 133.89 (C10), 136.51 (C15), 138.36 (C3), 146.60 (C9), 171.35 (C1), assignments to C4 and C19 are interchangeable, assignments to C5 and C6 are interchangeable, assignments to C13 and C18 are interchangeable, assignments to C11, C12, C16 and C17 are interchangeable. HRMS (EI). Anal. Calcd for $C_{22}H_{21}NO$ ($M^{+\cdot}$): 315.1623. Found: 315.1624. Anal. Calcd for $C_{22}H_{21}NO$: C, 83.78; H, 6.71; N, 4.44. Found: C, 83.71; H, 6.60; N, 4.40.



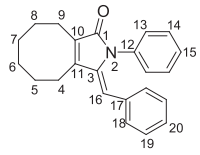
(3Z)-3-Benzylidene-2,3,5,6-tetrahydro-2-phenylcyclopenta[*c*]pyrrol-1(4*H*)-one (**7 g**)

Solid; m.p. 141–143 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44–2.51 (m, 2H, CH_2), 2.69–2.73 (m, 2H, CH_2), 2.80–2.85 (m, 2H, CH_2), 6.17 (s, 1H, vinyl CH), 6.81–6.84 (m, 2H, 2CH), 6.87–6.91 (m, 2H, 2CH), 6.93–7.06 (m, 6H, 6CH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.59 (C5), 27.20 (C6), 27.96 (C4), 112.47 (C13), 126.23 (C12), 126.98 (C10), 127.16 (C17), 127.41 (C15), 128.31 (C16), 129.49 (C11), 133.54 (C7), 135.21 (C9), 136.84 (C14), 139.68 (C3), 160.02 (C8), 167.80 (C1), assignments to C4–C6 are interchangeable, assignments to C12 and C17 are interchangeable, assignments to C10, C11, C15 and C16 are interchangeable. HRMS (EI). Anal. Calcd for $C_{20}H_{17}NO$ ($M^{+\cdot}$): 287.1310. Found: 287.1310. Anal. Calcd for $C_{20}H_{17}NO$: C, 83.59; H, 5.96; N, 4.87. Found: C, 83.50; H, 6.03; N, 4.50.



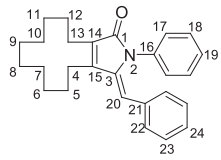
(3Z)-3-Benzylidene-2,3,5,6,7,8-hexahydro-2-phenylcyclohepta[*c*]pyrrol-1(4*H*)-one (**7 h**)

Solid; m.p. 140–141 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.68–1.73 (m, 2H, CH_2), 1.78–1.83 (m, 2H, CH_2), 1.87–1.93 (m, 2H, CH_2), 2.58–2.61 (m, 2H, CH_2), 2.70–2.73 (m, 2H, CH_2), 6.39 (s, 1H, vinyl CH), 6.83–7.04 (m, 10H, 10CH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.64 (C7), 26.27 (C5), 26.94 (C8), 27.06 (C6), 31.31 (C4), 110.19 (C15), 126.10 (C14), 126.82 (C19), 126.99 (C12), 127.35 (C17), 128.15 (C18), 129.43 (C13), 132.71 (C9), 134.23 (C11), 136.67 (C16), 138.60 (C3), 149.11 (C10), 171.66 (C1), assignments to C4–C8 are interchangeable, assignments to C12, C13, C17 and C18 are interchangeable, assignments to C15 and C20 are interchangeable, assignments to C14 and C19 are interchangeable. HRMS (EI). Anal. Calcd for $C_{22}H_{21}NO$ ($M^{+\cdot}$): 315.1623. Found: 315.1620. Anal. Calcd for $C_{22}H_{21}NO$: C, 83.78; H, 6.71; N, 4.44. Found: C, 83.69; H, 6.58; N, 4.38.



(3Z)-3-Benzylidene-2,3,4,5,6,7,8,9-octahydro-2-phenylcycloocta[*c*]pyrrol-1-one (**7i**)

Solid; m.p. 137–138 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54–1.62 (m, 4H, 2CH_2), 1.70–1.76 (m, 2H, CH_2), 1.81–1.87 (m, 2H, CH_2), 2.58–2.61 (m, 2H, CH_2), 2.78–2.81 (m, 2H, CH_2), 6.35 (s, 1H, vinyl CH), 6.84–7.06 (m, 10H, 10CH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.73 (C7), 23.44 (C6), 26.04 (C8), 26.27 (C5), 29.07 (C9), 29.27 (C4), 109.98 (C16), 126.06 (C15), 126.86 (C20), 126.90 (C13), 127.33 (C18), 128.15 (C19), 129.50 (C14), 131.37 (C10), 134.08 (C12), 136.65 (C17), 138.02 (C3), 147.83 (C11), 171.65 (C1), assignments to C4–C9 are interchangeable, assignments to C13, C14, C18 and C19 are interchangeable, assignments to C15 and C20 are interchangeable. HRMS (EI). Anal. Calcd for $C_{23}H_{23}NO$ ($M^{+\cdot}$): 329.1780. Found: 329.1779. Anal. Calcd for $C_{23}H_{23}NO$: C, 83.85; H, 7.04; N, 4.25. Found: C, 83.70; H, 6.90; N, 4.20.



(3Z)-3-Benzylidene-2,3,4,5,6,7,8,9,10,11,12,13-dodecahydro-2-phenylcyclododeca[c]pyrrol-1-one (**7j**)

Solid; m.p. 134–136 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32–1.54 (m, 12H, 6CH_2), 1.75–1.87 (m, 4H, 2CH_2), 2.44–2.47 (m, 2H, CH_2), 2.64–2.68 (m, 2H, CH_2), 6.36 (s, 1H, vinyl CH), 6.83–7.05 (m, 10H, 10CH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.91 (C11), 22.33 (C8), 22.36 (C9), 22.53 (C7), 24.81 (C10), 24.91 (C6), 25.37 (C12), 26.04 (C5), 26.25 (C13), 28.74 (C4), 110.78 (C20), 126.09 (C19), 126.81 (C24), 126.95 (C17), 127.35 (C22), 128.14 (C23), 129.46 (C18), 131.46 (C14), 134.21 (C16), 136.48 (C21), 138.52 (C3), 147.70 (C15), 171.93 (C1), assignments to C17, C18, C22 and C23 are interchangeable, assignments to C19 and C24 are interchangeable. HRMS (EI). Anal. Calcd for $C_{27}H_{31}NO$ ($M^{+\cdot}$): 385.2406. Found: 385.2406. Anal. Calcd for $C_{27}H_{31}NO$: C, 84.11; H, 8.10; N, 3.63. Found: C, 84.04; H, 8.00; N, 3.52.

Acknowledgments

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2012-0002856) and Kyungpook National University Research Fund, 2012.

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