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Chiral Lewis Acid-Catalyzed Enantioselective Cycloadditions between Indoles and Cyclic Carbonyl Ylides Derived from Diazodiketone or Diazoketoester Derivatives

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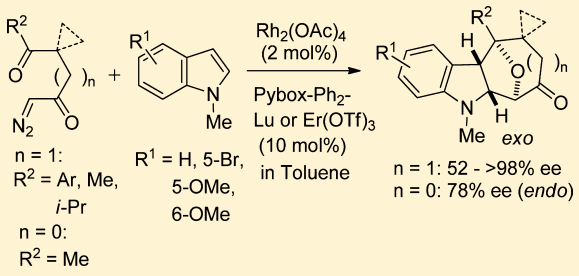
Supporting Information

ABSTRACT: Asymmetric 1,3-dipolar cycloaddition reactions between *N*-methylindoles and several cyclic carbonyl ylides that were derived from diazodiketone or diazoketoester precursors in the presence of both achiral Rh and chiral lanthanoid metal catalysts are described. For the six-membered cyclic carbonyl ylides derived from 1-diazo-5-aryl-2,5-pentanedione precursors, the cycloaddition reactions were carried out using $Rh_2(OAc)_4$ (2 mol %) and the chiral Pybox-Ph_2–$Lu(OTf)_3$ complex (10 mol %) as catalysts, resulting in high enantioselectivities (83% to >98% ee (*exo*)) along with relatively good *exo*-selectivities (*exo*:*endo* = 65:35 to 94:6) and yields (63–85%). For the five-membered cyclic carbonyl ylide derived from 1-diazo-2,4-pentandione precursor, the cycloaddition reaction with 5-bromo-1-methylindole was carried out in the presence of $Rh_2(OAc)_4$ (2 mol %) and the chiral Pybox-Ph_2–$Er(OTf)_3$ complex (30 mol %) as catalysts, resulting in relatively good enantioselectivity (78% ee) and *endo*-selectivity (*endo*:*exo* = 81:19).



INTRODUCTION

Development of an efficient and asymmetric methodology for the construction of optically active fused indoline derivatives, which include a large number of biologically active terpenoid indoline alkaloids such as aspidosperma and kopsifoline alkaloids,[1] has attracted considerable attention in the field of organic synthesis of heterocyclic compounds. Recently, Boger reported on the efficient total syntheses of (−)-vindoline,[2] (−)-vindorosine,[2d] vinblastine[3] and its analogues,[2d,4] (−)-kopsifoline D,[5] (+)-fendleridine,[6] and related aspidosperma alkaloids,[7] featuring a powerful intramolecular [4 + 2]/[3 + 2] cycloaddition cascade reaction of 1,3,4-oxadiazole,[8] which includes the 1,3-dipolar cycloaddition of a cyclic carbonyl ylide with a tethered indole C^2–C^3 double bond. The total syntheses of optically active alkaloids can either involve the resolution of a key intermediate or employ a highly diastereoselective tandem [4 + 2]/[3 + 2] cycloaddition reaction of the chiral 1,3,4-oxadiazole substrates. In 1992, Padwa reported on the pioneering investigations of intramolecular 1,3-dipolar cycloadditions between indole derivatives (dipolarophiles) and cyclic carbonyl ylides, which were generated via intramolecular carbenoid–carbonyl cyclizations from diazoimide derivatives.[9] This efficient synthetic scheme was subsequently applied toward the construction of the core skeletons of aspidosperma[10] and kopsifoline alkaloids,[11] and toward the total synthesis of (±)-aspidophytine.[12] Intermolecular 1,3-dipolar cycloadditions between indole derivatives and five-membered cyclic carbonyl ylides generated by intramolecular carbenoid–carbonyl cyclizations were also reported.[26] Recently, Hashimoto reported on the excellent asymmetric version of the intermolecular catalytic reaction, in which chiral Rh(II) complexes were shown to possess highly enantioselective catalytic activities for the 1,3-dipolar cycloaddition between indole derivatives and six- or five-membered cyclic carbonyl ylides derived from diazodiketoesters.[13a] Furthermore, the chiral Rh(II) catalyst was also effective for the asymmetric intramolecular carbonyl ylide cycloadditions using diazoimides that contained a tethered indole; this synthetic scheme was applied toward the construction of the pentacyclic skeleton of aspidosperma alkaloids, resulting in moderate yields with enantioselectivities of up to 66% ee.[13b] In fact, over the past decade, Hodgson[15] and Hashimoto[16] have separately developed intra- and intermolecular enantioselective carbonyl ylide cycloadditions with several other dipolarophiles.[14]

On the other hand, recently we reported our dual-activation methodology involving an achiral Rh(II)-catalyzed carbonyl ylide formation followed by an asymmetric 1,3-dipolar cycloaddition, in the presence of a Lewis acid catalyst, for the tandem carbonyl ylide formation–cycloaddition sequence with high levels of asymmetric induction. Our methodology could be applied to not only *normal* electron-demand cycloadditions[17] involving electron-deficient dipolarophiles such as (benzyloxy)-acetoaldehyde, *β*-keto esters, and 2-alkenoyl-3-oxazolidinones, but also *inverse* electron-demand cycloadditions[18] involving vinyl ethers as electron-donating dipolarophiles. To evaluate

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Scheme 1. Cycloaddition Reaction between Indole 2a and the Carbonyl Ylide Derived from Diazodiketone 1a

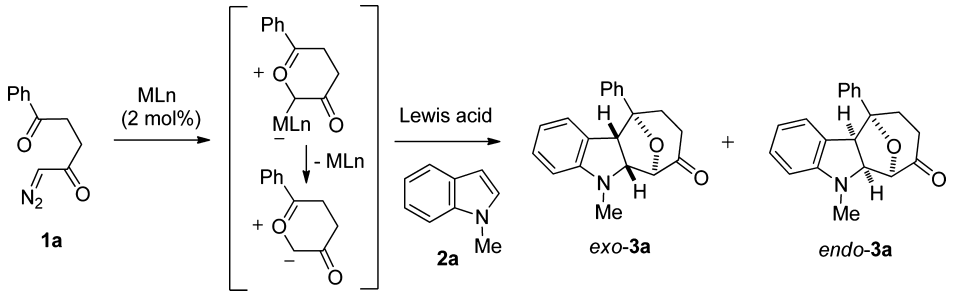

Table 1. Cycloaddition Reaction between Indole 2a and the Carbonyl Ylide Derived from Diazodiketone 1a[a]

entry	MLn	Lewis acid	solvent	addition condition[b]	yield (%)	*exo*:*endo* ratio[c]	ee[d] (%) (*exo*/*endo*)
1	$Rh_2(OAc)_4$	none	toluene	A	5	*endo* only	
2	$Rh_2(OAc)_4$	$Lu(OTf)_3$	toluene	A	84	44:56	
3	$Rh_2(OAc)_4$	Pybox-Ph_2–$Lu(OTf)_3$	toluene	A	77	75:25	79/22
4	$Rh_2(OAc)_4$	Pybox-Ph_2–$Lu(OTf)_3$	CH_2Cl_2	A	79	72:28	64/19
5	$Rh_2(OAc)_4$	Pybox-Ph_2–$Lu(OTf)_3$	CH_2Cl_2[e]	A	80	74:26	36/6
6	$Rh_2(OAc)_4$	Pybox-Ph_2–$Lu(OTf)_3$	toluene	B	77	78:22	90/32
7	$Rh_2(OAc)_4$	Pybox-Ph_2–$Lu(OTf)_3$	$CF_3C_6H_5$	B	64	66:34	83/17
8	$Rh_2(piv)_4$	Pybox-Ph_2–$Lu(OTf)_3$	toluene	B	57	54:46	85/14
9	$Rh_2(tfa)_4$	Pybox-Ph_2–$Lu(OTf)_3$	toluene	B	34	84:16	83/49
10	$Cu(acac)_2$	Pybox-Ph_2–$Lu(OTf)_3$	toluene	B	30	34:66	21/19
11	Rh_2(*S*-TCPTTL)$_4$	none	toluene	A	14	43:57	91/94
12	Rh_2(*S*-TCPTTL)$_4$	none	$CF_3C_6H_5$	B	17	66:34	92/85
13	Rh_2(*S*-TCPTTL)$_4$	$Lu(OTf)_3$	toluene	B	54	61:39	48/31
14	Rh_2(*S*-TCPTTL)$_4$	Pybox-Ph_2–$Lu(OTf)_3$	toluene	B	79	59:41	92/69
15	Rh_2(*R*-TCPTTL)$_4$	Pybox-Ph_2–$Lu(OTf)_3$	toluene	B	71	44:56	−32/−32

[a]The reaction was carried out by addition condition A or B at 23 °C in the presence of MS 4 Å in the solvent cited in the table using diazodiketone **1a** (1 equiv), indole **2a** (2 equiv), Rh(II) or Cu(II) catalyst (2 mol %), and a Lewis acid (0 or 10 mol %). [b]Condition A: a solution of diazodiketone **1a** was added to a solution of indole **2a** and Rh(II) or Cu(II) catalyst in the presence or absence of Lewis acid over a period of 1 h. Condition B: a solution of diazodiketone **1a** and indole **2a** was added to a solution of Rh(II) or Cu(II) catalyst and a Lewis acid over a period of 1 h. [c]Determined by ^{1}H NMR using the crude mixture. [d]Determined by chiral HPLC after isolation of the cycloadduct. [e]MeOH (10 mol %) was included as an additive.

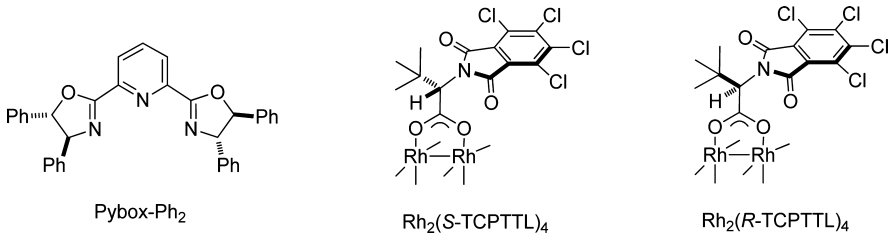

Figure 1. Structures of Pybox-Ph_2, Rh_2(*S*-TCPTTL)$_4$, and Rh_2(*R*-TCPTTL)$_4$.

the efficiency of the dual-activation methodology for the asymmetric synthesis of chiral fused indoline derivatives, we investigated the intermolecular asymmetric cycloaddition reactions between *N*-methylindole derivatives and six- or five-membered cyclic carbonyl ylides derived from the corresponding diazodiketone or diazoketoester, which have not been examined for the chiral Rh(II)-catalyzed cycloadditions with indole derivatives,[13a] under various combinations of achiral/chiral Rh or achiral Cu catalysts and chiral lanthanoid metal–2,6-bis(oxazolinyl)pyridine (Pybox) Lewis acids. Our results have revealed that the combination of $Rh_2(OAc)_4$ and chiral lanthanoid Pybox Lewis acid provided the highest enantioselectivities along with high diastereoselectivities and yields.

RESULTS AND DISCUSSION

Initially, the cycloaddition was carried out in the absence of any Lewis acids, and resulted in only cycloadduct *endo*-**3a** in merely 5% yield; specifically, 1-diazo-2,5-pentanedione **1a** was added to a solution of indole **2a** (2 equiv) and $Rh_2(OAc)_2$ (2 mol %) in toluene at room temperature over a period of 1 h (Scheme 1, Table 1, entry 1). The cycloaddition was repeated, but in the presence of Lewis acid $Lu(OTf)_3$ (10 mol %), to afford cycloadducts *exo*-**3a** and *endo*-**3a** in a combined yield of 84% with an *exo*:*endo* ratio of 44:56 (entry 2). Next, the cycloaddition was carried out in the presence of chiral lanthanoid metal catalyst (4*S*,5*S*)-Pybox-Ph_2–$Lu(OTf)_3$ (10 mol %) (Figure 1), which was prepared according to a previously reported procedure,[17,18] to give the cycloadducts in a combined yield of 77% with an *exo*:*endo* ratio of 75:25 with

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Scheme 2. Cycloaddition Reactions between Indoles 2a−d and Carbonyl Ylides Derived from Diazo Compounds 1a−g

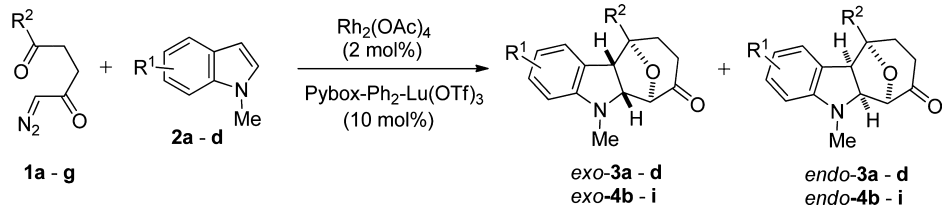

Table 2. Cycloaddition Reactions between Indoles 2a−d and Carbonyl Ylides Derived from Diazo Compounds 1a−g Catalyzed by the Chiral Pybox-Ph_2−Lu$(OTf)_3$ Complex[a]

entry	R^1	R^2	product	yield (%)	*exo*:*endo* ratio[b]	ee[c] (%) (*exo*/*endo*)
1	H (**2a**)	Ph (**1a**)	*exo*-**3a**/*endo*-**3a**	77	78:22	90/32
2	5-Br (**2b**)	Ph (**1a**)	*exo*-**3b**/*endo*-**3b**	76	88:12	96/ND[d]
3	5-OMe (**2c**)	Ph (**1a**)	*exo*-**3c**/*endo*-**3c**	77	71:29[e]	88/ND[d]
4	6-OMe (**2d**)	Ph (**1a**)	*exo*-**3d**/*endo*-**3d**	65	71:29	92/ND[d]
5	H (**2a**)	*p*-Me-C_6H_4 (**1b**)	*exo*-**4b**/*endo*-**4b**	85	65:35	83/18
6	H (**2a**)	*p*-Br-C_6H_4 (**1c**)	*exo*-**4c**/*endo*-**4c**	73	72:28	84/18
7	H (**2a**)	Me (**1d**)	*exo*-**4d**/*endo*-**4d**	56	57:43	52/11
8	H (**2a**)	*i*-Pr (**1e**)	*exo*-**4e**/*endo*-**4e**	39	71:29	68/39
9	5-Br (**2b**)	*p*-Me-C_6H_4 (**1b**)	*exo*-**4f**/*endo*-**4f**	63	90:10	92/ND[d]
10	5-Br (**2b**)	*p*-Et-C_6H_4 (**1f**)	*exo*-**4g**/*endo*-**4g**	71	93:7	85/ND[d]
11	5-Br (**2b**)	*p*-MeO-C_6H_4 (**1g**)	*exo*-**4h**/*endo*-**4h**	74	80:20	98/ND[d]
12	5-Br (**2b**)	*p*-Br-C_6H_4 (**1c**)	*exo*-**4i**/*endo*-**4i**	69	94:6	>98/ND[d]

[a]The reactions were carried out at 23 °C by adding a solution of diazodiketones **1a−g** and indoles **2a−d** in toluene to a solution of $Rh_2(OAc)_4$ (2 mol %) and the Pybox-Ph_2−Lu$(OTf)_3$ complex (10 mol %) in the presence of powdered MS 4 Å in toluene over a period of 1 h. [b]Determined by ^{1}H NMR using the crude mixture. [c]Determined by chiral HPLC after isolation of the cycloadduct. [d]Not determined. [e]Determined by isolated products.

enantiomeric excesses of 79% for *exo*-**3a** and 22% for *endo*-**3a** (entry 3). To further improve the diastereo- and enantioselectivities of the cycloaddition, studies were carried out to optimize the reaction conditions, which involved the choice of the reaction solvent, whether to include an alcohol as an additive, the procedures for the addition step, and the type of metal triflate in the preparation of the chiral Lewis acid (see the Supporting Information). Simply switching the reaction solvent to CH_2Cl_2 or $CF_3C_6H_5$ (entries 4 and 7) and/or including MeOH (10 mol %) as an additive in CH_2Cl_2 (entry 5) did not improve the selectivities. Surprisingly, however, by also modifying the addition step—specifically, adding a solution of both substrates **1** and **2a** into the catalyst solution (addition condition B)—the enantioselectivity of *exo*-**3a** was significantly improved to 90% ee, while the *exo*-selectivity increased slightly (*exo*:*endo* = 78:22) (entry 6).

To determine the influence of the metal catalysts on the yield and selectivity, the cycloadditions were carried out in the presence of a combination of the Pybox-Ph_2−Lu$(OTf)_3$ complex with either $Rh_2(piv)_4$, $Rh_2(tfa)_4$, or $Cu(acac)_2$ (entries 8−10). Although favorable results were not attained, it is interesting to note that both diastereo- and enantioselectivities were affected, during the generation of cyclic carbonyl ylide, by the choice of catalyst; especially, in the case of $Cu_2(acac)$ (entry 10), the *endo*-cycloadduct was favored (*exo*:*endo* = 34:66), whereas the enantioselectivtiy of the *exo*-cycloadduct decreased to 21% ee (compared to that of entry 6). Although the effect of the carbonyl ylide generation catalyst on the enantioselectivity is not clear at this point, the dissociation or association property of the corresponding catalyst for the carbonyl ylide could have an influence not only on the enantioselectivity but also on the diastereoselectivity. In those reactions, the metal-associated carbonyl ylide or the free carbonyl ylide is probably involved in the cycloaddition step depending on which carbonyl ylide generation catalyst was used. The rate of the background reaction corresponding to the metal-associated carbonyl ylide or the free carbonyl ylide also could affect the enantioselectivity. When the chiral Rh catalyst Rh_2(*S*-TCPTTL)$_4$ (2 mol %) was employed, in the absence of any Lewis acids, good enantioselectivities (85−94% ee) were observed for both the *exo*- and *endo*-cycloadducts (entries 11 and 12), albeit with moderate yields and diastereoselectivities. Under the same chiral Rh-catalyzed conditions, but in the presence of Lu$(OTf)_3$ (10 mol %), the cycloaddition resulted in an improved yield of the cycloadducts, but with lower enatioselectivities (entry 13). The yield was further improved (79%) using a combination of Rh_2(*S*-TCPTTL)$_4$ (2 mol %) and Pybox-Ph_2−Lu$(OTf)_3$ (10 mol %) (entry 14); in this case, although the enantioselectivity of the *exo*-cycloadduct was improved to 92% ee, the *exo*-selectivity (*exo*:*endo* = 59:41) was lower than that using a combination of $Rh_2(OAc)_4$ (2 mol %) and Pybox-Ph_2−Lu$(OTf)_3$ (10 mol %) (*exo*:*endo* = 78:22) (entry 6). In contrast to entry 14, reduced enantioselectivities (−32% ee) for both the *exo*- and *endo*-cycloadducts were observed using a combination of Rh_2(*R*-TCPTTL)$_4$ (2 mol %) and the chiral Pybox-Ph_2−Lu$(OTf)_3$ (10 mol %) (entry 15), which can be attributed to the mismatched combination of the catalysts.

To investigate the scope of the indole derivatives as dipolarophiles, cycloadditions of diazodiketone **1a** were carried out using 5-bromo-, 5-methoxy-, and 6-methoxyindoles (**2b−d**, respectively) in the presence of $Rh_2(OAc)_4$ (2 mol %) and the Pybox-Ph_2−Lu$(OTf)_3$ complex (10 mol %) (Scheme 2 and Table 2, entries 2−4). Although the *exo*-selectivities varied, the enantioselectivities of the *exo*-cycloadducts were good to excellent in all cases (entries 2−4). To investigate the scope of the diazo compounds, cycloadditions of indole **2a** or **2b** were

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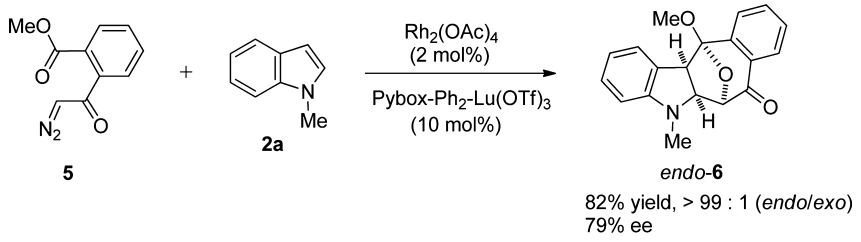
Scheme 3. Cycloaddition Reaction between Indole 2a and the Carbonyl Ylide Derived from Diazoketoester 5



Scheme 4. Cycloaddition Reaction between Indole 2b and the Carbonyl Ylide Derived from Diazodiketone 7

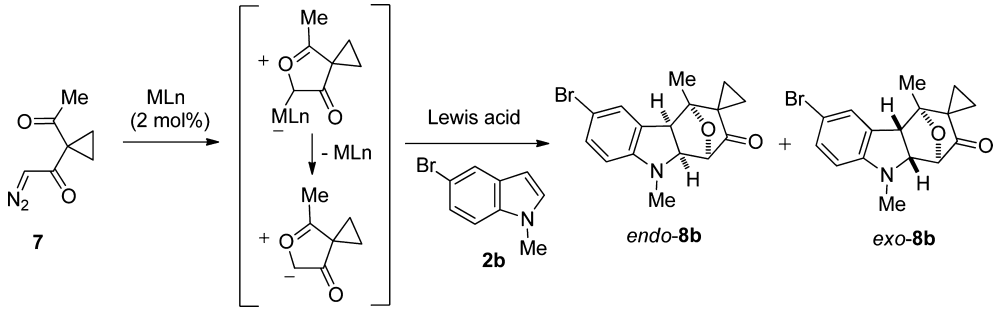


Table 3. Cycloaddition Reaction between Indole 2b and the Carbonyl Ylide Derived from Diazodiketone 7[a]

entry	MLn	Lewis acid	cat. loading (mol %)	addition time (h)	yield (%)	*endo*:*exo* ratio[b]	ee[c] (%) (*endo*/*exo*)
1	$Rh_2(OAc)_4$	none		1	trace	ND[d]	
2	$Rh_2(OAc)_4$	$Lu(OTf)_3$	10	1	42	35:65	
3	$Rh_2(OAc)_4$	Pybox-Ph_2–$Lu(OTf)_3$	10	1	12	62:38	68/ND[d]
4	$Rh_2(OAc)_4$	Pybox-Ph_2–$Ho(OTf)_3$	30	6	31	78:22	78/-4
5	$Rh_2(OAc)_4$	Pybox-Ph_2–$Er(OTf)_3$	30	6	32	81:19	78/1
6	$Cu(acac)_2$	none		6	trace	ND[d]	
7	$Cu(acac)_2$	Pybox-Ph_2–$Ho(OTf)_3$	30	6	33	13:87	12/66
8	Rh_2(*S*-TCPTTL)$_4$	none		6	17	71:29	−55/59
9	Rh_2(*S*-TCPTTL)$_4$	Pybox-Ph_2–$Ho(OTf)_3$	30	6	34	80:20	34/24
10	Rh_2(*R*-TCPTTL)$_4$	Pybox-Ph_2–$Ho(OTf)_3$	30	6	25	89:11[e]	70/−7

[a]The reactions were carried out at 23 °C by adding a solution of diazodiketone **7** and indole **2b** in toluene to a solution of Rh(II) or Cu(II) catalyst (2 mol %) and the $Lu(OTf)_3$ or Pybox-Ph_2–$M(OTf)_3$ complex (0–30 mol %) in the presence of powdered MS 4 Å in toluene over the period of time cited in the table. [b]Determined by ^{1}H NMR using the crude mixture. [c]Determined by chiral HPLC after isolation of the cycloadducts. [d]Not determined. [e]Determined by ^{1}H NMR after chromatography.

carried out using diazodiketones **1b–g** (entries 5–12, respectively). Although the 5-aryldiazodiketones, regardless of the electronic character of the *para*-substituent, showed good enantioselectivities of the *exo*-cycloadducts (entries 5, 6, and 9–12), 5-alkyldiazodiketones showed merely moderate enantioselectivities for the *exo*-cycloadducts (entries 7 and 8). Among the indole dipolarophiles, 5-bromo-1-methylindole (**2b**), in most cases, exhibited higher *exo*-selectivities (*exo*:*endo* = 80:20 to 94:6) and enantioselectivities (85% to >98% ee) (entries 2 and 9–12). In contrast to the above reactions of diazodiketones **1a–g**, the reaction of diazoketoester **5** with indole **2a**, under the same reaction conditions (condition B), resulted in only the *endo*-cycloadduct with a relatively good enantioselectivity (79% ee) (Scheme 3).

Next, cycloadditions were carried out between indole **2b** and 1-diazo-2,4-diketone **7**, which serves as the five-membered carbonyl ylide precursor, in an attempt to construct the hexahydrocarbazole framework found naturally in the *Aspidosperma* alkaloids (Scheme 4 and Table 3). Similar to that of 1-diazo-5-phenyl-2,5-pentanedione (**1a**), the cycloadditions of **7** in the absence of any Lewis acids, and carried out under $Rh_2(OAc)_4$- or $Cu(acac)_2$-catalyzed conditions at 23 °C in toluene, resulted in merely trace amounts of the cycloadducts (entries 1 and 6). Using a combination of $Lu(OTf)_3$ (10 mol %) and $Rh_2(OAc)_4$ (2 mol %), the corresponding cycloadducts were obtained in a combined yield of 42% with a slight preference for the *exo*-cycloaadduct (*exo*:*endo* = 65:35) (entry 2). Using a combination of Pybox-Ph_2–$Lu(OTf)_3$ (10 mol %) and $Rh_2(OAc)_4$ (2 mol %), the reaction afforded the cycloadducts with a combined yield of only 12%, but interestingly with a preference for the *endo*-cycloadduct (*exo*:*endo* = 38:62) with moderate enantioselectivity (68% ee) (entry 3). Furthermore, the cycloadditions were carried out under various conditions, including the addition time, the amount of Lewis acid, the reaction temperature, and the type of metal triflate for the preparation of the chiral Lewis acid (see the Supporting Information). The optimal yields (31–32%), diastereoselectivities (*endo*:*exo* = 78:22–81:19), and enantioselectivity (78% ee) were obtained using the reaction conditions of entries 4 and 5. It is noteworthy that, by utilizing $Cu(acac)_2$ as the catalyst for the diazo decomposition step (entry 7), the diastereoselectivity switches to favor the *exo*-

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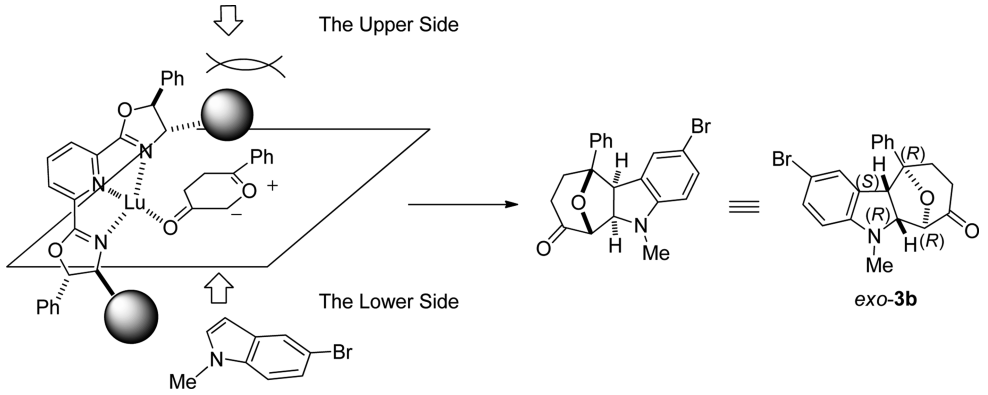

Figure 2. Proposed approaches for asymmetric induction based on the absolute configuration of *exo*-**3b**.

cycloadduct (*exo*:*endo* = 87:13) with moderate enantioselectivity (66% ee), which is a significant improvement over that of entry 4 (−4% ee). For Rh_2(*S*-TCPTTL)$_4$ (2 mol %) in the absence of any Lewis acids, moderate enantioselectivities (55−59% ee) were observed for both the *exo*- and *endo*-cycloadducts, albeit with a low yield (17%) and moderate diastereoselectivity (entry 8). Using a combination of Rh_2(*S*-TCPTTL)$_4$ and the chiral Pybox-Ph_2−Ho(OTf)$_3$ complex, the cycloadducts were obtained in a higher yield along with a good diastereoselectivity, but with reduced enantioselectivities (24−34% ee) for both the *exo*- and *endo*-cycloadducts. By contrast, the higher enantioselectivity of the *endo*-cycloadduct compared with those of entries 8 and 9 and the highest *endo*-selectivity were observed using a combination of Rh_2(*R*-TCPTTL)$_4$ and the chiral Pybox-Ph_2−Ho(OTf)$_3$ complex (entry 10). From these results, the reduced enantioselectivity of the *endo*-cycloadduct shown in entry 9 can be attributed to the mismatched combination of the catalysts.

To gain insight into the mechanism behind the asymmetric induction, X-ray crystal analysis was carried out using a single crystal of *exo*-**3b** after recrystallization from AcOEt/hexane (see the Supporting Information). The results indicate that cycloadduct *exo*-**3b** possesses a (5a*S*,6*R*,10*R*,10a*R*)-configuration, as depicted in Figure 2. This structure suggests that the coordination between the chiral Pybox-Ph_2−Lu(OTf)$_3$ complex and the carbonyl ylide effectively shields the approach of 5-bromo-1-methylindole from the upper side. Accordingly, the formation of cycloadduct *exo*-**3b**, with its (5a*S*,6*R*,10*R*,10a*R*)-configuration, would involve the approach of 5-bromo-1-methylindole from the lower side with an *exo*-orientation (Figure 2).

CONCLUSIONS

In summary, enantioselective 1,3-dipolar cycloaddition reactions were carried out between *N*-methylindoles and cyclic carbonyl ylides derived from diazodiketone or diazoketoester precursors under dual-activation conditions in the presence of achiral Rh and chiral lanthanoid metal catalysts. For six-membered cyclic carbonyl ylides that are derived from 1-diazo-5-aryl-2,5-pentanedione derivatives, high enantioselectivities (83−>98% ee (*exo*)) and relatively good diastereoselectivities (*exo*:*endo* = 65:35 to 94:6) and yields (63−85%) were obtained using a combination of $Rh_2(OAc)_4$ (2 mol %) and the chiral Pybox-Ph_2−Lu(OTf)$_3$ complex (10 mol %) as catalysts. For the cycloaddition between 5-bromo-1-methylindole and a five-membered cyclic carbonyl ylide derived from the 1-diazo-2,4-pentandione precursor, relatively good enantioselectivity (78% ee) and *endo*-selectivity (81:19) were obtained using $Rh_2(OAc)_4$ (2 mol %) and the chiral Pybox-Ph_2−Er(OTf)$_3$ complex (30 mol %) as catalysts.

EXPERIMENTAL SECTION

General Methods. Melting points were determined on a melting point apparatus and are uncorrected. IR spectra were taken with an FTIR spectrophotometer. ^{1}H NMR spectra were recorded on 300, 400, and 500 MHz spectrometers. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. ^{13}C NMR spectra were recorded on 75, 100, and 125 MHz spectrometers using broad-band proton decoupling. Chemical shifts are expressed in parts per million using the middle resonance of $CDCl_3$ (77.0 ppm) as an internal standard. Hydrogen multiplicity (C, CH, CH_2, CH_3) information was obtained from the carbon DEPT spectrum. All reactions were carried out under an argon atmosphere in dried glassware.

Materials. *o*-(Methoxycarbonyl)-*α*-diazoacetophenone (**5**) was prepared by the procedure described in a previous paper.[19] 1-Diazo-2,5-alkanediones **1a**, **1b**, **1d**, **1e**, and **1g** were prepared according to the procedure reported by Padwa.[16a,g,20] 1-Acetyl-1-(diazoacety1)-cyclopropane (**7**) was also prepared according to the procedure reported by Padwa.[21] *N*-Methylindoles **2b**−**d** were prepared from the corresponding commercially available indoles according to the reported procedure.[22] *N*-Methylindole (**2a**) and $Rh_2(OAc)_4$ were commercially available and used without further purification. Lanthanoid triflates were commercially available and dried in vacuo at 200 °C for 12 h before use. 2,6-Bis[(4*S*,5*S*)-4,5-diphenyl-2-oxazolin-2-yl]pyridine (Pybox-Ph_2) was prepared by the procedure described in the literature.[23] Powdered 4 Å molecular sieves (MS 4 Å) were commercially available and dried in vacuo at 200 °C for 12 h before use. Dehydrated dichloromethane was commercially available and treated with the Glass Contour solvent system before use. Toluene and $CF_3C_6H_5$ were distilled from a sodium benzophenone ketyl still under argon.

General Procedure for the Reaction of Diazodiketones 1a−g with *N*-Methylindole Derivatives 2a−d Exemplified by the Reaction of 1-Diazo-5-Phenyl-2,5-hexandione (1a) with *N*-Methylindole (2a) Catalyzed by the Pybox-Ph_2−Lu(III) Complex. A solution of Pybox-Ph_2 (26.1 mg, 0.05 mmol) in THF (1.5 mL) was added to a solution of Lu(OTf)$_3$ (31.1 mg, 0.05 mmol) in THF (1 mL). After the mixture was stirred for 2 h, the solvent was removed under reduced pressure, and the resulting solid was dried in vacuo at room temperature for 5 h. After addition of MS 4 Å (0.5 g), $Rh_2(OAc)_4$ (4.4 mg, 0.01 mmol), and toluene (4.0 mL), successively, a solution of diazo compound **1a** (101.1 mg, 0.50 mmol) and **2a** (125 μL, 1.00 mmol) in toluene (5 mL) was added over a period of 1 h using a syringe pump at 23 °C. The syringe was washed with toluene (1 mL) in one portion, and the reaction was immediately worked up. After removal of MS 4 Å through Celite, the reaction mixture was filtered through a plug of silica gel (3 cm) with AcOEt/hexane (6:4, 80 mL) as the eluent. The solvent was removed in vacuo, and the residue

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was purified by column chromatography (97:3 to 90:10 hexane/AcOEt) to provide 86.1 mg (56.4%) of *exo*-**3a** and 25.0 mg (16.4%) of *endo*-**3a** (combined yield 73%). The relative stereochemistry (*exo*/*endo*) of the products could be determined by ^{1}H NMR analysis on the basis of a coupling constant between H-5a and H-6, which was reported previously (*exo*-**3a**, 0 Hz; *endo*-**3a**, 7.1 Hz).[18b] The diastereomer ratio, 78:22 (*exo*-**3a**:*endo*-**3a**), was determined by ^{1}H NMR analysis of the crude mixture.

Cycloadducts *exo*-**3b** (130.8 mg, 68%) and *endo*-**3b** (16.0 mg, 8%) were synthesized according to the general procedure (combined yield 76%). The diastereomer ratio, 88:12 (*exo*-**3b**:*endo*-**3b**), was determined by ^{1}H NMR analysis of the crude mixture.

Cycloadducts *exo*-**3c** (90.6 mg, 54%) and *endo*-**3c** (37.7 mg, 23%) were synthesized according to the general procedure (combined yield 77%).

Cycloadducts *exo*-**3d** (76.3 mg, 46%) and *endo*-**3d** (31.9 mg, 19%) were synthesized according to the general procedure (combined yield 65%). The diastereomer ratio, 71:29 (*exo*-**3d**:*endo*-**3d**), was determined by ^{1}H NMR analysis of the crude mixture.

Cycloadducts *exo*-**4b** (75.4 mg, 47%) and *endo*-**4b** (61.0 mg, 38%) were synthesized according to the general procedure (combined yield 85%). The diastereomer ratio, 65:35 (*exo*-**4b**:*endo*-**4b**), was determined by ^{1}H NMR analysis of the crude mixture.

Cycloadducts *exo*-**4c** (95.9 mg, 50%) and *endo*-**4c** (44.1 mg, 23%) were synthesized according to the general procedure (combined yield 73%). The diastereomer ratio, 72:28 (*exo*-**4c**:*endo*-**4c**), was determined by ^{1}H NMR analysis of the crude mixture.

Cycloadducts *exo*-**4d** (41.2 mg, 34%) and *endo*-**4d** (26.5 mg, 22%) were synthesized according to the general procedure (combined yield 56%). The diastereomer ratio, 57:43 (*exo*-**4d**:*endo*-**4d**), was determined by ^{1}H NMR analysis of the crude mixture.

Cycloadducts *exo*-**4e** (31.0 mg, 23%) and *endo*-**4e** (21.6 mg, 16%) were synthesized according to the general procedure (combined yield 39%). The diastereomer ratio, 71:29 (*exo*-**4e**:*endo*-**4e**), was determined by ^{1}H NMR analysis of the crude mixture.

Cycloadducts *exo*-**4f** (116.0 mg, 58%) and *endo*-**4f** (9.1 mg, 5%) were synthesized according to the general procedure (combined yield 63%). The diastereomer ratio, 90:10 (*exo*-**4f**:*endo*-**4f**), was determined by ^{1}H NMR analysis of the crude mixture.

Cycloadducts *exo*-**4g** (136.2 mg, 66%) and *endo*-**4g** (10.2 mg, 5%) were synthesized according to the general procedure (combined yield 71%). The diastereomer ratio, 93:7 (*exo*-**4g**:*endo*-**4g**), was determined by ^{1}H NMR analysis of the crude mixture.

Cycloadducts *exo*-**4h** (122.6 mg, 59.2%) and *endo*-**4h** (29.9 mg, 14.4%) were synthesized according to the general procedure (combined yield 74%). The diastereomer ratio, 80:10 (*exo*-**4h**:*endo*-**4h**), was determined by ^{1}H NMR analysis of the crude mixture.

Cycloadducts *exo*-**4i** (150.2 mg, 65%) and *endo*-**4i** (9.0 mg, 4%) were synthesized according to the general procedure (combined yield 69%). The diastereomer ratio, 94:6 (*exo*-**4i**:*endo*-**4i**), was determined by ^{1}H NMR analysis of the crude mixture.

Cycloadduct *endo*-**6** (126.4 mg) was synthesized according to the general procedure (yield 82%).

*Data for exo-6,10-epoxy-5-methyl-10-phenyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (exo-**3a**):* pale yellow prisms; mp 181−183 °C; $[\alpha]_D^{25}$ +270.92 (*c* 1.00, $CHCl_3$) (90% ee); IR (KBr) 2862, 1721, 1605, 1492, 1379, 1219, 1174, 1039, 892, 863, 757, 744, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46−2.66 (2H, m), 2.68−2.78 (2H, m), 2.88 (3H, s), 4.09 (1H, d, *J* = 8.5 Hz), 4.23 (1H, d, *J* = 8.5 Hz), 4.52 (1H, d, *J* = 1.2 Hz), 5.99 (1H, m), 6.19 (1H, m), 6.33 (1H, m), 6.93 (1H, m), 7.14−7.25 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.5 (CH_2), 34.3 (CH_3), 36.1 (CH_2), 55.6 (CH), 75.2 (CH), 86.6 (CH), 87.7 (C), 105.7 (CH), 116.7 (CH), 125.2 (CH), 126.0 (CH), 126.4 (C), 127.1 (CH), 127.6 (CH), 127.9 (CH), 140.3 (C), 152.2 (C), 206.6 (C); MS (EI) *m*/*z* 305 (M^+), 174, 145, 104, 77, 15. Anal. Calcd for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.68; H, 6.25; N, 4.59. The enantiomeric excess of *exo*-**3a** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 24.9 min, t_{major} = 26.3 min.

*Data for endo-6,10-epoxy-5-methyl-10-phenyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (endo-**3a**):* pale yellow prisms; mp 136−138 °C; $[\alpha]_D^{25}$ +63.39 (*c* 0.220, $CHCl_3$) (32% ee); IR (KBr) 2902, 1724, 1600, 1490, 1315, 1220, 1040, 907, 883, 756, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.09−2.37 (4H, m), 2.77 (3H, s), 4.13 (1H, d, *J* = 11.7 Hz), 4.60 (1H, dd, *J* = 7.3, 11.7 Hz), 4.76 (1H, dd, *J* = 1.2, 7.3 Hz), 6.46 (1H, d, *J* = 8.2 Hz), 6.72 (1H, dt, *J* = 0.9, 7.4 Hz), 7.17−7.21 (2H, m), 7.35 (1H, m), 7.43−7.47 (2H, m), 7.57−7.60 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.8 (CH_2), 33.4 (CH_2), 34.7 (CH_3), 57.8 (CH), 74.6 (CH), 85.6 (CH), 86.5 (C), 107.5 (CH), 117.8 (CH), 124.5 (CH), 124.9 (CH), 126.7 (C), 127.4 (CH), 128.6 (CH), 129.2 (CH), 145.3 (C), 154.1 (C), 206.4 (C); MS (EI) *m*/*z* 305 (M^+), 139, 90, 28. Anal. Calcd for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.85; H, 6.22; N, 4.45. The enantiomeric excess of *endo*-**3a** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 16.0 min, t_{major} =17.7 min.

*Data for exo-2-bromo-6,10-epoxy-5-methyl-10-phenyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (exo-**3b**):* colorless needles; mp 192−195 °C (AcOEt/hexane); $[\alpha]_D^{25}$ +191.35 (*c* 0.736, $CHCl_3$) (96% ee); IR (KBr) 2950, 2880, 1723, 1560, 1489, 1276, 1048, 803, 752, 695 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46−2.64 (2H, m), 2.65−2.78 (2H, m), 2.86 (s, 3H), 4.02 (1H, d, *J* = 8.3 Hz), 4.25 (1H, d, *J* = 8.3 Hz), 4.5 (1H, s), 5.99 (1H, m), 6.17 (1H, d, *J* = 8.3 Hz), 7.00 (1H, dd, *J* = 1.4, 8.3 Hz), 7.15−7.38 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.4 (CH_2), 33.9 (CH_3), 35.7 (CH_2), 55.6 (CH), 75.2 (CH), 86.6 (CH), 87.7 (C), 106.8 (CH), 108.1 (C), 125.2 (CH), 127.7 (CH), 128.0 (CH), 128.7 (C), 129.1 (CH), 130.7 (CH), 140.1 (C), 151.3 (C), 206.7 (C); HRMS (APCI-TOF) *m*/*z* calcd for $C_{20}H_{19}NO_2Br$ [(M + H)$^+$] 384.0594, found 384.0594. The enantiomeric excess of *exo*-**3b** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 31.0 min, t_{major} = 42.5 min.

*Data for endo-2-bromo-6,10-epoxy-5-methyl-10-phenyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (endo-**3b**):* pale brown oil; IR ($CHCl_3$) 2907, 1720, 1599, 1495, 1279, 1062, 1041, 800, 766, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.03−2.41 (4H, m), 2.75 (3H, s), 4.10 (1H, d, *J* = 11.5 Hz), 4.62 (1H, dd, *J* = 7.3, 11.5 Hz), 4.75 (1H, d, *J* = 7.3 Hz), 6.32 (1H, d, *J* = 8.3 Hz), 7.20−7.61 (7H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.8 (CH_2), 33.3 (CH_2), 34.6 (CH_3), 57.5 (CH), 74.6 (CH), 85.5 (CH), 86.5 (C), 108.7 (CH), 109.3 (C), 124.4 (CH), 127.7 (CH), 127.8 (CH), 128.8 (CH), 128.9 (C), 132.0 (CH), 144.9 (C), 153.1 (C), 206.0 (C); HRMS (APCI-TOF) *m*/*z* calcd for $C_{20}H_{19}NO_2Br$ [(M + H)$^+$] 384.0594, found 384.0574.

*Data for exo-6,10-epoxy-2-methoxy-5-methyl-10-phenyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (exo-**3c**):* pale yellow needles; mp 145−147 °C (AcOEt/hexane); $[\alpha]_D^{25}$ +43.32 (*c* 0.264, $CHCl_3$) (88% ee); IR (KBr) 2943, 2881, 1722, 1499, 1427, 1366, 1274, 1232, 1147, 1047, 1027, 808, 755, 696 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.47−2.75 (4H, m), 2.83 (3H, s), 3.34 (3H, s), 4.05 (1H, d, *J* = 8.6 Hz), 4.16 (1H, d, *J* = 8.6 Hz), 4.52 (1H, d, *J* = 1.2 Hz), 5.63 (1H, d, *J* = 2.6 Hz), 6.28 (1H, d, *J* = 8.6 Hz), 6.53 (1H, dd, *J* = 2.6, 8.6 Hz), 7.20−7.27 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.4 (CH_2), 35.8 (CH_3), 35.9 (CH_2), 55.9 (CH_3), 56.1 (CH), 76.2 (CH), 87.2 (CH), 87.5 (C), 106.9 (CH), 112.6 (CH), 114.7 (CH), 125.5 (CH), 127.3 (CH), 127.8 (C), 128.0 (CH), 140.6 (C), 147.1 (C), 152.3 (C), 207.0 (C); HRMS (APCI-TOF) *m*/*z* calcd for $C_{21}H_{22}NO_3$ [(M + H)$^+$] 336.1594, found 336.1589. The enantiomeric excess of *exo*-**3c** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 34.8 min, t_{major} = 43.6 min.

*Data for endo-6,10-epoxy-2-methoxy-5-methyl-10-phenyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (endo-**3c**):* pale yellow oil; IR ($CHCl_3$) 2950, 1726, 1686, 1594, 1494, 1448, 1234, 1146, 1034, 814, 757, 701 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.15−2.37 (4H, m), 2.71 (3H, s), 3.76 (3H, s), 4.06 (1H, d, *J* = 11.5 Hz), 4.53 (1H, dd, *J* = 7.1, 11.5 Hz), 4.73 (1H, dd, *J* = 1.3, 7.1 Hz), 6.40 (1H, d, *J* = 8.5 Hz), 6.76 (1H, dd, *J* = 2.5, 8.5 Hz), 6.80 (1H, d, *J* = 2.5 Hz), 7.32−7.59 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ

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30.5 (CH_2), 33.4 (CH_2), 36.0 (CH_3), 56.1 (CH_3), 58.2 (CH), 75.5 (CH), 85.6 (CH), 86.2 (C), 108.2 (CH), 112.6 (CH), 113.5 (CH), 124.4 (CH), 127.5 (CH), 128.2 (C), 128.7 (CH), 145.3 (C), 148.8 (C), 152.8 (C), 206.2 (C); HRMS (APCI-TOF) m/z calcd for $C_{21}H_{22}NO_3$ $[(M + H)^+]$ 336.1594, found 336.1596.

*Data for exo-6,10-epoxy-3-methoxy-5-methyl-10-phenyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (exo-**3d**):* colorless needles; mp 101−103 °C (AcOEt/hexane); $[\alpha]_D^{25}$ +59.37 (c 0.264, $CHCl_3$) (92% ee); IR (KBr) 2930, 1728, 1617, 1499, 1372, 1235, 1174, 1080, 1034, 885, 820, 754, 695, 573 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.45−2.76 (4H, m), 2.86 (3H, s,), 3.66 (3H, s), 4.03 (1H, d, J = 8.5 Hz), 4.25 (1H, d, J = 8.5 Hz), 4.50 (1H, s), 5.72 (1H, dd, J = 2.4, 8.2 Hz), 5.85 (1H, dd, J = 0.8, 8.2 Hz), 5.90 (1H, d, J = 2.4 Hz), 7.20−7.26 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.5 (CH_2), 34.0 (CH_3), 36.0 (CH_2), 55.1 (CH_3), 75.9 (CH), 86.6 (CH), 87.7 (C), 92.9 (CH), 101.5 (CH), 119.0 (C), 125.4 (CH), 126.5 (CH), 127.2 (CH), 127.9 (CH), 140.8 (C), 153.8 (C), 160.7 (C), 207.1 (C); HRMS (APCI-TOF) m/z calcd for $C_{21}H_{22}NO_3$ $[(M + H)^+]$ 336.1594, found 336.1622. The enantiomeric excess of *exo*-**3d** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 30.2 min, t_{major} = 36.9 min.

*Data for endo-6,10-epoxy-3-methoxy-5-methyl-10-phenyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (endo-**3d**):* pale yellow oil; IR ($CHCl_3$) 3019, 1725, 1618, 1498, 1215, 1039, 756, 668 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.08−2.39 (4H, m), 2.75 (3H, s), 3.79 (3H, s), 4.06 (1H, d, J = 11.8 Hz), 4.62 (1H, dd, J = 7.2, 11.8 Hz), 4.72 (1H, d, J = 7.2 Hz), 6.01 (1H, d, J = 2.3 Hz), 6.24 (1H, dd, J = 2.3, 8.2 Hz), 7.07 (1H, dd, J = 0.9, 8.2 Hz), 7.44 (2H, m), 7.54−7.58 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.0 (CH_2), 33.4 (CH_2), 34.5 (CH_3), 57.1 (CH_3), 75.1 (CH), 85.5 (CH), 86.6 (C), 94.3 (CH), 102.3 (CH), 119.1 (C), 124.4 (CH), 125.2 (CH), 127.4 (CH), 128.0 (CH), 128.6 (CH), 145.4 (C), 155.5 (C), 161.5 (C), 206.4 (C); HRMS (APCI-TOF) m/z calcd for $C_{21}H_{22}NO_3$ $[(M + H)^+]$ 336.1594, found 336.1601.

*Data for exo-6,10-epoxy-5-methyl-10-(p-tolyl)-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (exo-**4b**):* pale yellow prisms; mp 158−159 °C; $[\alpha]_D^{25}$ +253.04 (c 1.00, $CHCl_3$) (83% ee); IR (KBr) 1723, 1605, 1490, 1214, 1050, 806, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.29 (3H, s), 2.43−2.64 (2H, m), 2.64−2.79 (2H, m), 2.88 (3H, s), 4.07 (1H, d, J = 8.8 Hz), 4.23 (1H, d, J = 8.8 Hz), 4.51 (1H, s), 6.03 (1H, m), 6.22 (1H, m), 6.34 (1H, m), 6.94 (1H, m), 7.04 (2H, d, J = 8.1 Hz), 7.12 (2H, d, J = 8.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1 (CH_3), 33.5 (CH_2), 34.3 (CH_3), 36.2 (CH_2), 55.5 (CH), 75.2 (CH), 86.5 (CH), 87.6 (C), 105.6 (CH), 116.7 (CH), 125.1 (CH), 126.1 (CH), 126.5 (C), 127.8 (CH), 128.2 (CH), 136.5 (C), 137.3 (C), 152.2 (C), 206.6 (C); MS (EI) m/z 319 (M^+), 235, 189, 147, 132, 117, 92, 77, 15; HRMS (EI) m/z calcd for $C_{21}H_{21}NO_2$ (M^+) 319.1572, found 319.1573. The enantiomeric excess of *exo*-**4b** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 20.4 min, t_{major} = 24.2 min.

*Data for endo-6,10-epoxy-5-methyl-10-(p-tolyl)-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (endo-**4b**):* pale yellow prisms; mp 147−148 °C; $[\alpha]_D^{25}$ +40.28 (c 0.336, $CHCl_3$) (18% ee); IR (KBr) 2936, 1726, 1602, 1489, 1035, 808, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.08−2.35 (4H, m), 2.39 (3H, s), 2.76 (3H, s), 4.12 (1H, d, J = 11.9 Hz), 4.59 (1H, dd, J = 6.8, 11.9 Hz), 4.74 (1H, d, J = 6.8 Hz), 6.45 (1H, d, J = 8.5 Hz), 6.71 (1H, dt, J = 0.9, 7.4 Hz), 7.16−7.20 (2H, m), 7.24−7.27 (2H, m), 7.45−7.48 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1 (CH_3), 30.9 (CH_2), 33.4 (CH_2), 34.7 (CH_3), 57.9 (CH), 74.5 (CH), 85.6 (CH), 86.5 (C), 107.4 (CH), 117.7 (CH), 124.4 (CH), 124.9 (CH), 126.8 (C), 129.1 (CH), 129.3 (CH), 137.1 (C), 142.4 (C), 154.1 (C), 206.5 (C); MS (EI) m/z 319 (M^+), 235, 189, 147, 132, 117, 92, 77, 15; HRMS (EI) m/z calcd for $C_{21}H_{21}NO_2$ (M^+) 319.1572, found 319.1598. The enantiomeric excess of *endo*-**4b** was determined by HPLC analysis (Daicel Chiralpak OZ-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 17.9 min, t_{major} = 19.5 min.

*Data for exo-10-(p-bromophenyl)-6,10-epoxy-5-methyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (exo-**4c**):* pale yellow prisms; mp 150−152 °C; $[\alpha]_D^{25}$ +227.68 (c 1.00, $CHCl_3$) (84% ee); IR (KBr) 2876, 1724, 1490, 1047, 1008, 809, 745 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.47 (1H, m), 2.59 (1H, m), 2.67−2.74 (2H, m), 2.87 (3H, s), 4.07 (1H, d, J = 8.5 Hz), 4.23 (1H, d, J = 8.5 Hz), 4.51 (1H, s), 6.04 (1H, d, J = 7.4 Hz), 6.26 (1H, dt, J = 0.8, 7.4 Hz), 6.35 (1H, d, J = 7.9 Hz), 6.96 (1H, t, J = 7.9 Hz), 7.10−7.13 (2H, m), 7.34−7.37 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.3 (CH_2), 34.3 (CH_3), 35.8 (CH_2), 55.4 (CH), 75.31 (CH), 86.7 (CH), 87.4 (C), 106.1 (CH), 117.2 (CH), 121.3 (C), 126.2 (CH), 126.2 (C), 127.3 (CH), 128.3 (CH), 130.9 (CH), 139.6 (C), 152.4 (C), 206.5 (C); MS (EI) m/z 383 (M^+), 253, 183, 145, 132, 115, 77, 15; HRMS (EI) m/z calcd for $C_{20}H_{18}BrNO_2$ (M^+) 383.0521, found 383.0497. The enantiomeric excess of *exo*-**4c** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{major} = 26.2 min, t_{minor} = 37.9 min.

*Data for endo-10-(p-bromophenyl)-6,10-epoxy-5-methyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (endo-**4c**):* pale yellow prisms; mp 128−129 °C; $[\alpha]_D^{25}$ +43.10 (c 0.512, $CHCl_3$) (18% ee); IR (KBr) 2884, 1720, 1490, 1035, 1008, 820, 750 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.10−2.25 (3H, m), 2.32 (1H, m), 2.76 (3H, s), 4.05 (1H, d, J = 11.5 Hz), 4.59 (1H, dd, J = 7.3, 11.5 Hz), 4.75 (1H, dd, J = 1.3, 7.3 Hz), 6.47 (1H, d, J = 7.9 Hz), 6.72 (1H, dt, J = 0.8, 7.4 Hz), 7.13 (1H, d, J = 7.4 Hz), 7.19 (1H, t, J = 7.8 Hz), 7.44−7.47 (2H, m), 7.55−7.58 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.4 (CH_2), 33.2 (CH_2), 34.8 (CH_3), 58.0 (CH), 74.6 (CH), 85.6 (CH), 86.0 (C), 107.7 (CH), 117.9 (CH), 121.4 (C), 124.7 (CH), 126.3 (CH), 126.3 (C), 129.4 (CH), 131.7 (CH), 144.3 (C), 154.1 (C), 206.0 (C); MS (EI) m/z 383 (M^+), 253, 183, 157, 145, 132, 115, 77, 15; HRMS (EI) m/z calcd for $C_{20}H_{18}BrNO_2$ (M^+) 383.0521, found 383.0507. The enantiomeric excess of *endo*-**4c** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (10:90, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{major} = 15.0 min, t_{minor} = 16.5 min.

*Data for exo-5,10-dimethyl-6,10-epoxy-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (exo-**4d**):* colorless prisms; mp 94−96 °C; $[\alpha]_D^{25}$ +109.71 (c 0.464, $CHCl_3$) (52% ee); IR (KBr) 2966, 1731, 1607, 1493, 1296, 1036, 842, 789 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.32 (3H, s), 2.06 (1H, ddd, J = 2.2, 8.3, 13.4 Hz), 2.27 (1H, m), 2.44 (1H, ddd, J = 8.3, 10.0, 17.8 Hz), 2.44 (1H, ddt, J = 7.8, 17.8, 2.2 Hz), 2.84 (3H, s), 3.84 (1H, d, J = 8.8 Hz), 4.17 (1H, d, J = 8.8 Hz), 4.30 (1H, J = 2.2 Hz), 6.44 (1H, d, J = 8.1 Hz), 6.67 (1H, m), 7.03 (1H, m), 7.13 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.0 (CH_3), 33.6 (CH_2), 34.3 (CH_3), 37.7 (CH_2), 53.0 (CH), 75.8 (CH), 83.8 (C), 86.1 (CH), 106.6 (CH), 117.0 (CH), 125.9 (CH), 126.4 (C), 128.4 (CH), 152.6 (C), 206.5 (C); MS (EI) m/z 243 (M^+), 159, 145, 133, 112, 84, 55, 43, 15; HRMS (EI) m/z calcd for $C_{15}H_{17}NO_2$ (M^+) 243.1259, found 243.1297. The enantiomeric excess of *exo*-**4d** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (3:97, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 29.3 min, t_{major} = 30.9 min.

*Data for endo-5,10-dimethyl-6,10-epoxy-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (endo-**4d**):* colorless prisms; mp 81−83 °C; $[\alpha]_D^{25}$ +15.91 (c 0.37, $CHCl_3$) (11% ee); IR (KBr) 2917, 1725, 1600, 1489, 1038, 1020, 836, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.62 (3H, s), 1.72 (1H, ddd, J = 2.9, 9.3, 13.7 Hz), 1.87 (1H, m), 1.99 (1H, m), 2.21 (1H, m), 2.73 (3H, s), 3.87 (1H, m), 4.49−4.57 (2H, m), 6.42 (1H, d, J = 7.8 Hz), 6.69 (1H, m), 7.08 (1H, d, J = 7.1 Hz), 7.15 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.5 (CH_3), 31.0 (CH_2), 33.3 (CH_2), 34.8 (CH_3), 56.5 (CH), 74.8 (CH), 83.8 (C), 85.7 (CH), 107.3 (CH), 117.5 (CH), 124.1 (CH), 127.0 (C), 128.8 (CH), 153.5 (C), 206.3 (C); MS (EI) m/z 243 (M^+), 159, 145, 133, 112, 84, 55, 43, 15; HRMS (EI) m/z calcd for $C_{15}H_{17}NO_2$ (M^+) 243.1259, found 243.1241. The enantiomeric excess of *endo*-**4d** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 14.7 min, t_{major} = 18.6 min.

*Data for exo-6,10-epoxy-10-isopropyl-5-methyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (exo-**4e**):* colorless prisms; mp 81−83 °C; $[\alpha]_D^{25}$ +147.47 (c 0.424,

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$CHCl_3$) (68% ee); IR (KBr) 2962, 1731, 1601, 1490, 1059, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.01 (3H, d, J = 6.8 Hz), 1.10 (3H, d, J = 6.8 Hz), 1.77 (1H, m), 2.05 (1H, sept, J = 6.8 Hz), 2.25−2.46 (2H, m), 2.60 (1 H, m), 2.84 (3H, s), 3.93 (1H, d, J = 8.5 Hz), 4.16 (1H, d, J = 8.5 Hz), 4.30 (1H, s), 6.42 (1H, d, J = 7.8 Hz), 6.65 (1H, m), 7.07−7.20 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.2 (CH_3), 19.7 (CH_3), 28.0 (CH_2), 31.0 (CH), 33.6 (CH_2), 34.2 (CH_3), 54.8 (CH), 75.9 (CH), 85.9 (CH), 88.8 (C), 106.6 (CH), 116.9 (CH), 125.8 (C), 125.9 (CH), 128.5 (CH), 153.0 (C), 208.4 (C); MS (EI) m/z 271 (M^+), 229, 187, 145, 132, 111, 84, 69, 55, 42, 27; HRMS (EI) m/z calcd for $C_{17}H_{21}NO_2$ (M^+) 271.1572, found 271.1535. The enantiomeric excess of *exo*-**4e** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (3:97, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{major} = 12.7 min, t_{minor} = 17.6 min.

*Data for endo-6,10-epoxy-10-isopropyl-5-methyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (endo-**4e**):* colorless prisms; mp 103−104 °C; $[\alpha]_D^{25}$ +50.79 (*c* 0.146, $CHCl_3$) (39% ee); IR (KBr) 2964, 1720, 1603, 1494, 1049, 751, 417 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.16 (6H, d, J = 6.8 Hz), 1.80−1.95 (3H, m), 2.07 (1H, sept, J = 6.8 Hz), 2.19 (1H, m), 2.76 (3H, s), 3.99 (1H, m), 4.44−4.53 (2H, m), 6.36 (1H, d, J = 7.8 Hz), 6.64 (1H, m), 7.08−7.18 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0 (CH_3), 18.5 (CH_3), 26.8 (CH_2), 33.2 (CH_2), 34.3 (CH), 37.3 (CH_3), 52.7 (CH), 74.3 (CH), 85.1 (CH), 89.0 (C), 106.6 (CH), 117.0 (CH), 125.4 (CH), 127.0 (C), 128.6 (CH), 153.8 (C), 207.2 (C); MS (EI) m/z 271 (M^+), 229, 187, 146, 131, 111, 83, 43, 27, 15; HRMS (EI) m/z calcd for $C_{17}H_{21}NO_2$ (M^+) 271.1572, found 271.1591. The enantiomeric excess of *endo*-**4e** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (3:97, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 9.7 min, t_{major} = 14.8 min.

*Data for exo-2-bromo-6,10-epoxy-5-methyl-10-(p-tolyl)-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (exo-**4f**):* colorless needles; mp 206−208 °C; $[\alpha]_D^{25}$ +21.97 (*c* 0.369, $CHCl_3$) (92% ee); IR (KBr) 2947, 1722, 1602, 1491, 1373, 1312, 1277, 1216, 1185, 1043, 797 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.32 (3H, s), 2.47−2.62 (2H, m), 2.65−2.76 (2H, m), 2.84 (3H, s), 3.98 (1H, d, J = 8.6 Hz), 4.23 (1H, d, J = 8.6 Hz), 4.50 (1H, s), 5.96 (1H, m), 6.16 (1H, d, J = 8.3 Hz), 6.99 (1H, dd, J = 8.3, 2.0 Hz), 7.08 (4H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0 (CH_3), 33.4 (CH_2), 33.9 (CH_3), 35.7 (CH_2), 55.7 (CH), 75.2 (CH), 86.6 (CH), 87.8 (C), 106.8 (CH), 108.1 (C), 125.2 (CH), 128.6 (CH), 128.9 (C), 129.1 (CH), 130.6 (CH), 137.1 (C), 137.4 (C), 151.2 (C), 206.8 (C); HRMS (ESI-TOF) m/z calcd for $C_{21}H_{21}O_2NBr$ [$(M + H)^+$] 398.0750, found 398.0730. The enantiomeric excess of *exo*-**4f** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 23.3 min, t_{major} = 32.3 min.

*Data for endo-2-bromo-6,10-epoxy-5-methyl-10-(p-tolyl)-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (endo-**4f**):* colorless prisms; mp 204−206 °C; IR (KBr) 2914, 1721, 1600, 1486, 1255, 1041, 885, 806, 612, 523 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.04−2.13 (1H, m), 2.17−2.29 (2H, m), 2.31−2.37 (1H, m), 2.39 (3H, s), 2.74 (3H, s), 4.08 (1H. d, J = 11.8 Hz), 4.61 (1H, dd, J = 7.2, 11.8 Hz), 4.72 (1H, d, J = 7.2 Hz), 6.30 (1H, d, J = 8.4 Hz), 6.97−7.00 (2H, m), 7.20 (1H, br), 7.26 (1H, m), 7.45−7.48 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1 (CH_3), 30.8 (CH_2), 33.3 (CH_2), 34.5 (CH_3), 57.5 (CH), 74.6 (CH), 85.4 (CH), 86.4 (C), 108.6 (CH), 109.2 (C), 124.3 (CH), 127.7 (CH), 128.9 (C), 129.4 (CH), 131.8 (CH), 137.3 (C), 141.9 (C), 153.0 (C), 206.1 (C); HRMS (APCI-TOF) m/z calcd for $C_{21}H_{21}O_2NBr$ [$(M + H)^+$] 398.0750, found 398.0729.

*Data for exo-2-bromo-6,10-epoxy-5-methyl-10-(p-ethylphenyl)-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (exo-**4g**):* colorless needles; mp 205−206 °C; $[\alpha]_D^{25}$ +21.01 (*c* 0.36, $CHCl_3$) (85% ee); IR (KBr) 2952, 1725, 1597, 1490, 1378, 1270, 1214, 1173, 1114, 1044, 802, 616 m^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.23 (3H, t, J = 7.6 Hz), 2.47−2.75 (6H, m), 2.84 (3H, s), 3.97 (1H, d, J = 8.6 Hz), 4.22 (1H, d, J = 8.6 Hz), 4.49 (1H, s), 5.93 (1H, m), 6.15 (1H, d, J = 8.4 Hz), 6.99 (1H, dd, J = 8.4, 2.0 Hz), 7.10 (4H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.8 (CH_3), 28.5 (CH_2), 33.3 (CH_2), 33.8 (CH_3), 35.5 (CH_2), 55.7 (CH), 76.0 (CH), 86.6 (CH), 87.7 (C), 106.7 (CH), 108.0 (C), 125.2 (CH), 127.4 (CH), 128.8 (C), 129.0 (CH), 130.6 (CH), 137.3 (C), 143.9 (C), 151.2 (C), 206.8 (C); HRMS (ESI-TOF) m/z calcd for $C_{22}H_{23}O_2NBr$ [$(M + H)^+$] 412.0907, found 412.0917. The enantiomeric excess of *exo*-**4g** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 22.5 min, t_{major} = 31.0 min.

*Data for endo-2-bromo-6,10-epoxy-5-methyl-10-(p-ethylphenyl)-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (endo-**4g**):* colorless needles; mp 223−224 °C; IR (KBr) 2961, 1731, 1600, 1496, 1458, 1410, 1278, 1140, 1054, 906, 826 m^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.28 (1H, t, J = 7.7 Hz), 2.10 (1H, m), 2.19−2.30 (2H, m), 2.35 (1H, m), 2.70 (2H, q, J = 7.7 Hz), 2.75 (3H, s), 4.11 (1H, d, J = 11.7 Hz), 4.62 (1H, dd, J = 7.1, 11.7 Hz), 4.73 (1H, d, J = 7.1 Hz), 6.31 (1H, d, J = 8.4 Hz), 7.23−7.31 (4H, m), 7.45−7.48 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.5 (CH_3), 28.5 (CH_2), 30.9 (CH_2), 33.4 (CH_2), 34.5 (CH_3), 57.4 (CH), 74.6 (CH), 85.4 (CH), 86.5 (C), 108.6 (CH), 109.2 (C), 124.4 (CH), 127.8 (CH), 128.2 (CH), 129.0 (C), 131.8 (CH), 142.1 (C), 143.7 (C), 153.0 (C), 206.2 (C); HRMS (APCI-TOF) m/z calcd for $C_{22}H_{23}O_2NBr$ [$(M + H)^+$] 412.0907, found 412.0897.

*Data for exo-2-bromo-6,10-epoxy-10-(p-methoxyphenyl)-5-methyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (exo-**4h**):* colorless needles; mp 208−209 °C; $[\alpha]_D^{25}$ +19.96 (*c* 0.314, $CHCl_3$) (98% ee); IR (KBr) 2935, 1727, 1604, 1514, 1491, 1377, 1248, 1182, 1043, 798, 542 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.48−2.60 (2H, m), 2.67−2.73 (2H, m), 2.85 (3H, s), 3.80 (3H, s), 3.97 (1H, d, J = 8.7 Hz), 4.23 (1H, d, J = 8.7 Hz), 4.48 (1H, s), 5.99 (1H, d, J = 1.9 Hz), 6.17 (1H, d, J = 8.7 Hz), 6.79−6.82 (2H, m), 7.01 (1H, dd, J = 8.7, 1.9 Hz), 7.10−7.13 (2H,m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.3 (CH_2), 33.4 (CH_3), 35.7 (CH_2), 55.5 (CH_3), 55.6 (CH), 75.1 (CH), 86.5 (CH), 87.5 (C), 106.8 (CH), 108.1 (C), 113.4 (CH), 126.5 (CH), 128.9 (C), 129.2 (CH), 130.6 (CH), 132.2 (C), 151.2 (C), 159.1 (C), 206.7 (C); HRMS (APCI-TOF) m/z calcd for $C_{21}H_{21}O_3NBr$ [$(M + H)^+$] 414.0699, found 414.0702. The enantiomeric excess of *exo*-**4h** was determined by HPLC analysis (Daicel Chiralpak IC, EtOAc/hexane (10:90, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 39.2 min, t_{major} = 27.6 min.

*Data for endo-2-bromo-6,10-epoxy-10-(p-methoxyphenyl)-5-methyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (endo-**4h**):* colorless needles; mp 207−208 °C; IR (KBr) 2923, 1721, 1598, 1510, 1490, 1248, 1184, 1093, 1031, 814 m^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.09 (1H, m), 2.17−2.28 (2H, m), 2.34 (1H, m), 2.74 (3H, s), 3.85 (3H, s), 4.09 (1H. d, J = 11.7 Hz), 4.61 (1H, dd, J = 7.3, 11.7 Hz), 4.72 (1H, d, J = 7.3 Hz), 6.30 (1H, d, J = 8.4 Hz), 6.97−7.00 (2H, m), 7.20 (1H, m), 7.25 (1H, m), 7.45−7.48 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.9 (CH_2), 33.3 (CH_2), 34.5 (CH_3), 55.3 (CH_3), 57.6 (CH), 74.5 (CH), 85.4 (CH), 86.3 (C), 108.6 (CH), 109.2 (C), 114.1 (CH), 125.7 (CH), 127.7 (CH), 129.0 (C), 131.8 (CH), 137.0 (C), 153.0 (C), 159.0 (C), 206.0 (C); HRMS (APCI-TOF) m/z calcd for $C_{21}H_{21}O_3NBr$ [$(M + H)^+$] 414.0699, found 414.0690.

*Data for exo-2-bromo-10-(p-bromophenyl)-6,10-epoxy-5-methyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (exo-**4i**):* colorless needles; mp 204−205 °C; $[\alpha]_D^{25}$ +22.84 (*c* 0.435, $CHCl_3$) (>98% ee); IR (KBr) 2953, 1725, 1597, 1490, 1378, 1271, 1215, 1173, 1115, 1044, 802, 616 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.45−2.60 (2H, m), 2.65−2.74 (2H, m), 2.84 (3H, s), 3.99 (1H, d, J = 8.5 Hz), 4.24 (1H, d, J = 8.5 Hz), 4.50 (1H, s), 6.03 (1H, m), 6.17 (1H, d, J = 8.4 Hz), 7.02 (1H, dd, J = 2.0, 8.4 Hz), 7.09 (2H, d, J = 8.6 Hz), 7.41 (2H, d, J = 8.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.2 (CH_2), 33.9 (CH_3), 35.4 (CH_2), 55.4 (CH), 75.2 (CH), 86.5 (CH), 87.4 (C), 107.0 (CH), 108.2 (C), 121.7 (C), 127.1 (CH), 128.4 (C), 129.0 (CH), 130.9 (CH), 131.1 (CH), 139.2 (C), 151.3 (C), 206.1 (C); HRMS (APCI-TOF) m/z calcd for $C_{20}H_{18}O_2NBr_2$ [$(M + H)^+$] 463.9699, found 463.9697. The enantiomeric excess of *exo*-**4i** was determined by HPLC analysis (Daicel Chiralpak IA, EtOAc/hexane (15:85, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 31.3 min, t_{major} = 39.7 min.

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*Data for endo-2-bromo-10-(p-bromophenyl)-6,10-epoxy-5-methyl-5,5a,6,8,9,10,10a-heptahydrocyclohepta[β]indol-7(5H)-one (endo-**4i**):* colorless prisms; mp 205−206 °C; IR (KBr) 2933, 1726, 1600, 1489, 1390, 1250, 1045, 1009, 888, 813, 522 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.07−2.38 (4H, m), 2.74 (3H, s), 4.01 (1H, d, *J* = 11.7 Hz), 4.61 (1H, dd, *J* = 7.2, 11.7 Hz), 4.74 (1H, d, *J* = 7.2 Hz), 6.32 (1H, d, *J* = 8.5 Hz), 7.18 (1H, m), 7.27 (1H, m), 7.41−7.44 (2H, m), 7.57−7.60 (2H,m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.4 (CH_2), 33.1 (CH_2), 34.6 (CH_3), 57.6 (CH), 74.6 (CH), 85.4 (CH), 86.0 (C), 108.8 (CH), 109.3 (C), 121.7 (C), 126.2 (CH), 127.6 (CH), 128.5 (C), 131.9 (CH), 132.1 (CH), 143.9 (C), 153.0 (C), 205.6 (C); HRMS (APCI-TOF) *m*/*z* calcd for $C_{20}H_{18}O_2NBr_2$ [(M + H)$^+$] 463.9699, found 463.9684.

*Data for endo-5-methoxybenzo[c]-N-methylindolino[3,2-f]-8-oxabicyclo[3.2.1]octan-2-one (endo-**6**):* yellow prisms; mp 142−145 °C; $[\alpha]_D^{25}$ −37.14 (*c* 1.00, $CHCl_3$) (79% ee); IR (KBr) 1705, 1602, 1490, 1179, 887 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.62 (3H, s), 3.52 (3H, s), 4.21 (1H, d, *J* = 11.0 Hz), 4.72 (1H, dd, *J* = 7.3, 11.0 Hz), 5.11 (1H, d, *J* = 7.3 Hz), 6.02 (1H, m), 6.50 (1H, m), 6.84 (1H, m), 7.09 (1H, m), 7.14 (1H, m), 7.20 (1H, m), 7.26 (1H, m), 7.79 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.9 (CH_3), 52.6 (CH_3), 56.2 (CH), 71.7 (CH), 84.7 (CH), 106.8 (CH), 110.5 (C), 117.1 (CH), 124.4 (CH), 125.3 (CH), 125.6 (CH), 128.1 (CH), 128.3 (CH), 131.1 (C), 131.7 (CH), 140.8 (C), 152.4 (C), 192.7 (C); MS (EI) *m*/*z* 307 (M$^+$), 276, 176, 145, 133, 77, 15; HRMS (EI) *m*/*z* calcd for $C_{19}H_{17}NO_3$ (M$^+$) 307.1208, found 307.1177. The enantiomeric excess of *endo*-**6** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 14.1 min, t_{major} = 19.6 min.

Reaction of Diazodiketone 7 with 5-Bromo-*N*-methylindole (2b) Catalyzed by the Pybox-Ph_2−Er(III) Complex. A solution of Pybox-Ph_2 (39.2 mg, 0.075 mmol) and $Er(OTf)_3$ (46.1 mg, 0.075 mmol) in THF (2.5 mL) was stirred at room temperature for 2 h. The solvent of the mixture was removed under reduced pressure, and the resulting solid was dried in vacuo at room temperature for 2.5 h. After addition of MS 4 Å (0.25 g), $Rh_2(OAc)_4$ (2.2 mg, 0.005 mmol), and toluene (2.0 mL), successively, a solution of diazo compound **7** (38.1 mg, 0.25 mmol) and **2b** (105.0 mg, 0.50 mmol) in toluene (2.5 mL) was added over a period of 6 h using a syringe pump at 23 °C. The syringe was washed with toluene (0.5 mL) in one portion, and the reaction was immediately worked up. After removal of MS 4 Å through Celite, the reaction mixture was filtered through a plug of silica gel (3 cm) with AcOEt/hexane (6:4, 80 mL) as the eluent. The solvent was removed in vacuo, and the residue was purified by column chromatography (95:5 hexane/AcOEt) to provide 26.9 mg of *endo*-**8b** and *exo*-**8b** (combined yield 32%, *endo*:*exo* = 82:18). The diastereomer ratio was determined to be 81:19 (*endo*-**8b**:*exo*-**8b**) by ^1H NMR analysis of the crude mixture.

*Data for endo- and exo-spiro[1,4-epoxy-6-bromo-4-methyl-2,3,4,4a,9,9a-hexahydro-1H-carbazol-2-one-3,1′-cyclopropane] (endo-**8b** and exo-**8b**):* pale yellow oil; $[\alpha]_D^{25}$ +8.22 (*c* 0.054, $CHCl_3$) (*endo*:*exo* = 82:18; *endo*, 78% ee; *exo*, 1% ee); IR ($CHCl_3$) 3021, 1752, 1492, 1215, 757, 669 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.18 (1H × 82/100, ddd, *J* = 5.0, 7.7, 9.6 Hz, *endo*), 0.60 (1H × 82/100, ddd, *J* = 5.0, 7.1, 9.8 Hz, *endo*), 0.74 (1H × 82/100, ddd, *J* = 4.3, 7.7, 9.8 Hz, *endo*), 0.77 (1H × 18/100, ddd, *J* = 4.3, 7.6, 9.6 Hz, *exo*), 0.93 (1H × 82/100, ddd, *J* = 4.3, 7.1, 9.6 Hz, *endo*), 1.10 (1H × 18/100, ddd, *J* = 4.3, 7.6, 9.6 Hz, *exo*), 1.24−1.30 (1H × 18/100, m, *exo*), 1.27 (3H × 18/100, s, *exo*), 1.38 (1H × 18/100, ddd, *J* = 4.3, 6.8, 9.6 Hz, *exo*), 1.43 (3H × 82/100, s, *endo*), 2.76 (3H × 82/100, s, *endo*), 2.86 (3H × 18/100, s, *exo*), 3.68 (1H × 18/100, d, *J* = 8.2 Hz, *exo*) 3.78 (1H × 82/100, d, *J* = 10.4 Hz, *endo*), 4.20 (1H × 18/100, d, *J* = 8.2 Hz, *exo*), 4.52 (1H × 82/100, dd, *J* = 5.5, 10.4 Hz, *endo*), 4.54 (1H × 18/100, s, *exo*), 4.72 (1H × 82/100, d, *J* = 5.5 Hz, *endo*), 6.18 (1H × 82/100, d, *J* = 8.5 Hz, *endo*), 6.25 (1H × 18/100, d, *J* = 8.4 Hz, *exo*), 7.02−7.03 (1H, m, *endo* and *exo*), 7.17−7.20 (1H, m, *endo* and *exo*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.2 (CH_2, *endo*), 11.9 (CH_2, *endo*), 12.5 (CH_2, *exo*), 13.7 (CH_3, *exo*), 15.0 (CH_2, *exo*), 17.2 (CH_3, *endo*), 31.6 (C, *exo*), 33.3 (CH_3, *exo*), 33.5 (CH_3, *endo*), 35.0 (C, *endo*), 54.2 (CH, *exo*), 56.8 (CH, *endo*), 71.7 (CH, *exo*), 72.6 (CH, *endo*), 84.5 (CH, *exo*), 84.6 (CH, *endo*), 87.4 (C, *endo*), 88.0 (C, *exo*), 107.2 (CH, *exo*), 107.7 (CH, *endo* and C, *exo*), 107.9 (C, *endo*), 126.7 (CH, *endo*), 127.8 (C, *exo*), 128.1 (CH, *exo*), 128.6 (C, *endo*), 131.3 (CH, *exo*), 131.6 (CH, *endo*), 152.4 (C, *endo*), 152.8 (C, *exo*), 210.0 (C, *endo*), 212.5 (C, *exo*); HRMS (APCI-TOF) *m*/*z* calcd for $C_{16}H_{17}NO_2Br$ [(M + H)$^+$] 334.0437, found 334.0465. The enantiomeric excess of *endo*-**8b** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 13.9 min, t_{major} = 12.1 min. The enantiomeric excess of *exo*-**8b** was determined by HPLC analysis (Daicel Chiralpak AD-3, *i*-PrOH/hexane (5:95, v/v), detector UV 254 nm, flow rate 0.5 mL/min, 35 °C): t_{minor} = 24.0 min, t_{major} = 18.4 min.

Preparation of 1-Diazo-5-(*p*-bromophenyl)-2,5-pentanedione (1c). To a solution of 3-(*p*-bromobenzoyl)propionic acid[24] (5.14 g, 20.0 mmol) and ethyl chloroformate (1.90 mL, 20 mmol) in 60 mL of ether was added triethylamine (3.0 mL, 21.5 mmol). The resulting mixture was stirred at room temperature for 2 h. The precipitated triethylamine hydrochloride was removed by filtration, and the resulting solution was immediately treated with 50 mmol of freshly prepared diazomethane at 0 °C. The mixture was allowed to warm to room temperature overnight. The solvent was removed under reduced pressure, and the resulting residue was chromatographed on a silica gel column (80:20, hexane/AcOEt) to give 1.52 g (27%) of **1c**: yellow prisms; mp 84−85 °C; IR (KBr) 3090, 2111, 1673, 1637, 1583, 1385, 1349, 1110, 781 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.77 (2H, br s, CH_2), 3.35 (2H, t, *J* = 6.3 Hz), 5.40 (1H, br s), 7.56−7.63 (2H, m), 7.79−7.87 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.0, 34.1, 54.7, 128.4, 129.5, 131.9, 135.2, 193.2, 197.4; HRMS (EST-TOF) *m*/*z* calcd for $C_{11}H_9O_2N_2BrNa$ [(M + Na)$^+$] 302.9740, found 302.9739. Anal. Calcd for $C_{11}H_9N_2O_2Br$: C, 47.00; H, 3.23; N, 9.97. Found: C, 47.20; H, 3.07; N, 9.92.

Preparation of 1-Diazo-5-(*p*-ethylphenyl)-2,5-pentanedione (1f). To a solution of 3-(*p*-ethylbenzoyl)propionic acid[25] (3.09 g, 15.0 mmol) and ethyl chloroformate (1.43 mL, 20 mmol) in 45 mL of ether was added triethylamine ((2.1 mL, 16.1 mmol). The resulting mixture was stirred at room temperature for 2 h. The precipitated triethylamine hydrochloride was removed by filtration, and the resulting solution was immediately treated with 38 mmol of freshly prepared diazomethane at 0 °C. The mixture was allowed to warm to room temperature overnight. The solvent was removed under reduced pressure, and the resulting residue was chromatographed on a silica gel column (90:10, hexane/AcOEt) to give 1.14 g (33%) of **1f**: pale yellow plates; mp 69−70 °C; IR (KBr) 3098, 2967, 2113, 1670, 1630, 1604, 1352, 1106, 787 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.25 (3H, t, *J* = 7.5 Hz), 2.70 (2H, q, *J* = 7.5 Hz), 2.76 (2H, br), 3.34 (2H, t, *J* = 6.6 Hz), 5.41 (1H, br s), 7.27−7.29 (2H, m), 7.90−7.91 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.1 (CH_3), 28.8 (CH_2), 33.0 (CH_2), 34.2 (CH_2), 54.5 (CH), 128.0 (CH), 128.2 (CH), 134.1 (C), 150.1 (C), 193.6 (C), 197.9 (C); HRMS (EST-TOF) *m*/*z* calcd for $C_{13}H_{14}O_2N_2Na$ [(M + Na)$^+$] 253.0947, found 253.0956.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Relationship between the lanthanoid metals on selectivities and yield in the cycloaddition reactions, X-ray crystallographic data of *exo*-**3b**, including CIF data, and copies of ^1H and ^{13}C NMR spectra of cycloadducts. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00835.

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Notes

The authors declare no competing financial interest.

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