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Samarium(II)-Mediated Spirocyclization by Intramolecular Aryl Radical Addition onto an Aromatic Ring

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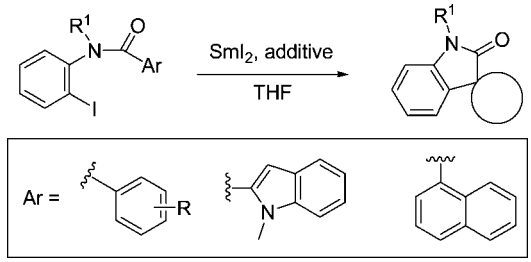

Samarium(II)-mediated spirocyclization by intramolecular addition of aryl radicals onto an aromatic ring was achieved by the reaction of *N*-(2-iodophenyl)-*N*-alkylbenzamides with SmI_2 in the presence of HMPA, yielding spirocyclic indolin-2-one derivatives. The ether congeners afford spirocyclic benzofuran derivatives in moderate yields by aryl radical addition onto a benzene ring without having an electron-withdrawing group. The reaction with other aryl groups such as naphthalene and indole rings is also described.

Introduction

Recently, the synthesis of spirocycles has attracted a great deal of attention due to their unique structure and diverse biological activities.[1] A variety of methods for the synthesis of spirocyclic compounds are reported, such as transition-metal-catalyzed cyclization,[2] rearrangement of epoxides or cyclopropanes,[3] and cycloaddition reactions.[4] Among them, radical cyclization is one of the important methods for spirocyclization: spirocycles can be efficiently synthesized by an intramolecular radical attack onto a cyclic olefin,[5] intramolecular addition of tertiary cyclic radicals to an alkene[6] or alkyne,[7] or cyclization of a radical species possessing a preformed quaternary carbon center.[8] In contrast, synthesis of spirocycles by a radical attack onto an aromatic ring is relatively limited, except for intramolecular radical addition onto the *para*-position of phenol derivatives, which is a convenient approach to spirocyclic cyclohexadienones.[9] Recently, some examples of the synthesis of spirocyclic compounds using the radical reaction onto an indole or benzofuran ring mediated by tributyltin hydride have been reported.[10] However, there are some problems with these reactions such as the toxicity of the tin reagent, harsh reaction

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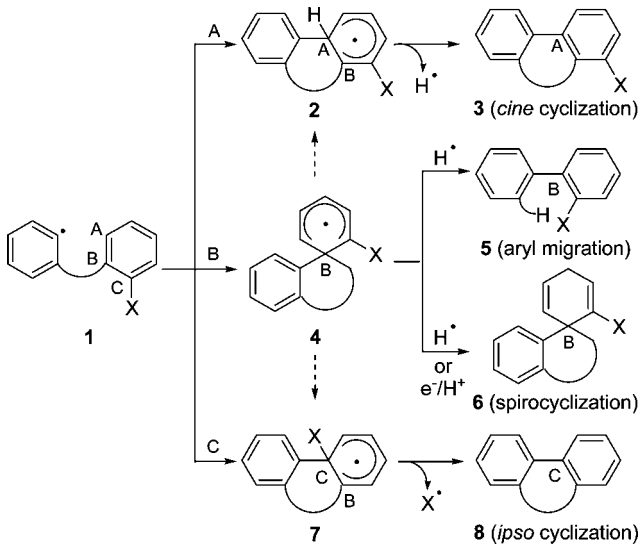
SCHEME 1



conditions, and the difficulty to obtain spiro compounds selectively due to the unstable spirocyclic radical intermediates.

More recently, we have reported samarium(II)-mediated spirocyclization through the addition of a ketyl radical onto an aromatic ring.[11,12] On the basis of this study, we next turned our attention to samarium(II)-mediated spirocyclization by the intramolecular addition of an aryl radical with an aromatic ring. As shown in Scheme 1, (1) the intramolecular addition of aryl radical **1** onto carbon A forms the cyclohexadienyl radical intermediate **2**, which is easily converted into the fused ring **3** by abstraction of a hydrogen atom on the carbon A (cine cyclization).[13,14] (2) The reaction at carbon B followed by facile aryl migration of the unstable spirocyclohexadienyl radical intermediate **4** gives biaryl compound **5**.[15] On the other hand, trapping of the intermediate **4** by hydrogen radical or reduction-protonation affords the spirocyclic compounds such as **6**.[16] (3) Ipso substitution via attack of the aryl radical at carbon C followed by elimination of the X radical gives the fused ring **8**.[17] In general, the aryl radical cyclization onto an aromatic ring to form spirocycles such as **6** is extremely difficult, producing a considerable amount of the *cine*-cyclized product of the type **3**,[16] except for the reaction of indole derivatives.[10] Presumably this is because spirocyclohexadienyl radical intermediate **4** is extremely unstable in the reversible radical reactions, and in some cases, rearrangement readily takes place to form a fused-ring radical such as **2** or **7**.[13,15c] We expected that SmI_2 in the presence of a proton source would effectively trap the key intermediate **4** by single electron transfer followed by protonation, which could realize the spirocyclization via reductive biaryl coupling.[10] Herein, we present a full account of our investigation into the aryl radical spirocyclization onto various aromatic rings mediated by SmI_2.[18]

Results and Discussion

SmI_2-Mediated Spirocyclization of Benzoate Derivatives. First, we examined the aryl radical coupling reaction of 2-iodophenyl benzoates **9a** and **9b** mediated by SmI_2 with HMPA. However, the reaction in the presence or absence of *i*-PrOH led to decomposition of the starting materials, without producing any detectable amounts of the desired spirocyclic product (Scheme 2).

Considering that the phenyl ester moiety of **9a** and **9b** would be labile under the reductive reaction conditions, we next investigated the reaction of the *N*-methylbenzamide derivatives **10a**−**h** in the presence of *i*-PrOH. The results are summarized in Table 1. Fortunately, the reaction of **10a** without a substituent on the benzene ring could act as a radical acceptor with the

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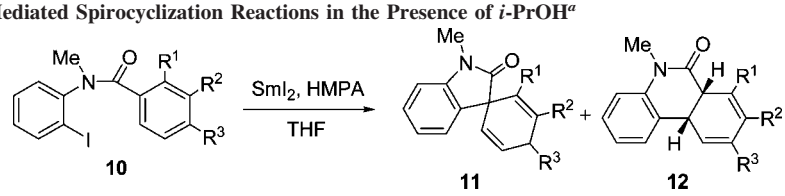
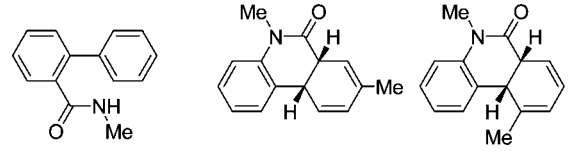
TABLE 1. Samarium(II)-Mediated Spirocyclization Reactions in the Presence of *i*-PrOH[a]

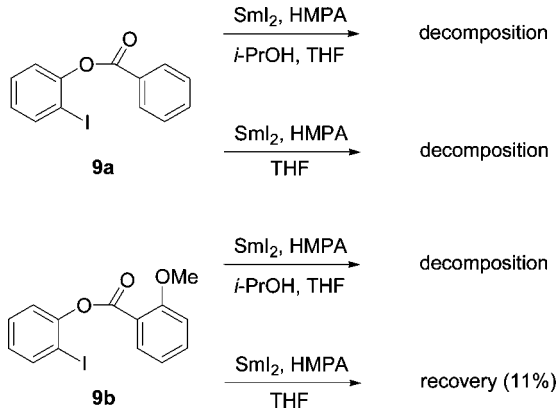


							product yield (%)	
entry	substrate	R^1	R^2	R^3	*i*-PrOH (equiv)	*T* (°C)	**11**	**12**
1	**10a**	H	H	H	2	0	34	tr
2	**10a**	H	H	H	20	0	39	28
3	**10a**	H	H	H	2	−35	36	30
4	**10b**	Me	H	H	2	−35	89	6
5	**10c**	OMe	H	H	2	−35	89	9
6	**10d**	Br	H	H	2	−35	34[b]	0
7	**10e**	NO_2	H	H	2	−35	no reaction	
8	**10f**	H	Me	H	2	−35	29	65[c]
9	**10g**	H	H	Me	2	−35	31	53
10	**10h**	H	H	OMe	2	−35	complex mixture	

[a] All reactions were carried out in THF using SmI_2 (5 equiv) and HMPA (18 equiv). [b] Gave a known biaryl compound **A** (40%). [c] Obtained as a mixture of regioisomers **12fA** and **12fB** (1:1).



SCHEME 2



THF solution of SmI_2 (5 equiv)[19] in the presence of HMPA and *i*-PrOH at 0 °C to give the desired spirocyclic compound **11** in 34% yield, as well as a trace amount of fused cyclic compound **12** (entry 1). Increased loading of *i*-PrOH (20 equiv, entry 2) or lowering of the reaction temperature to −35 °C (entry 3) was not effective for improvement of the yield of spirocycle **11**, and a considerable amount of a reduced fused ring **12** was obtained in both cases (28% and 30% yield, respectively). Next, we investigated the spirocyclization of benzamides with a substituent on the benzene ring and found that the reaction of the *o*-methyl- or *o*-methoxy-substituted analogues **10b** and **10c** (entries 4 and 5) afforded the spirocycle **11** both in high yields (89%) and selectivities (ca. **11**:**12** = 9:1). This is the first example of selective spirocyclization by an aryl radical addition onto a benzene ring. The reaction of benzamide derivative **10d**, which has a bromine atom at the *ortho*-position, afforded the spirocycle **11d** in low yield of 34% and a known biaryl compound (40%) (entry 6). Similarly, the reaction of **10e** having a nitro group at the *ortho*-position at −35 °C did not give any cyclized products leading to recovery of unchanged starting material (entry 7).[20] Comparing entries 4 and 5 with entries 6 and 7, the electron-rich benzene ring is more appropriate as a radical acceptor in the samarium(II)-mediated aryl coupling reaction than the electron-deficient benzene ring. Interestingly, a methyl substituent at the *meta*- (entry 8) or *para*-position (entry 9) increased the yields of the fused rings **12**. Compared to other radical aryl coupling reactions using Bu_3SnH/AIBN,[13b,c,14b,c] which mainly yield biaryl products, formation of the spirocycles **11** and fused rings **12** with a loss of aromaticity is a unique reactivity of the SmI_2/HMPA/*i*-PrOH system. This can be attributed to facile trapping of the unstable bicyclic hexadienyl radical intermediates by SmI_2 as the single electron transfer reductant (vide infra).

As shown in Table 2, when the reaction of **10a**−**h** was conducted in the absence of *i*-PrOH, the biaryl coupling products **13** were selectively obtained in low to moderate yields in almost all cases (entries 1−8). For a reason that is unclear, the *para*-substituted benzamide derivatives **10g** and **10h** afforded the biaryl product **13** most efficiently in 57−60% yields, without isolation of other cyclized products (entries 7 and 8). From these results, we found that the cyclization mode (path A vs path B in Scheme 1) could be completely controlled by simply changing the reaction conditions and the substituent pattern (compare Table 1, entries 4 and 5 vs Table 2, entries 7 and 8).

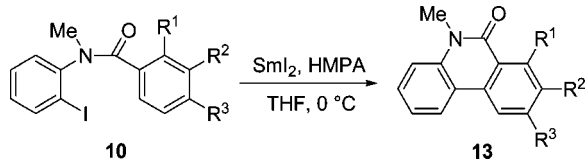
In order to investigate the steric effect of the substituent on the nitrogen atom,[21] we next examined the reaction of benzamide derivatives **14a**−**c**, which have the sterically more hindered *N*-alkyl substituent rather than a methyl group. The reaction of

(19) When the reaction was conducted with 2 equiv of SmI_2, a considerable amount of the unchanged starting materials was observed on TLC.

(20) The reaction at a higher temperature (0 °C) gave a complex mixture of unidentified products.

(21) The reaction of substrates having no substituent or Ms group on the nitrogen atom led to decomposition of the starting materials without producing the desired products.

TABLE 2. Samarium(II)-Mediated Biaryl Coupling Reactions in the Absence of *i*-PrOH[a]



10 13

entry	substrate	R^1	R^2	R^3	**13** (%)
1	**10a**	H	H	H	26
2	**10b**	Me	H	H	26
3	**10c**	OMe	H	H	15
4	**10d**	Br	H	H	35 (R^1 = H)
5	**10e**	NO_2	H	H	complex mixture
6	**10f**	H	Me	H	29[b]
7	**10g**	H	H	Me	60
8	**10h**	H	H	OMe	57[c]

[a] All reactions were carried out in THF using SmI_2 (5 equiv) and HMPA (18 equiv). [b] Obtained as a mixture of regioisomers **13fA** and **13fB** (2:1). [c] The reaction was conducted at −78 °C, and a regioisomeric fused ring **13h′** was also formed.

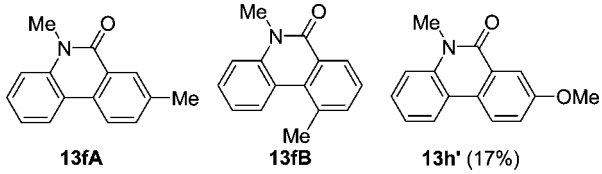
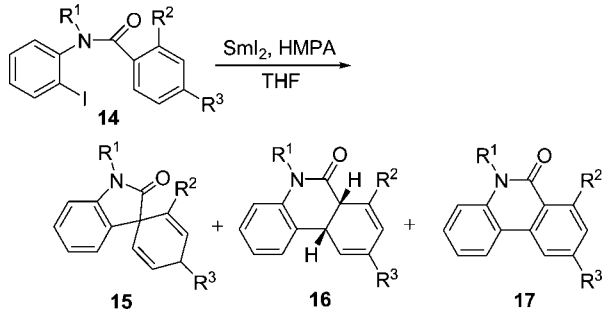


TABLE 3. Steric Effect of Substituent on the Nitrogen Atom[a]



							product yield (%)		
entry	substrate	R^1	R^2	R^3	*i*-PrOH (equiv)	*T* (°C)	**15**	**16**	**17**
1	**14a**	Bu	Me	H	2	−35	75	tr	0
2	**14a**	Bu	Me	H	0	0	0	0	19[b]
3	**14b**	Bu	H	Me	2	−35	27	tr	0
4	**14b**	Bu	H	Me	0	0	0	0	46
5	**14c**	*i*-Pr	Me	H	2	−35	75	tr	0
6	**14c**	*i*-Pr	Me	H	0	0	0	0	4[b]

[a] All reactions were carried out in THF using SmI_2 (5 equiv) and HMPA (18 equiv). [b] A complex mixture of unidentified products was also obtained.

N-alkyl derivatives **14a** and **14c** with an *ortho*-substituent gave the corresponding spirocycles **15** in good yields (Table 3, entries 1 and 5). When the reaction of **14b** was conducted in the absence of *i*-PrOH, the expected biaryl coupling product was selectively obtained in 46% yield (entry 4).

A plausible mechanism for the samarium(II)-mediated radical aryl coupling reaction is shown in Scheme 3. Single electron transfer (SET) to the iodide **18** by SmI_2 generates the aryl radical, which would undergo a 5-*exo*-type intramolecular cyclization onto the benzene ring producing the spirohexadienyl radical intermediate **A**. The unstable intermediate **A** can be easily rearranged to the more stable intermediate **C**. However; further SET and protonation of the resulting cyclohexadienyl anion **B** would be promoted by SmI_2 in the presence of *i*-PrOH to afford the spirocyclic 1,4-cyclohexadiene **19**. In contrast, rearrangement of the unstable intermediate **A** to the fused ring **C** followed by SET and the subsequent protonation would give the reduced fused ring **21**, while in the absence of *i*-PrOH, the hydrogen abstraction from **C** yields the aromatized product **20**. The fact that the reaction in the absence of *i*-PrOH gave the biaryl product **13** selectively (Table 2) indicates that *i*-PrOH would promote the SET to **B**, by trapping this anionic intermediate. The selective formation of spirocyclic compounds **11** from the *ortho*-substituted benzamide derivatives **10b** and **10c** (R^1 = Me or OMe; Table 1, entries 4 and 5) can be explained by the unfavorable steric interaction in the rearrangement of **A** to **C** as shown in the structure **D**. The relatively long lifetime of **A** with an *ortho*-substituent would assist further SET by SmI_2 and the subsequent protonation to **19** without rearrangement to **C**.

Substrate Scope and Limitation. We next examined the reaction of substrates **22a**−**g** that contained an ether tether with SmI_2 in the absence of *i*-PrOH. Isomeric spirocyclic dienes **23** and **24** were obtained in only low yields (Table 4, entry 1); however, this result clearly shows that the benzene ring without an activating substituent such as a carbonyl group can also serve as the acceptor of aryl radicals. Introduction of a methoxy substituent at the *ortho*-position slightly improved the yield of spirocycles **23** and **24** (entry 2), which is in good agreement with the results with the amide congeners (Table 1). For a reason that is unclear, formation of a fused ring was not observed with the substrates having an ether tether. Instead, hydrodeiodination/reduction products **25** were observed in most cases. We found that introduction of a methyl group at the tether carbon also improves the yield of the spirocycle (entry 5). This can be partly attributed to stabilization of a favorable conformation for spirocyclization due to the steric hindrance around the ether tether, as with the *N*-alkylanilide derivatives. The best result was gained with **22g**, which has a methyl group at the ether tether and a methoxy group at the *para*-position of the benzene ring (entry 7).

Next, we planned to investigate the reactivity of other aromatic rings as the radical acceptor to expand the synthetic utility of this reaction and explore the limitation of its scope. First, we chose the indole ring as the radical acceptor[10a] and investigated the reaction under the standard conditions for spirocyclization (SmI_2/HMPA/*i*-PrOH). Unfortunately, spirocycle **27** and reduced fused ring **28** were obtained in low yields (Table 5, entry 1). With this unsatisfactory result in terms of both yield and selectivity, we next examined the reaction in the presence of alkali metal salts, according to Flower's report, which uses LiBr or LiCl in a SmI_2-mediated pinacol coupling reaction.[22] Use of LiBr and LiCl as an additive gave better results in the spirocyclization, leading to formation of the desired spirocycle **27** in 57% yield (entries 4−6). In contrast, other salts such as LiI, NaBr, and KBr were ineffective (entries 7−9).

We also examined the substrate **29** with an amide side chain at the 3-position of the indole ring. The reaction of **29** with SmI_2 in the presence of LiBr at room temperature gave

(22) (a) Fuchs, J. R.; Mitchell, M. L.; Shabangi, M.; Flowers, R. A., II. *Tetrahedron Lett.* **1997**, *38*, 8157–8158. (b) Miller, R. S.; Sealy, J. M.; Shabangi, M.; Kuhlman, M. L.; Fuchs, J. R.; Flowers, R. A., II *J. Am. Chem. Soc.* **2000**, *122*, 7718–7722, They speculated that the addition of bromide or chloride to samarium iodide would form another samarium halide species with improved reducing ability.

SCHEME 3

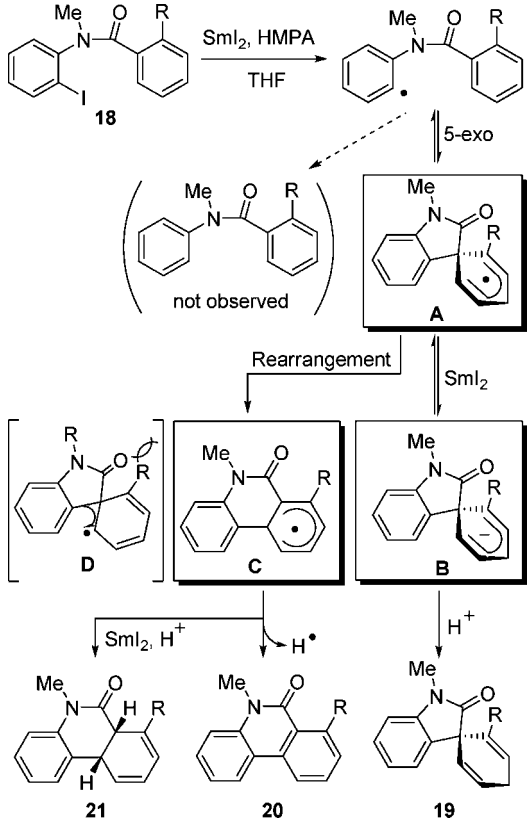
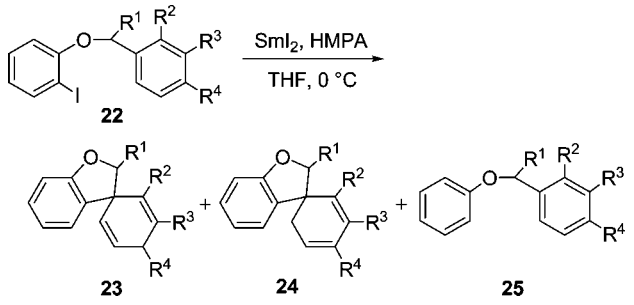
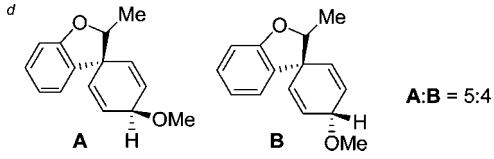


TABLE 4. Reactions of Substrates Having an Ether Tether[a]



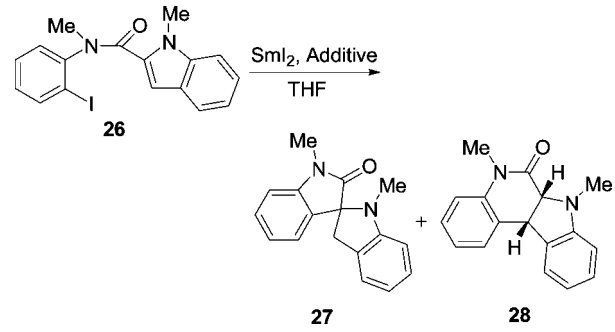
						product yield (%)[b]		
entry	substrate	R^1	R^2	R^3	R^4	**23**	**24**	**25**
1	**22a**	H	H	H	H	19	10	47
2	**22b**	H	OMe	H	H	28	28	41
3	**22c**	H	H	OMe	H	28	6	62
4	**22d**	H	H	H	OMe	41[c]	0	31
5	**22e**	Me	H	H	H	38	0	24
6	**22f**	Me	OMe	H	H	35	18	13
7	**22g**	Me	H	H	OMe	67[d]	0	0

[a] All reactions were carried out in THF using SmI_2 (3 equiv) and HMPA (10.8 equiv). [b] Yields were based on ^1H NMR. [c] As a 23:18 mixture of diastereomers. [d]



spirocycle **30**, reduced fused ring **31**, and dehalogenated product **32** without selectivity (Table 6, entry 1). Lowering the reaction temperature did not improve the yield or selectivity (entries 2−4). These results revealed that the indole ring can work as the radical acceptor in the aryl radical coupling reaction; however, the spirocyclization by the aryl radical addition onto an indole ring proceeds more easily at the 2-position.

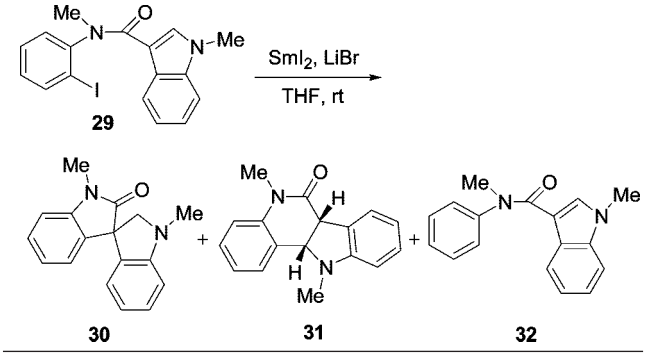
TABLE 5. Reactions of Indole-2-carboxamide Derivative 26[a]



			product yield (%)	
entry	additive[b]	T (°C)	**27**	**28**
1	HMPA, *i*-PrOH	−35	16	17
2	HMPA	0	complex mixture	
3	none	rt	no reaction	
4	LiBr	rt	57	8
5	LiBr, *i*-PrOH	rt	57	0
6	LiCl	rt	57	0
7	LiI	rt	no reaction	
8	NaBr	rt	no reaction	
9	KBr	rt	no reaction	

[a] Reactions were carried out with 3.5 equiv (with HMPA) or 5 equiv (with other additives) of SmI_2 in THF. [b] HMPA (4 equiv relative to SmI_2), metal salts (8 equiv relative to SmI_2), and *i*-PrOH (2 equiv relative to **26**) were used.

TABLE 6. Reactions of Indole-3-carboxamide Derivative 29[a]

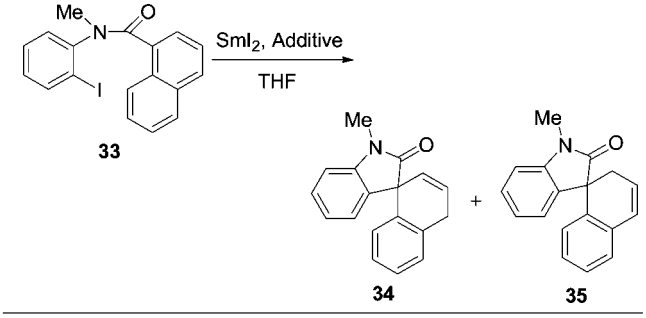


		product yield (%)		
entry	T (°C)	**30**	**31**	**32**
1	rt	22	34	28
2	0	16	29	41
3	−30	0	tr	tr
4	−78		no reaction	

[a] All Reactions were carried out in THF using SmI_2 (3.5 equiv) and LiBr (8 equiv relative to SmI_2).

We next evaluated naphthalene ring as the radical acceptor. The standard conditions for the spirocyclization (SmI_2/HMPA/*i*-PrOH) yielded the spirocycle **34** in ca. 75% yield, although isolation of **34** from the starting material was difficult (Table 7, entry 1). Interestingly, treatment of **33** with SmI_2 and HMPA in the absence of *i*-PrOH selectively gave spirocycle **35**, which has a conjugated double bond (entry 2), whereas the reaction

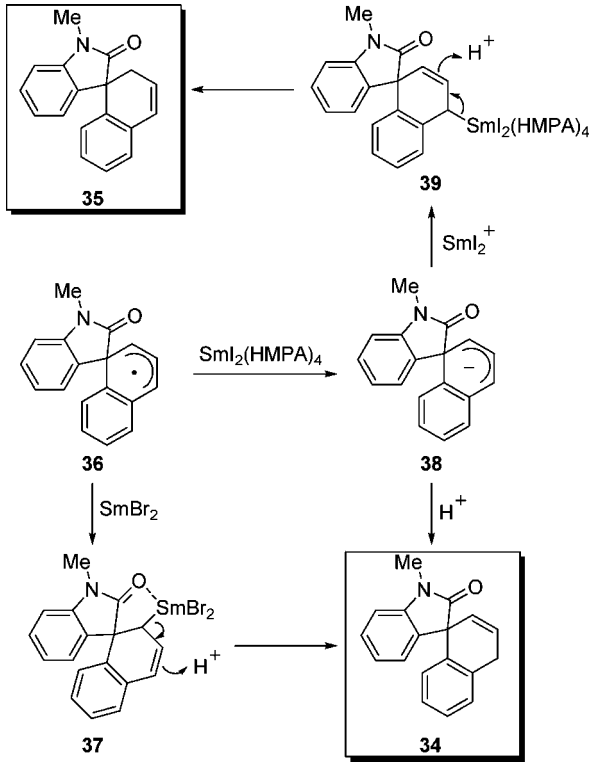
TABLE 7. Reactions of 1-Naphthamide Derivative 33[a]



entry	additive[b]	T (°C)	product yield (%) 34	35
1	HMPA, *i*-PrOH	−35	<75	0
2	HMPA	0	0	58
3	LiBr	rt	75	0
4	LiBr, *i*-PrOH	rt	74	0
5	LiBr	0	no reaction	

[a] Reactions were carried out with 3.5 equiv (with HMPA) or 5 equiv (with LiBr) of SmI_2 in THF. [b] HMPA (4 equiv relative to SmI_2), metal salts (8 equiv relative to SmI_2) and *i*-PrOH (2 equiv relative to **33**) were used.

SCHEME 4



with SmI_2/LiBr gave spirocycle **34** with an isolated double bond in good yields, irrespective of the presence or absence of *i*-PrOH (entries 3 and 4).

A possible rationalization for the observed results with the naphthalene derivative **33**, in which the position of the double bond was controlled by changing the reaction conditions, is shown in Scheme 4. In the presence of LiBr, the generated $SmBr_2$[22] would react with the radical species **36**, coordinating with the amide oxygen to produce an organosamarium intermediate **37**, and the spirocycle **34** was then formed by subsequent protonation. In contrast, in the case using HMPA,

SCHEME 5

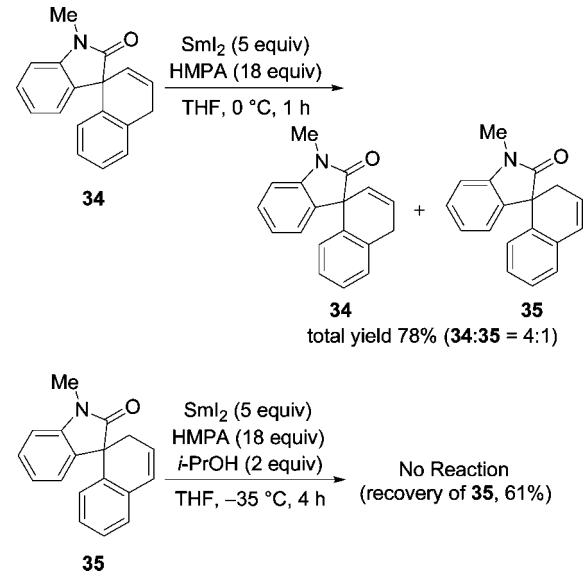
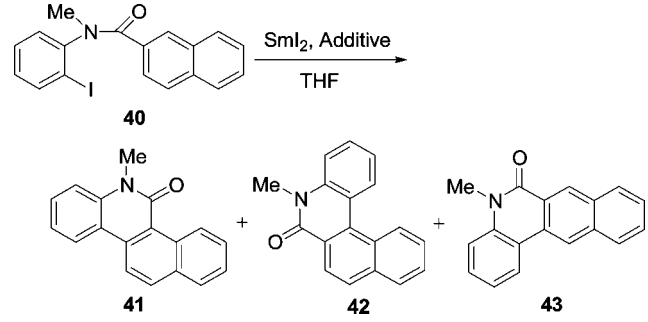


TABLE 8. Reactions of 2-Naphthamide Derivative 40[a]



entry	additive	T (°C)	product yield (%) 41	42	43
1	HMPA, *i*-PrOH	−78	complex mixture		
2	HMPA	−78	14	22	15
3	LiBr	rt	complex mixture		
4	LiBr	rt	complex mixture		

[a] Reactions were carried out with 3.5 equiv (with HMPA) or 5 equiv (with LiBr) of SmI_2 in THF. [b] HMPA (4 equiv relative to SmI_2), LiBr (8 equiv relative to SmI_2) and *i*-PrOH (2 equiv relative to **40**) were used.

formation of the organosamarium intermediate of type **37** would be relatively difficult since the coordination site of samarium can be saturated by HMPA. Accordingly, SET to the spiro radical **36** by SmI_2 followed by protonation by *i*-PrOH at the less hindered position of the resulting anionic intermediate **38** gives spirocycle **34**. In the absence of *i*-PrOH, protonation occurred during workup at the less hindered position after formation of the organosamarium species **39** to give the spirocycle **35** having a conjugated double bond.[23] It should be noted that isomerization of **34** to the conjugated isomer **35** did proceed to some extent (**34**:**35** = 4:1, Scheme 5) under the cyclization conditions without *i*-PrOH, while the reverse reaction from **35** was not observed under the protic conditions (SmI_2/HMPA/*i*-PrOH in THF). Accordingly, isomerization to **35** might

(23) The key intermediate **39** would be formed only in the absence of proton source, because isopropanol could protonate the intermediate **38** leading to **34**, before formation of **39**.

partly assist the selective formation of **35** in the absence of *i*-PrOH, although it has been proven that formation of **34** using *i*-PrOH is kinetically controlled.[24]

Finally, we examined substrate **40** with an amide side chain at the 2-position of the naphthalene ring. The reaction of **40** with SmI_2/HMPA gave fused ring **41** (formed by the rearrangement of the carbonyl group to the 1-position), fused ring **42** (formed by the rearrangement of the phenyl group to the 1-position), and fused ring **43** (formed by the rearrangement of the phenyl ring to the 3-position) (Table 8, entry 2). We have revealed that the spirocyclization by the aryl radical addition onto a naphthalene ring proceeds more efficiently with substrate **33** having an amide side chain at the 1-position of the naphthalene ring.

Conclusions

We have demonstrated a reductive cyclization of aryl radicals onto an aromatic ring mediated by SmI_2 and an appropriate additive such as HMPA, *i*-PrOH, and LiBr. When *ortho*-substituted benzamide derivatives were used, the corresponding spirocyclic compounds were selectively obtained. This is the first example of the synthesis of spirocycles by the aryl radical addition onto a benzene ring. It has also been revealed that an indole or naphthalene ring can work as the radical acceptor, yielding various spirocycles and reduced fused ring compounds. The radical cyclization reaction with the substrates having an ether tether also proceeds to give spirocycles, and we found that introduction of a substituent onto the tether is effective for improvement of the yield of the spirocycles. These results demonstrate that product distribution is highly dependent on the reaction conditions and substrate structure; however, samarium(II)-mediated cyclization of appropriate substrates is useful for the synthesis of various spirocycles.

Experimental Section

General Procedure for Samarium(II)-Mediated Spirocyclization. Synthesis of 1′-Methylspiro[cyclohexa[2,5]diene-1,3′-indolin]-2′-one (11a) and 5-Methyl-6a,10a-dihydrophenanthridin-6(5*H*)-one (12a) (Table 1, entry 3). A mixture of samarium (232 mg, 1.54 mmol) and 1,2-diiodoethane (335 mg, 1.19 mmol) in THF (12 mL) was stirred for 1.5 h. After cooling to 0 °C, HMPA (0.742 mL, 4.27 mmol) was added to the mixture, and stirring was continued for 20 min at this temperature. After cooling to −35 °C, a solution of the amide **10a** (80 mg, 0.237 mmol) and *i*-PrOH (0.036 mL, 0.474 mmol) in THF (2 mL) was added to the mixture, and the mixture was stirred for 15 min. After the mixture was exposed to air, saturated $NaHCO_3$ was added to the mixture, and the whole was extracted with Et_2O. The extract was washed with saturated $NaHCO_3$ and brine and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to leave a residue, which was purified by column chromatography over silica gel with *n*-hexane−EtOAc (6:1) to give spirocycle **11a** (18 mg, 36% yield) and fused cyclic compound **12a** (15 mg, 30% yield).

Compound **11a**: colorless oil; IR (KBr) cm^{-1} 1716 (C═O); ^1H NMR (500 MHz, $CDCl_3$) δ 2.82−3.01 (m, 2H, CH_2), 3.23 (s, 3H, NMe), 5.39 (ddd, J = 10.5, 2.0, 2.0 Hz, 2H, 2 × *C*═CH), 6.12−6.15 (m, 2H, 2 × *C*═CH), 6.83−6.85 (m, 1H, Ar), 7.05−7.13 (m, 2H, Ar), 7.26−7.30 (m, 1H, Ar); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 25.7, 26.6, 51.8, 108.0, 122.9, 123.8 (2C), 124.7, 127.2, 128.4 (2C), 134.2, 143.0, 177.9; MS (FAB) *m*/*z* (%) 212 (MH^+, 100); HRMS (FAB) calcd for $C_{14}H_{14}NO$ (MH^+) 212.1075, found 212.1077.

(24) As we expected, isomerization from **35** to **34** or its reverse reaction did not proceed under SmI_2/HMPA in the presence of *i*-PrOH.

Compound **12a**: pale yellow oil; IR (KBr) cm^{-1} 1666 (C═O); ^1H NMR (500 MHz, $CDCl_3$) δ 3.32−3.36 (m, 1H, CH), 3.37 (s, 3H, NMe), 3.78 (ddd, J = 9.0, 3.0, 3.0 Hz, 1H, CH), 5.77 (ddd, J = 9.0, 4.0, 3.5 Hz, 1H, *C*═CH), 5.96−5.99 (m, 1H, *C*═CH), 6.08−6.15 (m, 2H, CH═CH), 6.98 (d, J = 8.0 Hz, 1H, Ar), 7.05−7.08 (m, 1H, Ar), 7.22−7.31 (m, 2H, Ar); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 29.8, 35.6, 39.3, 114.4, 123.1, 124.2, 125.5, 125.7, 126.5, 127.6 (2C), 127.8, 139.8, 170.2; MS (FAB) *m*/*z* (%) 212 (MH^+, 49), 210 (100); HRMS (FAB) calcd for $C_{14}H_{14}NO$ (MH^+) 212.1075, found 212.1084.

General Procedure for Samarium(II)-Mediated Spirocyclization in the Absence of *i*-PrOH. Synthesis of 5-Methylphenanthridin-6(5*H*)-one (13a) (Table 2, entry 1). A mixture of samarium (293 mg, 1.95 mmol) and 1,2-diiodoethane (423 mg, 1.50 mmol) in THF (15.0 mL) was stirred for 1.5 h. After cooling to 0 °C, HMPA (0.939 mL, 5.40 mmol) was added to the mixture, and stirring was continued for 20 min at this temperature. A solution of amide **10a** (100 mg, 0.300 mmol) in THF (3.0 mL) was added to the mixture, and the mixture was stirred for 30 min at this temperature. After the mixture was exposed to air, saturated $NaHCO_3$ was added to the mixture, and the whole was extracted with Et_2O. The extract was washed with saturated $NaHCO_3$ and brine and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to leave a residue, which was purified by column chromatography over silica gel with *n*-hexane−EtOAc (6:1) to give a biaryl coupling product **13a** (16.2 mg, 26% yield): colorless oil; IR (KBr) cm^{-1} 1651 (C═O); ^1H NMR (500 MHz, $CDCl_3$) δ 3.80 (s, 3H, NMe), 7.31 (ddd, J = 8.0, 8.0, 1.5 Hz, 1H, Ar), 7.39 (d, J = 8.5 Hz, 1H, Ar), 7.52−7.59 (m, 2H, Ar), 7.74 (ddd, J = 7.5, 7.5, 1.5 Hz, 1H, Ar), 8.25 (dd, J = 7.5, 4.5 Hz, 2H, Ar), 8.54 (dd, J = 8.0, 1.5 Hz, 1H, Ar); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 29.9, 115.0, 119.2, 121.6, 122.4, 123.2, 125.5, 127.9, 128.8, 129.5, 132.3, 133.5, 138.0, 161.6; MS (FAB) *m*/*z* (%) 210 (MH^+, 60), 154 (100); HRMS (FAB) calcd for $C_{14}H_{12}NO$ (MH^+) 210.0919, found 210.0916.

General Procedure for Samarium(II)-Mediated Spirocyclization in the Presence of LiBr. Synthesis of 1,1′-Dimethyl-2,3′-spirobi[indolin]-2-one (27) and (±)-(6a*R*,11b*R*)-5,7-Dimethyl-5,6a,7,11b-tetrahydroindolo[2,3-*c*]quinolin-6-one (28) (Table 5, entry 4). A mixture of samarium (90 mg, 0.599 mmol) and 1,2-diiodoethane (131 mg, 0.466 mmol) in THF (4.6 mL) was stirred for 2 h. After cooling to 0 °C, a solution of LiBr (323 mg, 3.72 mmol) in THF (3.5 mL) was added to the mixture, and stirring was continued for 40 min at room temperature. A solution of indole **26** (50 mg, 0.133 mmol) in THF (2.0 mL) was added to the mixture, and the mixture was stirred for 30 min at this temperature. After the mixture was exposed to air, $Na_2S_4O_7$ was added to the mixture, and the whole was extracted with Et_2O. The extract was washed with $Na_2S_4O_7$ and brine and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to leave a residue, which was purified by column chromatography over silica gel with *n*-hexane−EtOAc (10:1). Further purification by recrystallization from EtOAc gave the spirocycle **27** (20.1 mg, 57% yield) and fused cyclic compound **28** (2.8 mg, 8% yield).

Compound **27**: colorless crystals; mp 176−178 °C; IR (KBr) cm^{-1} 1716 (C═O); ^1H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, 3H, NMe), 3.21 (d, J = 15.6 Hz, 1H, C*H*H), 3.25 (s, 3H, NMe), 3.54 (d, J = 15.6 Hz, 1H, CH*H*), 6.47 (d, J = 7.8 Hz, 1H, Ar), 6.72 (ddd, J = 7.5, 7.5, 1.0 Hz, 1H, Ar), 6.88 (d, J = 7.5 Hz, 1H, Ar), 7.01 (ddd, J = 7.5, 7.5, 1.0 Hz, 1H, Ar), 7.06−7.17 (m, 3H, Ar), 7.33 (ddd, J = 7.5, 7.5, 1.2 Hz, 1H, Ar); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 26.3, 30.6, 40.8, 73.9, 106.6, 108.3, 118.1, 123.0, 123.4, 124.1, 126.8, 127.9, 129.3, 129.5, 143.0, 151.9, 176.9; MS (FAB) *m*/*z* (%) 287 (MNa^+, 73), 264 (100); HRMS (FAB) calcd for $C_{17}H_{16}N_2NaO$ (MNa^+) 287.1130, found 287.1154.

Compound **28**: colorless oil; IR (KBr) cm^{-1} 1668 (C═O); ^1H NMR (300 MHz, $CDCl_3$) δ 2.96 (s, 3H, NMe), 3.42 (s, 3H, NMe), 4.01 (d, J = 8.1 Hz, 1H, 11b-H), 4.49 (d, J = 8.1 Hz, 1H, 6a-H), 6.56 (d, J = 8.1 Hz, 1H, Ar), 6.82 (ddd, J = 7.5, 7.5, 0.6 Hz, 1H,

Ar), 6.99−7.06 (m, 2H, Ar), 7.18 (ddd, J = 7.5, 7.5, 1.2 Hz, 1H, Ar), 7.23−7.28 (m, 1H, Ar), 7.33−7.36 (m, 2H, Ar); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 29.7, 35.3, 42.0, 68.4, 108.5, 114.7, 119.0, 122.9, 123.2, 124.8, 127.9, 128.5, 128.7, 130.5, 138.5, 151.8, 166.6; MS (FAB) m/z (%) 287 (MNa^+, 75), 264 (100); HRMS (FAB) calcd for $C_{17}H_{16}N_2NaO$ (MNa^+) 287.1160, found 287.1158.

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Supporting Information Available: Synthetic procedure, characterization, and ^{1}H NMR for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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