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Stereoselectivity of 6-*Exo* Cyclization of α-Carbamoyl Radicals

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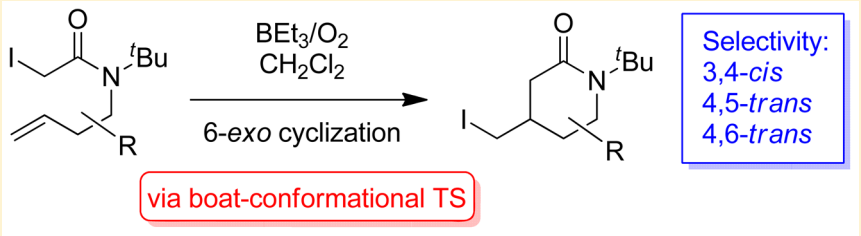
Supporting Information

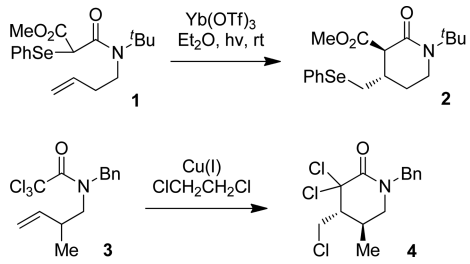


ABSTRACT: The stereoselectivity in the 6-*exo* cyclization of α-carbamoyl radicals was investigated experimentally and theoretically. The BEt_3/O_2-initiated iodine-atom-transfer radical cyclization reactions of substituted *N*-(but-3-en-1-yl)-*N*-(*tert*-butyl)-2-iodoalkanamides were carried out, which led to the predominant formations of 3,4-*cis*, 4,5-*trans*, or 4,6-*trans* substituted δ-lactams. Density functional calculations at the B3LYP/6-31G* level revealed that the 6-*exo* radical cyclization proceeds via boat-conformational transition states. Furthermore, a mechanistic insight into the stereoselectivity was provided and the calculation results were in excellent agreement with the experimental observations.

INTRODUCTION

Radical cyclizations provide a facile entry to various carbo- and heterocycles with unique chemo-, regio-, and stereoselectivities and thus have gained increasing popularity in organic synthesis in the past decades.[1] Among various modes of radical cyclization, 5-*exo* and 6-*exo* cyclizations are perhaps the most extensively studied types of reactions. In particular, the 6-*exo* cyclization of α-carbamoyl radicals has been demonstrated to be a viable means for the construction of δ-lactam skeletons and thus of great potential in organic synthesis.[2−9] For example, Bonjoch and co-workers studied extensively the 6-*exo* cyclization of unsaturated trichloroacetamides leading to the construction of 2-azabicyclo[3.3.1]nonanes and perhydroisoquinolines.[2] This strategy was successfully applied to the total synthesis of indole alkaloids (±)-melinonine-E and (±)-strychnoxanthine.[2d]

Despite the extensive study on the 6-*exo* cyclization of α-carbamoyl radicals, we were surprised to find that little was known on the general pattern of stereoselectivity in this type of cyclization. Yang et al. reported the Lewis acid promoted phenylseleno-group-transfer reaction of amide **1** in which the 3,4-*trans*-substituted product **2** was obtained as the only product in high yield (eq 1).[8] Curran et al. also observed the same 3,4-*trans*-selectivity in the Bu_3SnH-mediated reactions of *N*-(2-vinylphenyl)-2-bromoalkanamide derivatives.[9] Clark and co-workers reported the Cu(I)-catalyzed cyclization of trichloroacetamide **3** leading to the exclusive formation of the 4,5-*trans*-substituted δ-lactam **4** in quantitative yield (eq 2).[3a]



We have long been interested in the cyclization of α-carbonyl and α-carbamoyl radicals.[10−13] During our recent investigation[10] on the behaviors of α-carbamoyl radical reactions, we found that, in the presence of $Mg(ClO_4)_2$ and a bis(oxazoline) ligand (**L**), the *N*-ethoxycarbonyl-substituted *N*-allyl-2-iodoalkanamides **5** underwent efficient and stereoselective 5-*exo* iodine-atom-transfer radical cyclization[14,15] to afford exclusively the 3,4-*trans*-configued γ-lactams **6**. Furthermore, the analogous 8-*endo* cyclization reactions (**7** to **8**) also proceeded in high stereoselectivities (Scheme 1).[10] It is certainly interesting to see if this remarkable Lewis acid effect could be extended to control the stereoselectivity of 6-*exo* cyclization. Herein we report that efficient and highly stereoselective 6-*exo* cyclization reactions can be successfully implemented for α-carbamoyl radicals. The control of stereoselectivity is further analyzed by our theoretical calculations.

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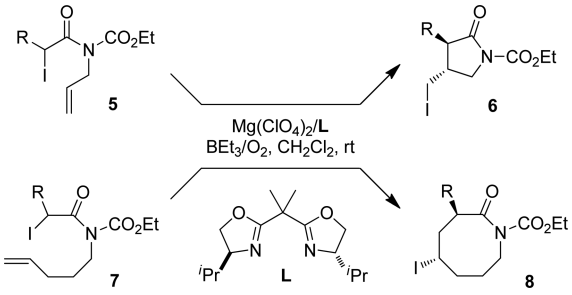
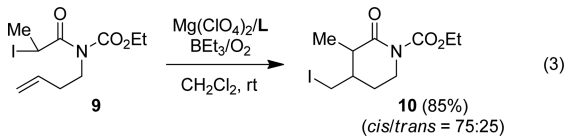
Scheme 1. Lewis Acid Promoted Stereoselective 5-*Exo* and 8-*Endo* Cyclization



RESULTS AND DISCUSSION

The *N*-ethoxycarbonyl-substituted iodoamide **9** was chosen as the model substrate to examine the effect of a Lewis acid on the control of stereoselectivity. With the presence of $Mg(ClO_4)_2$/**L**, the BEt_3/O_2-initiated reaction of **9** proceeded smoothly in dichloromethane at room temperature to give the expected 6-*exo* cyclization product **10** in 85% yield (eq 3). However, the stereoselectivity was only 3:1 in favor of the *cis* isomer.

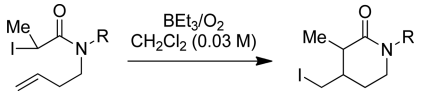


(3)

The above-mentioned results prompted us to examine the *N*-substituent effect. Several substituents were thus screened without the presence of a Lewis acid (Table 1). The cyclization of substrate **9** at room temperature gave the product **10** in 79% yield as a 1:1 mixture of stereoisomers. The reaction did not proceed at −78 °C (entries 1−2, Table 1). With an *N*-*para*-methoxyphenyl (PMP) group, amide **11** failed to give any cyclized product at room temperature. When its reaction was carried out in refluxing benzene, the corresponding cyclization product **12** was obtained as a 2:1 mixture of two stereoisomers in favor of the 3,4-*cis* isomer (entries 3−4, Table 1). Apparently the PMP group is not bulky enough to direct the substrate to the Z-conformation required for cyclization. Raising the reaction temperature helps the interconversion.[16] We then prepared *N*-tosyl iodoamide **13**. Surprisingly, the reaction of **13** at room temperature yielded no cyclized product while all the starting material was consumed (entry 5, Table 1). When the cyclization was performed at −78 °C, the expected lactam **14** was observed by the crude NMR as the mixture of two isomers in about a 9:1 ratio in favor of the *cis* isomer (entry 6, Table 1). However, the 3,4-*trans* isomer decomposed during the purification step. Thus, the ratio might not reflect the true stereoselectivity of cyclization. Finally, we turned to the *N*-*tert*-butyl group. The reaction of substrate **15a** at room temperature afforded the corresponding *δ*-lactam **16a** in approximately quantitative yield as a 72:28 mixture of two isomers (entry 7, Table 1). Again the 3,4-*cis* isomer predominated. When the temperature was lowered to −78 °C, the cyclization also proceeded smoothly and the stereoselectivity was improved to 82:18 (entry 8, Table 1).

We then screened a number of *N*-*tert*-butyl-substituted substrates on 6-*exo* cyclization (Table 2). Clean reactions were observed in all cases, and the desired cyclization products were secured in moderate to excellent yields. The stereochemistry of *δ*-lactams was unambiguously assigned either by ^{1}H NMR or by 2D NOESY experiments. It is noteworthy that the *α*-carbonyl substituents R in substrates **15** exhibited an impact on the stereoselectivity. The stereochemical control was enhanced as the size of R increased, resulting in the predominance of 3,4-*cis*

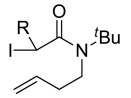
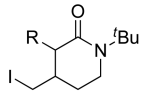
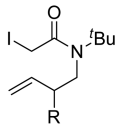
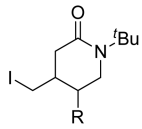
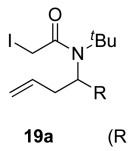
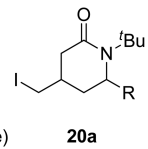
Table 1. Effect of *N*-Substituent on the Stereoselectivity of 6-*Exo* Cyclization



entry[a]	substrate	R	product	temp	yield (%)[b]	*cis*/*trans*[c]
1	**9**	CO_2Et	**10**	rt	79	50:50
2	**9**	CO_2Et	**10**	−78 °C	0	−
3	**11**	PMP	**12**	rt	0	−
4	**11**	PMP	**12**	reflux[d]	54	67:33
5	**13**	Ts	**14**	rt	dec[e]	−
6	**13**	Ts	**14**	−78 °C	61	~90:10
7	**15a**	*t*-Bu	**16a**	rt	97	72:28
8	**15a**	*t*-Bu	**16a**	−78 °C	92	82:18

[a]Reaction conditions: iodoamide (0.3 mmol), BEt_3 (0.09 mmol), air (3 × 10 mL), CH_2Cl_2 (10 mL), 1 h. [b]Isolated yield based on the corresponding iodoamide substrate. [c]Determined by the crude ^{1}H NMR (400 MHz). [d]Benzene was used as the solvent. [e]Decomposed.

Table 2. 6-*Exo* Cyclization of *N*-(*tert*-Butyl)-Substituted Iodoamides

entry[a]	substrate		product	yield (%)[b]	*cis* : *trans*[c]
					
1	**15a**	(R = Me)	**16a**	92	82 : 18
2	**15b**	(R = Et)	**16b**	90	92 : 8
3	**15c**	(R = *n*-Bu)	**16c**	81	> 95 : 5
4	**15d**	(R = *i*-Pr)	**16d**	93	> 95 : 5
5	**15e**	(R = *c*-Hex)	**16e**	87	> 95 : 5
6	**15f**	(R = *t*-Bu)	**16f**	72	> 95 : 5
					
7	**17a**	(R = Me)	**18a**	81	12 : 88
8	**17b**	(R = *n*-Pr)	**18b**	89	< 5 : 95
9	**17c**	(R = Ph)	**18c**	82	< 5 : 95
					
10[d]	**19a**	(R = Me)	**20a**	62	9 : 91
11[d]	**19b**	(R = *n*-Bu)	**20b**	60	< 5 : 95
12[d]	**19c**	(R = Ph)	**20c**	42	< 5 : 95

[a]Reaction conditions: iodoamide (0.3 mmol), BEt_3 (0.09 mmol), air (3 × 10 mL), CH_2Cl_2 (10 mL), −78 °C, 1 h. [b]Isolated yield based on the starting iodoamide. [c]Determined by ^{1}H NMR (400 MHz). [d]The reaction was run at rt.

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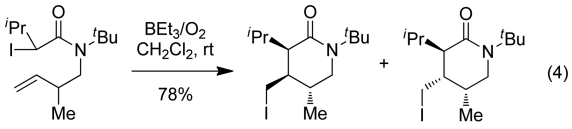
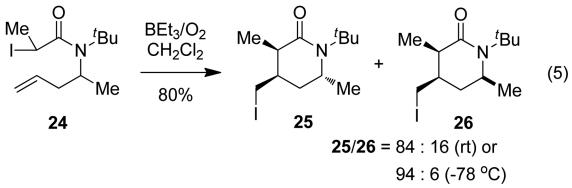
isomers (entries 1−6, Table 2). As a comparison, for substrates **17** with the R group at the allylic position, the stereoselectivity of cyclization was improved and the 4,5-*trans* isomers prevailed (entries 7−9, Table 2). Furthermore, for iodoamides **19** having a substituent at the homoallylic position, the cyclization also exhibited excellent stereoselectivity to give predominantly the 4,6-*trans* isomers **20** (entries 10−12, Table 2). The structure of **20c** was further confirmed by its X-ray diffraction analysis (see the Supporting Information).

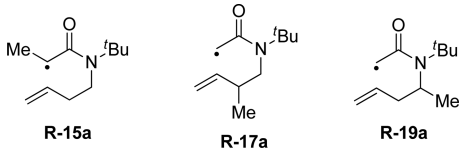
We then went on to examine the stereoselectivity of 6-*exo* cyclization of multisubstituted substrates. As shown in eq 4, the





iodine-atom-transfer cyclization of iodoamide **21** led to the formation of two stereoisomers **22** and **23** in the ratio of 91:9. Both isomers have the 3,5-*trans* configuration. In another experiment, substrate **24** bearing two methyl groups was subjected to the above reaction conditions, from which only two stereoisomers **25** and **26** were isolated. Both isomers have the 3,4-*cis* configuration (eq 5). When the reaction of **24** was carried out at room temperature, the ratio of **25** to **26** was 84:16. When the reaction temperature was lowered to −78 °C, the ratio was raised to 94:6. Again, the stereochemistry of cyclized products was unambiguously determined by their NOESY experiments.

It is thus clear that the 6-*exo* cyclization of α-carbamoyl radicals can be highly stereoselective even without the help of Lewis acids. The excellent stereoselectivity in favor of 3,4-*cis*, 4,5-*trans*, and 4,6-*trans* configurations was clearly observed. To understand this unique stereoselectivity pattern, we carried out density functional calculations on model radicals **R-15a**, **R-17a**, and **R-19a** derived from representative substrates **15a**, **17a**, and **19a**. All the calculations were performed at the UB3LYP/6-31G* level using the Gaussian09 suite of programs,[17] a widely used and fairly accurate method for treating radical reactions.[18] The computed transition state structures and the calculated activation free energies were thus obtained and grouped in Figure 1 and Table 3, respectively.



The calculations indicate that the *Z*-rotamer is at least 1.5 kcal/mol lower in energy than the corresponding *E*-rotamer for all the substrate radicals, which should be attributed to the steric hindrance of the bulky *tert*-butyl group. This allows the α-

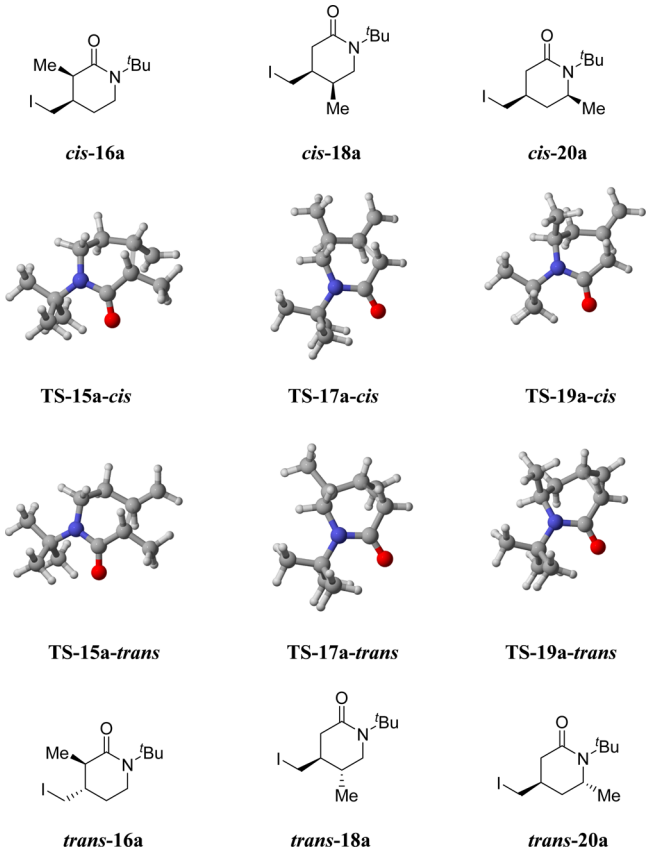


Figure 1. Computed (UB3LYP/6-31G*) transition state structures and corresponding products.

carbamoyl radicals readily undergo cyclization even at low temperature. The calculations also indicate that all the transition states are in boat-like conformations. For the cyclization of radical **R-15a**, two transition states, **TS-15a-*cis*** and **TS-15a-*trans***, were computed. The pseudoequatorial configuration of the C═C bond in **TS-15a-*trans*** results in the steric hindrance between the methylene moiety and the two flagpole hydrogen atoms, their distances being estimated to be 3.021 and 3.720 Å. Such steric interactions are not observed in **TS-15a-*cis*** in which the C═C bond is at the pseudoaxial position. As a result, **TS-15a-*cis*** is slightly lower in energy (0.5 kcal/mol) than **TS-15a-*trans***, in good agreement with the *cis*/*trans* ratio of stereoisomers in the cyclized product **16a**.

For the cyclization of radical **R-17a**, two transition states, **TS-17a-*cis*** and **TS-17a-*trans***, were also computed. The vinylic methylene moiety and the allylic methyl group are much closer in **TS-17a-*cis*** (2.939 Å) than in **TS-17a-*trans*** (3.459 Å). Thus, **TS-17a-*cis*** would face more steric hindrance and its free energy is higher. This is consistent with the predominant 4,5-*trans* stereoselectivity observed in the cyclization of **17a**.

In the cyclization of radical **R-19a**, two transition states, **TS-19a-*cis*** and **TS-19a-*trans***, were also obtained. In both structures the methyl substituent is at the pseudoaxial position in order to ease steric congestion caused by the adjacent *N*-*tert*-butyl group. In **TS-19a-*cis*** the vinylic methylene moiety is at the pseudoequatorial position, suffering steric interactions not only with the flagpole hydrogen atom but also with the flagpole methyl group. Such a steric congestion is not observed in **TS-19a-*trans*** with the vinylic methylene moiety at the pseudoaxial position. Therefore, **TS-19a-*trans*** is of lower energy than **TS-**

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Table 3. Relative Free Energies (kcal/mol) Calculated at the UB3LYP/6-31G* Level

entry	radical	*Z*-rotamer	*E*-rotamer	transition states
1	**R-15a**	0	2.7	11.6 (**TS-15a-*cis***), 12.1 (**TS-15a-*trans***)
2	**R-17a**	0	2.9	8.7 (**TS-17a-*cis***), 7.3 (**TS-17a-*trans***)
3	**R-19a**	0	1.5	8.9 (**TS-19a-*cis***), 7.6 (**TS-19a-*trans***)

19a-*cis*, in excellent agreement with our experimental observations.

The boat-like conformational transition states nicely explain the preference of the 3,4-*cis*, 4,5-*trans*, and 4,6-*trans* configuration in the 6-*exo* cyclization products. It is assumed that as the substituent gets more bulky, the corresponding transition-state conformations become more rigid, leading to the increased steric instability of the disfavored transition states. As a result, the energy difference is enlarged and improved stereoselectivity is anticipated. These analyses are in excellent qualitative agreement with the experimental data.

CONCLUSION

In summary, the experiments detailed above in combination with theoretical calculations have clearly demonstrated that the introduction of the *N*-*tert*-butyl group to the radical precursor not only significantly elevates the efficiency of 6-*exo* radical cyclization but also pushes the α-carbamoyl radicals to cyclize via fixed *Z*-conformational transition states. The boat-like conformational transition states are responsible for the predominant 3,4-*cis*, 4,5-*trans*, or 4,6-*trans* configurations and a high degree of stereochemical control. The calculations furnish a quantitative view of the mechanism of 6-*exo* cyclization of α-carbamoyl radicals. These understanding should be of significance in the further development of an α-carbamoyl radical-based strategy in organic synthesis.

EXPERIMENTAL SECTION

General Information. Melting points were measured with a melting point instrument and were uncorrected. ^{1}H and ^{13}C NMR spectra were recorded using a 400 MHz NMR spectrometer. The chemical shifts are referenced to $CDCl_3$ (signals at 7.26 and 77.0 ppm, respectively) with TMS as the internal standard. IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with a spectrometer. High-resolution mass spectrometry (HRMS) was performed on a TOF MS instrument with an ESI source.

Ethyl But-3-enyl(2-iodopropanoyl)carbamate (9). Typical Procedure: A 50 mL two-necked flask equipped with a condensor was charged with $LiAlH_4$ (456 mg, 12 mmol) and dry ether (20 mL) under nitrogen. Allyl cyanide (0.67 g, 10 mmol) dissolved in ether (10 mL) was added dropwise. After the addition was completed, the mixture was heated to reflux overnight. The reaction mixture was cooled to 0 °C with an ice−water bath and quenched carefully with H_2O (0.5 mL) and a 10% aqueous solution of NaOH (1.0 mL) and H_2O (1.5 mL). The resulting mixture was then filtered, and the filtrate was dried with anhydrous $MgSO_4$ to afford the solution of 3-butenamine in ether. To the solution was added triethylamine (2.10 mL, 15 mmol) and 4-dimethylamino pyridine (DMAP, 122 mg, 1.0 mmol). The resulting solution was cooled to 0 °C with an ice−water bath, and ethyl chloroformate (0.95 mL, 10.0 mol) was added dropwise under nitrogen. After completion of the addition, the resulting mixture was allowed to warm to room termperature and stirred overnight. The reaciton mixture was quenched by addition of water (20 mL). The organic fractions were collected, and the aqueous phase was extracted with ether (3 × 20 mL). The combined organic fractions were washed with 1 M citric acid (10 mL), sat. $NaHCO_3$ (10 mL) and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using petroleum ether/ethyl acetate (5:1) to afford ethyl 3-butenylcarbamate (900 mg, 63% yield over 2 steps) as a colorless oil.

To a solution of ethyl 3-butenylcarbamate (900 mg, 6.3 mmol) in dry THF (5 mL) at 0 °C was added *n*-Butyllithium (3.9 mL, 1.6 M in hexane, 6.24 mmol) under nitrogen. The resulting mixture was stirred for 5 min at 0 °C. Then 2-iodopropanoyl chloride (1.38 g, 6.3 mmol) dissolved in dry THF (5 mL) was added dropwise, and the mixture was stirred for an additional 30 min at 0 °C. The reaction was quenched with saturated aqueous NH_4Cl (10 mL). The organic fractions were collected, and the aqueous phase was extracted with ethyl acetate (3 × 10 mL). The combined organic fractions were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) to give **9** (1.10 g, 54% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2978, 2922, 1736, 1694, 1447, 1372, 1356, 1199, 1152, 1020. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (3H, t, J = 7.2 Hz), 1.99 (3H, d, J = 6.8 Hz), 2.28−2.38 (2H, m), 3.72−3.78 (1H, m), 3.85−3.92 (1H, m), 4.25−4.36 (2H, m), 5.02−5.10 (2H, m), 5.72−5.82 (1H, m), 5.90 (1H, q, J = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 17.6, 23.5, 32.4, 44.2, 63.3, 117.1, 134.6, 153.9, 174.1. EIMS: m/z (rel intensity) 325 (M^+, 1), 198 (77), 183 (38), 155 (34), 116 (48), 102 (100), 84 (27), 56 (41), 55 (32). HRMS calcd for $C_{10}H_{16}INO_3$ (M): 325.0175. Found: 325.0180.

***N*-(But-3-enyl)-2-iodo-*N*-tosylpropanamide (13).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (100:1) gave the product (928 mg, 76% yield) as a colorless oil. IR (neat): ν (cm^{-1}) 2976, 2921, 1693, 1596, 1445, 1355, 1205, 1168, 1086. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90 (3H, d, J = 6.8 Hz), 2.39−2.53 (5H, m), 3.70−3.77 (1H, m), 3.90−3.97 (1H, m), 5.08−5.17 (3H, m), 5.70−5.80 (1H, m), 7.36 (2H, d, J = 8.0 Hz), 7.82 (2H, d, J = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 21.7, 23.3, 33.7, 46.8, 118.2, 127.9, 129.9, 133.7, 135.9, 145.2, 171.4. EIMS: m/z (rel intensity) 407 (M^+, 1), 366 (20), 280 (27), 236 (26), 184 (74), 183 (34), 155 (100), 91 (81), 56 (21). HRMS calcd for $C_{14}H_{18}INO_3S$ (M): 407.0052. Found: 407.0050.

***N*-(But-3-enyl)-*N*-*tert*-butyl-2-iodopropanamide (15a). Typical Procedure**: To a solution of *tert*-butylamine (8.0 mL, 75 mmol) in dimethylformamide (DMF, 40 mL) were added sodium carbonate (5.30 g, 50 mmol) and sodium iodide (0.30 g, 2 mmol), and the mixture was stirred at room temperature for an additional 5 min. 4-Bromo-1-butene (6.75 g, 50 mmol) dissolved in DMF (5 mL) was added dropwise. After completion of the addition, the resulting mixture was allowed to stir at room termperature for 48 h. Water (100 mL) was added to quench the reaction. The aqueous phase was extracted with ether (3 × 100 mL). The combined organic fractions were concentrated and treated with excess 5% hydrochloric acid. The aqueous phase was extracted with ether (3 × 20 mL), and the organic fractions were discarded. The aqueous phase was cooled to 0 °C with an ice−water bath and alkalized with saturated aqueous NaOH. The aqueous phase was extracted with ether (3 × 30 mL). The combined organic fractions were washed with brine and dried with anhydrous $MgSO_4$ and concentrated under reduced pressure to give *N*-(*tert*-butyl)-3-buten-1-amine (2.16 g, 34% yield) as a yellowish liquid.

To a solution of *N*-(*tert*-butyl)-3-buten-1-amine (254 mg, 2 mmol) in dry CH_2Cl_2 (10 mL) were added triethylamine (0.56 mL, 4 mmol) and DMAP (25 mg, 0.2 mmol). The resulting solution was cooled to 0 °C with an ice−water bath, and then 2-iodopropanoyl chloride (460 mg, 2.1 mmol) dissolved in dry CH_2Cl_2 (2 mL) was added dropwise. After completion of the addition, the reaction mixture was allowed to warm to room temperature and stirred overnight. The reaciton mixture was quenched by addition of water (10 mL). the organic

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J. Org. Chem. 2016, 81, 2442−2450

fractions were collected, and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic fractions were washed successively with 1 M citric acid (10 mL), saturated aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) to afford **15a** (501 mg, 81% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2973, 2918, 1649, 1448, 1397, 1362, 1193, 1108, 919. ^1H NMR (400 MHz, $CDCl_3$) δ 1.45 (9H, s), 1.94 (3H, d, J = 6.8 Hz), 2.16−2.25 (1H, m), 2.45−2.54 (1H, m), 3.28−3.43 (2H, m), 4.57 (1H, q, J = 6.8 Hz), 5.10−5.15 (2H, m), 5.69−5.79 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4, 24.2, 28.5, 36.7, 44.9, 57.7, 117.7, 133.8, 171.2. EIMS: m/z (rel intensity) 309 (M^+, 1), 268 (79), 212 (100), 112 (26), 86 (14), 85 (13), 57 (65), 55 (14), 41 (17). HRMS calcd for $C_{11}H_{20}INO$ (M): 309.0590. Found: 309.0594.

***N*-(But-3-enyl)-2-iodo-*N*-(4-methoxyphenyl)propanamide (11).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (481 mg, 67% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2968, 2931, 2835, 1659, 1509, 1444, 1397, 1249, 1036. ^1H NMR (400 MHz, $CDCl_3$) δ 1.86 (3H, d, J = 6.8 Hz), 2.27−2.32 (2H, m), 3.72 (2H, t, J = 3.2 Hz), 3.85 (3H, s), 4.25 (1H, q, J = 6.8 Hz), 5.03−5.10 (2H, m), 5.72−5.82 (1H, m), 6.93−7.22 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 23.9, 31.7, 49.2, 55.5, 115.0, 116.9, 129.1, 134.1, 135.0, 159.4, 171.3. EIMS: m/z (rel intensity) 359 (M^+, 11), 359 (11), 318 (15), 162 (9), 137 (9), 136 (100), 135 (26), 120 (21), 55 (10). HRMS calcd for $C_{14}H_{18}INO_2$ (M): 359.0382. Found: 359.0385.

***N*-(But-3-enyl)-*N*-*tert*-butyl-2-iodobutanamide (15b).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (504 mg, 78% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2970, 2930, 2874, 1651, 1455, 1400, 1362, 1282, 1192, 1109. ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (3H, t, J = 7.2 Hz), 1.45 (9H, s), 2.02−2.16 (2H, m), 2.18−2.27 (1H, m), 2.46−2.55 (1H, m), 3.36−3.44 (2H, m), 4.31 (1H, t, J = 7.2 Hz), 5.10−5.16 (2H, m), 5.70−5.80 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 27.2, 28.5, 30.5, 36.8, 44.8, 57.8, 117.5, 133.9, 170.6. EIMS: m/z (rel intensity) 323 (M^+, 1), 282 (65), 226 (100), 112 (37), 86 (49), 70 (19), 57 (85), 55 (26), 41 (40). HRMS calcd for $C_{12}H_{22}INO$ (M): 323.0746. Found: 323.0745.

***N*-(But-3-enyl)-*N*-*tert*-butyl-2-iodohexanamide (15c).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (527 mg, 75% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2959, 2928, 2872, 1654, 1399, 1362, 1192, 1112, 919. ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (3H, t, J = 7.2 Hz), 1.26−1.40 (4H, m), 1.45 (9H, s), 1.99−2.13 (2H, m), 2.16−2.26 (1H, m), 2.46−2.55 (1H, m), 3.26−3.42 (2H, m), 4.37 (1H, t, J = 7.2 Hz), 5.10−5.15 (2H, m), 5.70−5.80 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.1, 25.6, 28.5, 31.6, 36.8, 44.9, 57.8, 117.5, 133.9, 170.6. EIMS: m/z (rel intensity) 351 (M^+, 1), 310 (53), 254 (95), 112 (41), 86 (93), 69 (33), 57 (100), 55 (58), 41 (47). HRMS calcd for $C_{14}H_{26}INO$ (M): 351.1059. Found: 351.1058.

***N*-(But-3-enyl)-*N*-*tert*-butyl-2-iodo-3-methylbutanamide (15d).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (533 mg, 79% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2962, 2929, 2870, 1654, 1469, 1399, 1363, 1193, 1113. ^1H NMR (400 MHz, $CDCl_3$) δ 0.99 (3H, d, J = 6.8 Hz), 1.18 (3H, d, J = 6.8 Hz), 1.45 (9H, s), 2.20−2.38 (2H, m), 2.47−2.56 (1H, m), 3.23−3.40 (2H, m), 4.11 (1H, d, J = 10.0 Hz), 5.10−5.15 (2H, m), 5.71−5.81 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.4, 24.0, 28.4, 33.2, 36.5, 36.8, 44.9, 57.9, 117.3, 134.0, 170.7. EIMS: m/z (rel intensity) 337 (M^+, 1), 296 (42), 240 (40), 112 (29), 86 (100), 69 (16), 57 (62), 55 (34), 41 (28). HRMS calcd for $C_{13}H_{24}INO$ (M): 337.0903. Found: 337.0899.

***N*-(But-3-enyl)-*N*-*tert*-butyl-2-cyclohexyl-2-iodoacetamide (15e).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (558 mg, 74% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2973, 2926, 2852, 1651, 1447, 1398, 1361, 1188, 917. ^1H NMR (400 MHz, $CDCl_3$) δ 0.76−0.92 (2H, m), 1.05−1.16 (1H, m), 1.23−1.36 (2H, m), 1.45 (9H, s), 1.59−1.65 (2H, m), 1.76−1.80 (1H, m), 1.88−2.04 (2H, m), 2.16−2.29 (2H, m), 2.46−2.56 (1H, m), 3.22−3.39 (2H, m), 4.12 (1H, d, J = 10.0 Hz), 5.10−5.15 (2H, m), 5.70−5.81 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 26.2, 26.4, 28.4, 30.8, 34.3, 36.0, 36.8, 41.7, 44.8, 57.9, 117.3, 134.0, 170.5. EIMS: m/z (rel intensity) 377 (M^+, 1), 336 (16), 280 (12), 112 (17), 95 (25), 86 (100), 57 (30), 55 (18), 41 (16). HRMS calcd for $C_{16}H_{28}INO$ (M): 377.1216. Found: 377.1219.

***N*-(But-3-enyl)-*N*-*tert*-butyl-2-iodo-3,3-dimethylbutanamide (15f).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (534 mg, 76% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2959, 2929, 2867, 1656, 1479, 1389, 1362, 1281, 1196, 1097. ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (9H, s), 1.44 (9H, s), 2.25−2.35 (1H, m), 2.48−2.58 (1H, m), 3.27−3.40 (2H, m), 4.40 (1H, s), 5.10−5.16 (2H, m), 5.72−5.82 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2, 28.5, 35.6, 36.6, 41.3, 45.3, 57.9, 117.3, 134.1, 170.8. EIMS: m/z (rel intensity) 351 (M^+, 1), 310 (38), 254 (19), 198 (11), 197 (10), 112 (19), 86 (100), 57 (32), 55 (10). HRMS calcd for $C_{14}H_{26}INO$ (M): 351.1059. Found: 351.1054.

***N*-*tert*-Butyl-2-iodo-*N*-(2-methylbut-3-enyl)acetamide (17a).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (451 mg, 73% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2964, 2926, 1645, 1456, 1423, 1392, 1362, 1198, 1060, 919. ^1H NMR (400 MHz, $CDCl_3$) δ 1.03 (3H, d, J = 6.4 Hz), 1.44 (9H, s), 2.42−2.53 (1H, m), 3.12−3.32 (2H, m), 3.75 (2H, AB, J = 10.0 Hz), 5.08−5.13 (2H, m), 5.64−5.73 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.3, 17.0, 28.4, 39.7, 52.5, 57.6, 116.2, 139.9, 168.6. EIMS: m/z (rel intensity) 309 (M^+, 1), 254 (75), 198 (100), 126 (8), 70 (10), 57 (96), 55 (11), 42 (9), 41 (29). HRMS calcd for $C_{11}H_{20}INO$ (M): 309.0590. Found: 309.0586.

***N*-*tert*-Butyl-2-iodo-*N*-(2-vinylpentyl)acetamide (17b).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (555 mg, 77% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 3076, 2959, 2928, 2871, 1644, 1456, 1424, 1393, 1362, 1195, 1150, 1073, 917. ^1H NMR (400 MHz, $CDCl_3$) 0.91 (3H, t, J = 6.8 Hz), 1.23−1.44 (13H, m), 2.25−2.34 (1H, m), 3.13 (1H, dd, J = 15.6, 9.6 Hz), 3.28 (1H, dd, J = 16.0, 4.8 Hz), 3.72 (2H, AB, J = 9.6 Hz), 5.06−5.16 (2H, m), 5.45−5.54 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.3, 14.0, 20.3, 28.5, 34.2, 46.2, 51.8, 57.7, 118.1, 139.1, 168.8. ESI-MS m/z 360 $(M + Na)^+$. HRMS calcd for $C_{13}H_{24}INNaO$ (M + Na): 360.0795. Found: 360.0801.

***N*-*tert*-Butyl-2-iodo-*N*-(2-phenylbut-3-enyl)acetamide (17c).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (591 mg, 75% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 3061, 3027, 2975, 2925, 1647, 1492, 1453, 1424, 1392, 1362, 1190, 1150, 1076, 1028, 1002, 921, 759, 702. ^1H NMR (400 MHz, $CDCl_3$) δ 1.47 (9H, s), 3.25−3.68 (5H, m), 5.15−5.24 (2H, m), 5.99−6.07 (1H, m), 7.20−7.37 (5H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.0, 28.6, 51.6, 52.5, 58.0, 117.5, 127.4, 127.8, 129.1, 137.8, 141.0, 168.8. ESI-MS m/z 372 $(M + H)^+$. HRMS calcd for $C_{16}H_{22}INNaO$ (M + Na): 394.0638. Found: 394.0640.

***N*-*tert*-Butyl-2-iodo-*N*-(pent-4-en-2-yl)acetamide (19a).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (415 mg, 67% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2963, 2925, 2853, 1639, 1431, 1363, 1340, 1314, 1195. ^1H NMR (400 MHz, $CDCl_3$) δ 1.38−1.45 (12H, m), 2.41−2.49 (1H, m), 2.53−2.60 (1H, m), 3.76−3.87 (3H, m), 5.07−5.14 (2H, m), 5.71−5.81 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.6, 20.7, 29.4, 41.2, 51.6, 58.7, 117.4, 135.4, 169.6. EIMS: m/z (rel intensity) 309 (M^+, 1), 268 (37), 212 (100), 84 (8), 58 (7), 57 (33), 44 (24), 42 (6), 41 (16). HRMS calcd for $C_{11}H_{20}INO$ (M): 309.0590. Found: 309.0591.

***N*-*tert*-Butyl-2-iodo-*N*-(oct-1-en-4-yl)acetamide (19b).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (487 mg, 65% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 3076, 2958, 2929, 2871, 1639, 1431, 1361, 1329, 1192, 1157, 1086, 996, 916. ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (3H, t, J = 6.8 Hz), 1.25−1.50 (13H, m), 1.71−1.76 (2H, m), 2.42−2.62 (2H, m), 3.53−3.92 (3H, m), 5.06−5.13 (2H, m), 5.71−5.81 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.5, 14.0, 22.6, 29.6, 30.1, 34.9, 40.1, 56.7, 58.6, 117.4, 135.6, 169.4. ESI-MS m/z 352 $(M + H)^+$. HRMS calcd for $C_{14}H_{26}INNaO$ (M + Na): 374.0951. Found: 374.0948.

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***N-tert*-Butyl-2-iodo-*N*-(1-phenylbut-3-enyl)acetamide (19c).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (497 mg, 63% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 3062, 2965, 2925, 2860, 1647, 1496, 1447, 1424, 1362, 1303, 1192, 1158, 1088, 1032, 997, 918, 744, 699. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.52 (9H, s), 2.75−2.83 (1H, m), 3.13−3.20 (1H, m), 3.41−3.58 (2H, m), 5.03 (1H, t, J = 6.8 Hz), 5.20−5.30 (2H, m), 5.93−6.03 (1H, m), 7.26−7.40 (5H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.7, 29.2, 39.6, 58.1, 59.5, 118.1, 126.1, 127.2, 129.0, 135.4, 141.9, 169.6. ESI-MS m/z 372 $(M + H)^+$. HRMS calcd for $C_{16}H_{22}INNaO$ (M + Na): 394.0638. Found: 394.0633.

***N-tert*-Butyl-2-iodo-3-methyl-*N*-(2-methylbut-3-enyl)-butanamide (21).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (569 mg, 81% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2962, 2927, 2870, 1650, 1470, 1398, 1363, 1197, 1101, 918. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98−1.06 (6H, m), 1.17 (3H, t, J = 6.8 Hz), 1.44 (9H, d, J = 10.0 Hz), 2.14−2.32 (1H, m), 2.38−2.54 (1H, m), 3.08−3.14 (1H, m), 3.22−3.31 (1H, m), 4.21−4.25 (1H, m), 5.05−5.15 (2H, m), 5.68−5.78 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.3/17.4, 20.0/20.1, 24.0/24.1, 28.4/28.5, 33.0/33.1, 38.2/38.7, 39.6/40.4, 51.1/51.7, 58.0/58.1, 115.4/116.3, 140.2/140.9, 170.9. EIMS: m/z (rel intensity) 351 (M^+, 1), 296 (51), 240 (56), 183 (13), 86 (100), 69 (14), 57 (48), 55 (21), 41 (22). HRMS calcd for $C_{14}H_{26}INO$ (M): 351.1059. Found: 351.1054.

***N-tert*-Butyl-2-iodo-*N*-(pent-4-en-2-yl)propanamide (24).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (50:1) gave the product (451 mg, 65% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 3076, 2972, 2925, 1737, 1651, 1447, 1422, 1364, 1339, 1196, 1152, 1119, 918. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26−1.44 (12H, m), 1.93−1.96 (3H, m), 2.31−2.65 (2H, m), 3.72−3.74 (1H, m), 4.78 (1H, q, J = 6.8 Hz), 5.06−5.17 (2H, m), 5.68−5.82 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 22.1, 23.8/24.0, 29.0, 41.4/41.6, 51.2, 58.4, 117.4/117.6, 135.4, 174.2. ESI-MS m/z 346 (M + Na)$^+$. HRMS calcd for $C_{12}H_{22}INNaO$ (M + Na): 346.0638. Found: 346.0635.

Typical Procedure for the 6-*Exo* Cyclization of α-Carbamoyl Radicals. A dry Schlenk tube with a nitrogen atmosphere was charged with iodoamide **15a** (93 mg, 0.30 mmol) and dry CH_2Cl_2 (10 mL). The solution was cooled to −78 °C, and Et_3B (0.09 mL, 1 M in hexane, 0.09 mmol) was added. Dry air (3 × 10 mL) was injected in 10 min. The mixture was then warmed up to room temperature and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using petroleum ether/ethyl acetate (20/1) to give separately pure *cis*-**16a** (70 mg, 75% yield) and *trans*-**16a** (16 mg, 17% yield). **(3*R**,4*R**)-1-*tert*-Butyl-3-methyl-4-(iodomethyl)piperidin-2-one (*cis*-16a)**: yellowish oil. IR (neat): ν (cm^{-1}) 2972, 1639, 1456, 1425, 1362, 1318, 1203, 1050, 1018. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (3H, d, J = 7.2 Hz), 1.42 (9H, s), 1.69−1.79 (1H, m), 1.92−1.99 (1H, m), 2.17−2.26 (1H, m), 2.60−2.67 (1H, m), 2.99 (1H, t, J = 9.6 Hz), 3.18−3.26 (2H, m), 3.39−3.45 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.2, 12.4, 26.9, 28.3, 38.7, 42.0, 42.3, 57.2, 173.3. EIMS: m/z (rel intensity) 309 (M^+, 67), 309 (67), 294 (45), 266 (63), 166 (37), 70 (41), 57 (100), 41 (58), 40 (60). HRMS calcd for $C_{11}H_{20}INO$ (M): 309.0590. Found: 309.0594. **(3*R**,4*S**)-1-*tert*-Butyl-3-methyl-4-(iodomethyl)piperidin-2-one (*trans*-16a)**: yellowish oil. IR (neat): ν (cm^{-1}) 2960, 2929, 2970, 1639, 1478, 1426, 1361, 1322, 1203. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (3H, d, J = 6.8 Hz), 1.37−1.48 (10 H, m), 1.52−1.61 (1H, m), 1.95−2.06 (1H, m), 2.10−2.17 (1H, m), 3.13 (1H, dd, J = 10.0, 7.2 Hz), 3.25−3.32 (1H, m), 3.36−3.42 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.3, 16.2, 28.3, 30.0, 40.4, 42.0, 44.0, 57.2, 173.1. EIMS: m/z (rel intensity) 309 (M^+, 48), 309 (48), 294 (38), 266 (49), 166 (34), 70 (37), 57 (100), 55 (35), 41 (53). HRMS calcd for $C_{11}H_{20}INO$ (M): 309.0590. Found: 309.0588.

(3*R,4*R**)-Ethyl 4-(Iodomethyl)-3-methyl-2-oxopiperidine-1-carboxylate (*cis*-10).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (39 mg, 40% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2979, 2934, 1767, 1705, 1531, 1456, 1384, 1257, 1175, 1037. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (3H, d, J = 7.2 Hz), 1.34 (3H, t, J = 6.8 Hz), 1.79−1.90 (1H, m), 2.05−2.13 (1H, m), 2.32−2.40 (1H, m), 2.81−2.88 (1H, m), 2.99 (1H, t, J = 10.0 Hz), 2.24 (1H, dd, J = 10.0, 6.0 Hz), 3.50−3.57 (1H, m), 3.95−4.01 (1H, m), 4.30 (2H, q, J = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.1, 12.1, 14.2, 26.9, 38.8, 42.5, 44.1, 63.3, 154.2, 173.4. EIMS: m/z (rel intensity) 325 (M^+, 10), 198 (100), 102 (29), 83 (27), 81 (25), 69 (32), 56 (32), 55 (67), 41 (36). HRMS calcd for $C_{10}H_{16}INO_3$ (M): 325.0175. Found: 325.0177.

(3*R,4*S**)-Ethyl 4-(Iodomethyl)-3-methyl-2-oxopiperidine-1-carboxylate (*trans*-10).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (38 mg, 39% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2978, 2933, 1771, 1716, 1464, 1368, 1287, 1229, 1181, 1024. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (3H, d, J = 6.8 Hz), 1.35 (3H, t, J = 7.2 Hz), 1.42−1.50 (1H, m), 1.68−1.77 (1H, m), 1.98−2.09 (1H, m), 2.36−2.43 (1H, m), 3.26 (1H, dd, J = 10.0, 5.2 Hz), 3.42 (1H, dd, J = 10.0, 2.8 Hz), 3.72−3.86 (2H, m), 4.31 (2H, q, J = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 14.5, 29.2, 29.7, 39.5, 43.8, 44.3, 63.6, 154.1, 173.2. EIMS: m/z (rel intensity) 325 (M^+, 7), 198 (100), 83 (34), 81 (33), 70 (24), 69 (48), 56 (38), 55 (83), 41 (54). HRMS calcd for $C_{10}H_{16}INO_3$ (M): 325.0175. Found: 325.0179.

(3*R,4*R**)-4-(Iodomethyl)-1-(4-methoxyphenyl)-3-methylpiperidin-2-one (*cis*-12).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (39 mg, 36% yield) as a colorless oil. IR (neat): ν (cm^{-1}) 2936, 2835, 1651, 1607, 1510, 1430, 1296, 1246, 1184, 1035, 829. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (3H, d, J = 7.2 Hz), 1.94−2.10 (2H, m), 2.37−2.46 (1H, m), 2.85−2.92 (1H, m), 3.15−3.27 (2H, m), 3.55−3.68 (2H, m), 3.80 (3H, s), 6.90 (2H, d, J = 8.8 Hz), 7.12 (2H, d, J = 8.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.3, 12.3, 25.6, 39.4, 40.6, 50.0, 55.5, 114.5, 127.4, 135.8, 158.2, 172.8. EIMS: m/z (rel intensity) 359 (M^+, 78), 359 (78), 204 (22), 176 (29), 149 (20), 136 (100), 135 (19), 134 (18), 120 (26). HRMS calcd for $C_{14}H_{18}INO_2$ (M): 359.0382. Found: 359.0383.

(3*R,4*S**)-4-(Iodomethyl)-1-(4-methoxyphenyl)-3-methylpiperidin-2-one (*trans*-12).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (20 mg, 18% yield) as a colorless oil. IR (neat): ν (cm^{-1}) 2963, 2931, 2830, 1651, 1510, 1430, 1328, 1296, 1246, 1033, 830. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (3H, d, J = 7.2 Hz), 1.57−1.65 (1H, m), 1.82−1.92 (1H, m), 2.07−2.14 (1H, m), 2.34−2.42 (1H, m), 3.27 (1H, dd, J = 10.0, 7.2 Hz), 3.49 (1H, dd, J = 10.0, 3.2 Hz), 3.58−3.72 (2H, m), 3.80 (3H, s), 6.90 (2H, d, J = 8.8 Hz), 7.13 (2H, d, J = 8.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.1, 15.4, 29.2, 40.9, 42.4, 49.4, 55.5, 114.5, 127.2, 136.2, 158.1, 171.9. EIMS: m/z (rel intensity) 359 (M^+, 100), 360 (17), 359 (100), 176 (15), 149 (18), 136 (66), 135 (18), 134 (16), 120 (23). HRMS calcd for $C_{14}H_{18}INO_2$ (M): 359.0382. Found: 359.0376.

(3*R,4*R**)-4-(Iodomethyl)-3-methyl-1-tosylpiperidin-2-one (*cis*-14).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (75 mg, 61% yield) as a colorless oil. IR (neat): ν (cm^{-1}) 2977, 2923, 1693, 1596, 1477, 1352, 1272, 1167, 1091, 1026. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (3H, d, J = 7.6 Hz), 1.89−1.99 (1H, m), 2.07−2.16 (1H, m), 2.22−2.31 (1H, m), 2.43 (3H, s), 2.68−2.75 (1H, m), 2.88 (1H, t, J = 9.6 Hz), 3.13 (1H, dd, J = 10.4, 6.4 Hz), 3.64−3.71 (1H, m), 4.16−4.22 (1H, m), 7.31 (2H, d, J = 8.0 Hz), 7.90 (2H, d, J = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 6.5, 11.8, 21.7, 26.8, 38.4, 42.1, 44.5, 128.7, 129.4, 135.9, 144.9, 172.7. ESI-MS m/z 430 (M + Na)$^+$. HRMS calcd for $C_{14}H_{19}INO_3S$ (M + H): 408.0125. Found: 408.0125.

(3*R,4*R**)-1-*tert*-Butyl-3-ethyl-4-(iodomethyl)piperidin-2-one (*cis*-16b).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (81 mg, 83% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2959, 2933, 2873, 1646, 1456, 1423, 1360, 1307, 1201. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (3H, t, J = 7.2 Hz), 1.33−1.45 (10H, m), 1.78−1.90 (2H, m), 1.95−2.03 (1H, m), 2.28−2.39 (2H, m), 2.87 (1H, t, J = 10.0 Hz), 3.20−3.32 (2H, m), 3.39−3.45 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.2, 12.5, 20.2, 28.4, 29.0, 36.9, 40.9, 48.9, 57.1, 172.3. EIMS: m/z (rel intensity) 323 (M^+, 26), 308 (31), 280 (35), 180 (33), 168 (31), 70 (43), 57 (100),

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J. Org. Chem. 2016, 81, 2442−2450

55 (43), 41 (58). HRMS calcd for $C_{12}H_{22}INO$ (M): 323.0746. Found: 323.0741.

(3*R,4*S**)-1-*tert*-Butyl-3-ethyl-4-(iodomethyl)piperidin-2-one (*trans*-16b).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (7.0 mg, 7% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2961, 2928, 2875, 1638, 1457, 1423, 1362, 1321, 1198. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 7.2 Hz), 1.42−1.73 (12H, m), 1.89−2.06 (2H, m), 2.10−2.14 (1H, m), 3.07 (1H, dd, J = 10.0, 8.0 Hz), 3.22−3.28 (1H, m), 3.34−3.43 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.2, 12.5, 23.3, 28.2, 29.8, 36.9, 42.1, 50.2, 57.5, 172.2. EIMS: m/z (rel intensity) 323 (M^+, 28), 308 (36), 180 (35), 168 (47), 112 (36), 70 (45), 57 (100), 55 (40), 41 (60). HRMS calcd for $C_{12}H_{22}INO$ (M): 323.0746. Found: 323.0744.

(3*R,4*R**)-1-*tert*-Butyl-3-butyl-4-(iodomethyl)piperidin-2-one (*cis*-16c).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (86 mg, 81% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2955, 2930, 2870, 1646, 1455, 1423, 1360, 1308, 1200. ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (3H, t, J = 6.8 Hz), 1.32−1.37 (5H, m), 1.41 (9H, s), 1.77−1.87 (2H, m), 1.95−2.01 (1H, m), 2.28−2.41 (2H, m), 2.87 (1H, t, J = 10.4 Hz), 3.20−3.26 (1H, m), 3.30 (1H, dd, J = 10.4, 4.8 Hz), 3.39−3.45 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.3, 14.0, 22.9, 26.9, 28.4, 29.0, 30.1, 37.2, 40.8, 47.3, 57.1, 172.5. EIMS: m/z (rel intensity) 351 (M^+, 2), 295 (20), 208 (14), 168 (100), 112 (55), 70 (22), 57 (52), 55 (27), 41 (31). HRMS calcd for $C_{14}H_{26}INO$ (M): 351.1059. Found: 351.1061.

(3*R,4*R**)-1-*tert*-Butyl-4-(iodomethyl)-3-isopropylpiperidin-2-one (*cis*-16d).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (94 mg, 93% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2959, 2870, 1658, 1458, 1408, 1361, 1329, 1308, 1200, 1124. ^1H NMR (400 MHz, $CDCl_3$) δ 0.97 (3H, d, J = 6.0 Hz), 1.03 (3H, d, J = 6.0 Hz), 1.42 (9H, s), 1.56−1.65 (1H, m), 2.01−2.12 (3H, m), 2.49−2.56 (1H, m), 2.74 (1H, dd, J = 11.6, 9.6 Hz), 3.17−3.24 (1H, m), 3.33 (1H, dd, J = 9.6, 3.6 Hz), 3.48−3.54 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.5, 21.0, 22.7, 25.3, 28.8, 30.8, 37.0, 40.7, 53.9, 57.0, 171.8. EIMS: m/z (rel intensity) 337 (M^+, 17), 210 (34), 194 (40), 168 (92), 112 (71), 70 (35), 57 (100), 55 (33), 41 (54). HRMS calcd for $C_{13}H_{24}INO$ (M): 337.0903. Found: 337.0906.

(3*R,4*R**)-1-*tert*-Butyl-3-cyclohexyl-4-(iodomethyl)-piperidin-2-one (*cis*-16e).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (99 mg, 87% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2923, 2850, 1655, 1448, 1407, 1361, 1320, 1200, 1185. ^1H NMR (400 MHz, $CDCl_3$) δ 0.83−0.93 (1H, m), 1.02−1.21 (2H, m), 1.24−1.37 (2H, m), 1.41 (9H, s), 1.54−1.61 (1H, m), 1.63−1.78 (5H, m), 1.99−2.06 (2H, m), 2.09 (1H, dd, J = 8.4, 5.2 Hz), 2.46−2.55 (1H, m), 2.74 (1H, dd, J = 11.2, 10.0 Hz), 3.16−3.23 (1H, m), 3.29 (1H, dd, J = 9.6, 3.6 Hz), 3.47−3.53 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.7, 26.3, 26.5, 26.7, 28.8, 30.5, 31.2, 33.2, 34.8, 36.4, 40.8, 52.8, 57.0, 171.8. EIMS: m/z (rel intensity) 377 (M^+, 2), 295 (23), 169 (13), 168 (100), 112 (98), 98 (15), 57 (35), 55 (21), 41 (25). HRMS calcd for $C_{16}H_{28}INO$ (M): 377.1216. Found: 377.1214.

(3*S,4*R**)-1,3-Di-*tert*-Butyl-4-(iodomethyl)piperidin-2-one (*cis*-16f).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (76 mg, 72% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2956, 2869, 1654, 1481, 1420, 1392, 1364, 1300, 1204, 1182, 1156. ^1H NMR (400 MHz, $CDCl_3$) δ 1.15 (9H, s), 1.41 (9H, s), 1.87−2.04 (2H, m), 2.20 (1H, d, J = 4.4 Hz), 2.51−2.68 (1H, m), 2.96 (1H, dd, J = 12.4, 9.6 Hz), 3.17−3.24 (1H, m), 3.36−3.43 (1H, m), 3.68 (1H, dd, J = 9.6, 2.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.8, 28.5, 30.1, 31.2, 33.6, 36.7, 39.8, 56.5, 57.0, 171.5. EIMS: m/z (rel intensity) 351 (M^+, 11), 336 (22), 295 (27), 208 (38), 168 (100), 112 (82), 70 (16), 57 (69), 41 (26). HRMS calcd for $C_{14}H_{26}INO$ (M): 351.1059. Found: 351.1061.

(4*S,5*S**)-1-*tert*-Butyl-4-(iodomethyl)-5-methylpiperidin-2-one (*cis*-18a).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (9.5 mg, 10% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2959, 2922, 1643, 1479, 1428, 1360, 1325, 1281, 1204, 1186. ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (3H, d, J = 7.2 Hz), 1.42 (9H, s), 2.12−2.28 (3H, m), 2.51−2.61 (1H, m), 3.05 (2H, d, J = 7.2 Hz), 3.23 (1H, dd, J = 12.0, 4.0 Hz), 3.32 (1H, dd, J = 12.0, 4.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.7, 11.1, 28.2, 31.3, 37.5, 39.0, 50.2, 57.4, 169.0. EIMS: m/z (rel intensity) 309 (M^+, 63), 309 (63), 266 (62), 166 (72), 126 (53), 71 (42), 57 (83), 55 (47), 41 (100). HRMS calcd for $C_{11}H_{20}INO$ (M): 309.0590. Found: 309.0591.

(4*S,5*R**)-1-*tert*-Butyl-4-(iodomethyl)-5-methylpiperidin-2-one (*trans*-18a).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (66 mg, 71% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2959, 2923, 1644, 1479, 1434, 1363, 1328, 1292, 1246, 1205. ^1H NMR (400 MHz, $CDCl_3$) δ 1.00 (3H, d, J = 6.8 Hz), 1.24−1.32 (1H, m), 1.43 (9H, s), 1.62−1.73 (1H, m), 2.24 (1H, dd, J = 16.8, 10.4 Hz), 2.45 (1H, dd, J = 16.8, 5.2 Hz), 2.92 (1H, dd, J = 12.0, 10.0 Hz), 3.19−3.29 (2H, m), 3.38 (1H, dd, J = 12.0, 4.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.9, 16.5, 28.3, 34.6, 38.8, 40.8, 49.9, 57.1, 170.2. EIMS: m/z (rel intensity) 309 (M^+, 18), 86 (50), 84 (100), 70 (20), 57 (30), 51 (22), 49 (71), 43 (58), 41 (31). HRMS calcd for $C_{11}H_{20}INO$ (M): 309.0590. Found: 309.0586. The structure was further confirmed by its 2D NOESY experiments.

(4*S,5*R**)-1-*tert*-Butyl-4-(iodomethyl)-5-propylpiperidin-2-one (*trans*-18b).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (90 mg, 89% yield) as a colorless oil. IR (neat): ν (cm^{-1}) 2958, 2927, 2872, 1650, 1480, 1457, 1433, 1360, 1331, 1297, 1249, 1205, 1157. ^1H NMR (400 MHz, $CDCl_3$) 0.96 (3H, t, J = 7.2 Hz), 1.20−1.52 (14H, m), 1.56−1.64 (1H, m), 2.27 (1H, dd, J = 16.4, 9.2 Hz), 2.45 (1H, dd, J = 16.4, 5.6 Hz), 3.01 (1H, dd, J = 12.8, 7.6 Hz), 3.20−3.27 (2H, m), 3.40 (1H, dd, J = 12.8, 4.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.3, 14.2, 19.9, 28.4, 34.1, 37.9, 39.2, 40.6, 46.6, 57.0, 170.6. EIMS: m/z (rel intensity) 337 (M^+, 35), 322 (50), 294 (77), 210 (39), 154 (100), 112 (48), 57 (62), 55 (44), 41 (77). HRMS calcd for $C_{13}H_{24}INO$ (M): 337.0903. Found: 337.0902.

(4*S,5*S**)-1-*tert*-Butyl-4-(iodomethyl)-5-phenylpiperidin-2-one (*trans*-18c).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (91 mg, 82% yield) as a colorless oil. IR (neat): ν (cm^{-1}) 3028, 2958, 2923, 2853, 1647, 1496, 1475, 1454, 1431, 1362, 1318, 1294, 1199, 1153, 765, 723, 701. ^1H NMR (400 MHz, $CDCl_3$) 1.42 (9H, s), 1.89−1.98 (1H, m), 2.40 (1H, dd, J = 17.2, 11.2 Hz), 2.65 (1H, dd, J = 17.2, 5.6 Hz), 2.76 (1H, td, J = 10.8, 5.2 Hz), 2.84 (1H, dd, J = 10.0, 6.0 Hz), 3.09 (1H, dd, J = 10.0, 3.2 Hz), 3.28 (1H, dd, J = 12.4, 10.8 Hz), 3.53 (1H, dd, J = 12.0, 5.2 Hz), 7.25−7.38 (5H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.0, 28.3, 37.7, 41.2, 47.0, 50.4, 57.5, 127.7, 128.1, 129.1, 139.6, 169.9. EIMS: m/z (rel intensity) 371 (M^+, 37), 371 (37), 188 (33), 117 (100), 115 (34), 91 (37), 84 (40), 57 (37), 41 (36). HRMS calcd for $C_{16}H_{22}INO$ (M): 371.0746. Found: 371.0747.

(4*R,6*R**)-1-*tert*-Butyl-4-(iodomethyl)-6-methylpiperidin-2-one (*trans*-20a).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (58 mg, 62% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2973, 2926, 1635, 1427, 1409, 1378, 1364, 1318, 1193. ^1H NMR (400 MHz, $CDCl_3$) δ 1.24 (3H, d, J = 6.8 Hz), 1.46−1.55 (10H, m), 1.86−1.91 (1H, m), 2.06 (1H, dd, J = 17.2, 10.4 Hz), 2.14−2.24 (1H, m), 2.61 (1H, ddd, J = 17.2, 6.8, 1.6 Hz), 3.05−3.17 (2H, m), 3.93−4.00 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.1, 22.8, 28.9, 30.7, 38.0, 40.4, 48.6, 57.4, 169.0. EIMS: m/z (rel intensity) 309 (M^+, 78), 309 (78), 294 (66), 266 (86), 238 (64), 84 (49), 70 (51), 57 (100), 41 (94). HRMS calcd for $C_{11}H_{20}INO$ (M): 309.0590. Found: 309.0593. The structure was further confirmed by its 2D NOESY experiments.

(4*R,6*R**)-1-*tert*-Butyl-6-butyl-4-(iodomethyl)piperidin-2-one (*trans*-20b).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (63 mg, 60% yield) as a colorless oil. IR (neat): ν (cm^{-1}) 2957, 2930, 2870, 1635, 1455, 1427, 1409, 1361, 1318, 1198, 1143. ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (3H, t, J = 6.8 Hz), 1.14−1.37 (5H, m), 1.39−1.52 (10H, m), 1.60−1.69 (1H, m), 2.01−2.19 (3H, m), 2.58−2.64 (1H, m), 3.05 (1H, dd, J = 9.6, 6.4 Hz), 3.16 (1H, dd, J = 9.6, 5.6 Hz), 3.67−3.72 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.0, 14.0, 22.6, 28.3, 29.0, 30.5, 33.3, 34.8, 40.3, 53.2, 57.6, 168.9. EIMS: m/z (rel intensity) 351 (M^+, 6), 294 (44), 238 (100), 224 (22), 195 (20), 168 (26), 57 (29), 55 (13),

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J. Org. Chem. 2016, 81, 2442−2450

41 (33). HRMS calcd for $C_{14}H_{26}INO$ (M): 351.1059. Found: 351.1057.

(4*R,6*S**)-1-*tert*-Butyl-4-(iodomethyl)-6-phenylpiperidin-2-one (*trans*-20c).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (47 mg, 42% yield) as a white solid. Mp 128−130 °C. IR (KBr): ν (cm^{-1}) 3026, 2949, 2926, 1616, 1454, 1423, 1408, 1348, 1325, 1302, 1260, 1194, 1183, 1160, 1127, 995, 955, 779, 749, 703. ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (9H, s), 1.70−1.85 (2H, m), 1.96−2.00 (1H, m), 2.18 (1H, dd, J = 17.6, 10.0 Hz), 2.69−2.75 (1H, m), 2.97−3.04 (2H, m), 5.02−5.04 (1H, m), 7.15−7.38 (5H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.1, 28.6, 29.3, 39.7, 40.7, 57.9, 58.8, 126.3, 127.4, 128.6, 143.2, 170.1. EIMS: m/z (rel intensity) 371 (M^+, 81), 371 (81), 314 (72), 146 (65), 132 (96), 130 (64), 104 (98), 91 (68), 58 (100). HRMS calcd for $C_{16}H_{22}INO$ (M): 371.0746. Found: 371.0743. The structure was further confirmed by its X-ray diffractional analysis.

(3*R,4*R**,5*R**)-1-*tert*-Butyl-4-(iodomethyl)-3-isopropyl-5-methylpiperidin-2-one (22).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (75 mg, 71% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2960, 2921, 2868, 1660, 1458, 1407, 1362, 1288, 1204, 1143. ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (3H, d, J = 6.8 Hz), 1.03 (6H, d, J = 6.8 Hz), 1.41 (9H, s), 1.71−1.78 (1H, m), 1.87 (1H, dd, J = 10.0, 4.8 Hz), 2.05−2.13 (2H, m), 2.65 (1H, dd, J = 12.0, 9.6 Hz), 2.80 (1H, dd, J = 13.6, 11.2 Hz), 3.29 (1H, dd, J = 9.6, 2.4 Hz), 3.52 (1H, dd, J = 13.6, 2.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.8, 19.4, 20.1, 23.2, 24.7, 29.0, 37.3, 44.2, 47.6, 52.7, 56.7, 172.0. EIMS: m/z (rel intensity) 351 (M^+, 12), 336 (50), 224 (98), 208 (30), 182 (100), 168 (35), 126 (60), 57 (43), 41 (28). HRMS calcd for $C_{14}H_{26}INO$ (M): 351.1059. Found: 351.1057. The structure was further confirmed by its 2D NOESY experiments.

(3*R,4*S**,5*R**)-1-*tert*-Butyl-4-(iodomethyl)-3-isopropyl-5-methylpiperidin-2-one (23).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (7.5 mg, 7% yield) as a yellowish oil. IR (neat): ν (cm^{-1}) 2958, 2926, 2875, 1640, 1463, 1427, 1362, 1286, 1245, 1206. ^1H NMR (400 MHz, $CDCl_3$) δ 0.91−0.98 (7H, m), 1.11 (3H, d, J = 6.8 Hz), 1.41 (9H, s), 1.57−1.65 (1H, m), 1.91−2.03 (1H, m), 2.13 (1H, dd, J = 7.2, 4.0 Hz), 2.94 (1H, dd, J = 12.0, 10.8 Hz), 3.27−3.36 (3H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.0, 16.8, 19.2, 21.4, 28.3, 31.5, 35.7, 42.6, 49.3, 55.3, 57.2, 172.3. EIMS: m/z (rel intensity) 351 (M^+, 9), 182 (57), 126 (40), 86 (68), 84 (46), 57 (100), 55 (35), 49 (38), 41 (48). HRMS calcd for $C_{14}H_{26}INO$ (M): 351.1059. Found: 351.1056. The structure was further confirmed by its 2D NOESY experiments.

(3*R,4*R**,6*R**)-1-*tert*-Butyl-4-(iodomethyl)-3,6-dimethylpiperidin-2-one (25).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (65 mg, 67% yield) as a colorless oil. IR (neat): ν (cm^{-1}) 2973, 2928, 1637, 1467, 1413, 1377, 1362, 1316, 1200, 1167, 1049. ^1H NMR (400 MHz, $CDCl_3$) δ 1.09 (3H, d, J = 7.2 Hz), 1.24 (3H, d, J = 6.4 Hz), 1.44 (9H, s), 1.67−1.71 (1H, m), 1.82 (1H, td, J = 12.4, 5.2 Hz), 2.41−2.51 (1H, m), 2.61−2.68 (1H, m), 3.03−3.12 (2H, m), 3.89−3.96 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.2, 12.9, 23.4, 28.8, 33.0, 35.0, 41.9, 48.5, 57.0, 173.9. EIMS: m/z (rel intensity) 323 (M^+, 57), 323 (57), 308 (76), 280 (79), 252 (81), 196 (57), 99 (65), 57 (100), 41 (74). HRMS calcd for $C_{12}H_{22}INO$ (M): 323.0746. Found: 323.0744. The structure was further confirmed by its 2D NOESY experiments.

(3*R,4*R**,6*S**)-1-*tert*-Butyl-4-(iodomethyl)-3,6-dimethylpiperidin-2-one (26).** Flash chromatography on silica gel using petroleum ether/ethyl acetate (20:1) gave the product (13 mg, 13% yield) as a colorless oil. IR (neat): ν (cm^{-1}) 2960, 2926, 2868, 1648, 1458, 1416, 1377, 1360, 1280, 1247, 1203. ^1H NMR (400 MHz, $CDCl_3$) δ 1.14 (3H, d, J = 6.8 Hz), 1.31 (3H, d, J = 6.8 Hz), 1.35−1.48 (11H, m), 2.15−2.25 (2H, m), 3.23 (1H, dd, J = 10.0, 6.0 Hz), 3.39 (1H, dd, J = 10.0, 2.4 Hz), 3.95−4.03 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 15.6, 25.3, 29.0, 36.4, 39.1, 42.1, 46.5, 57.2, 173.9. EIMS: m/z (rel intensity) 323 (M^+, 35), 323 (35), 308 (53), 280 (55), 252 (67), 84 (38), 57 (100), 55 (44), 41 (62). HRMS calcd for $C_{12}H_{22}INO$ (M): 323.0746. Found: 323.0749. The structure was further confirmed by its 2D NOESY experiments.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00008.

Crystallographic data for **20c** (CIF)

Copies of ^1H, ^{13}C NMR and 2D NOESY spectra, DFT calculation data, and complete ref 17 (PDF)

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Notes

The authors declare no competing financial interest.

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