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Synthetic Methods

A Formal Intermolecular Iodolactonization Reaction Based on a Radical-Ionic Sequence

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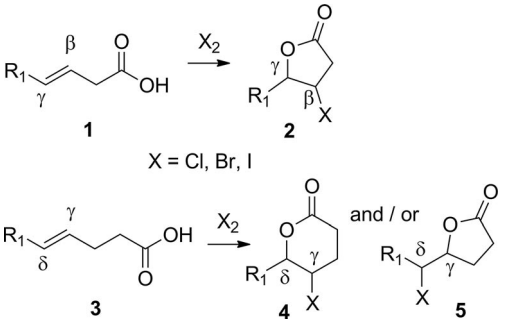
Abstract: We report herein a method based on a radical-ionic sequence between an allylic alcohol and an α-iodo acid in the presence of substoichiometric amounts of lauroyl peroxide (DLP) to produce an atom transfer radical addition (ATRA) adduct, which subseqently underwent an acid-mediated lactonization. This approach can be described as a free radical reaction followed by an intermolecular iodolactonization. Twenty-two experiments were carried out to evaluate the scope of the reaction, which afforded a wide variety of iodo lactones with diverse functionalities. The utility of this approach was demonstrated in the synthesis of the natural product (–)-de-*O*-methylcentrolobine.

Introduction

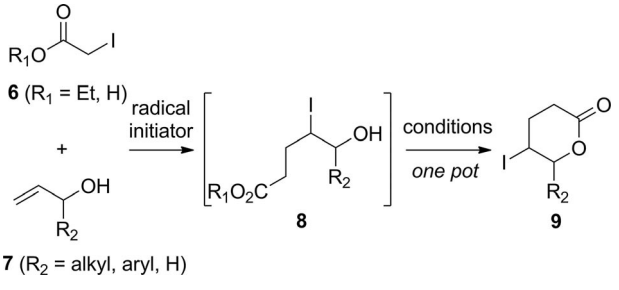
Since Boughoult's[1] discovery in 1904, the halolactonization reaction has received much attention and has become a current strategy for retrosynthetic analysis. The transformation involves the conversion of β,γ- and γ,δ-unsaturated carboxylic acids **1** and **3** into the corresponding five- or six-membered lactones that contain a halogen atom at the β-, γ-, or δ-position (i.e., **2**, **4**, and **5**; Scheme 1).[2] The compounds obtained by this method are valuable synthetic intermediates, as both carbonyl and halogen groups can be further functionalized.[3] The halolactonization of γ,δ-unsaturated carboxylic acid **3** is of special interest, because it allows for the possibility of preparing either γ- or δ-lactones. Both the regio-[3] and stereoselectivity[4] of the process depend on the ionic nature of the reaction, the Baldwin rules, and the reaction conditions. In fact, γ,δ-unsaturated carboxylic acid **3** typically affords the corresponding γ-lactone **5** unless special structural elements are used to control the regioselectivity of the transformation (i.e., R_1 = aryl group). To the best of our knowledge, halo- and selenolactonization reactions are intramolecular processes, which can present a challenge with regard to the preparation of the required unsaturated carboxylic acid.

However, atom transfer radical additions[5] (ATRAs or Kharash reactions) are powerful tools for the simultaneous construction of carbon–carbon and carbon–heteroatom bonds and produce valuable synthetic intermediates that are embedded with various functional groups for further synthetic manipulation. Recently, our group reported some new radical-ionic sequences



Scheme 1. Typical intramolecular halolactonizations.

for the synthesis of epoxides[6] and 1,4-dicarbonyl compounds[7] by employing an initial ATRA reaction, in which the adduct is not isolated but treated under ionic conditions (basic media or silica gel) to afford the desired molecular skeleton. On the basis of the above results, we propose that the application of an ATRA reaction between α-iodo acid or α-iodo ester **6** and allylic alcohol **7** would yield adduct **8**, which could be transformed into lactone **9** under standard conditions. Thus, the overall transformation might be rationalized as a formal intermolecular iodolactonization reaction (Scheme 2). This strategy would exclusively produce γ-iodo-δ-lactones regardless on the



Scheme 2. Proposed radical-ionic sequence based on an ATRA reaction.

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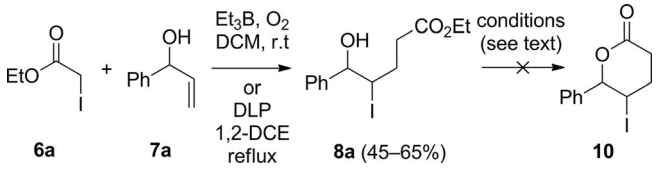
starting material substituents, as both the radical addition and the iodine transfer are highly regioselective.

Results and Discussion

The new protocol started with the reaction between ethyl iodoacetate (**6a**) and known allylic alcohol **7a**[8] (Scheme 3). The radical step could be initiated with either Et_3B/O_2 (0.6 equiv. added portionwise) or with lauroyl peroxide (DLP, 0.3 equiv. added portionwise) in refluxing 1,2-dichloroethane (1,2-DCE) to give hydroxy ester **8a** in 65 and 45 % yield, respectively. However, when **8a** was treated under a variety of acidic conditions [trifluoroacetic acid (TFA), *para*-toluenesulfonic acid (PTSA), HCl, or heating], **10** was not observed, but a complex mixture of degradation products was formed instead. Basic conditions were not evaluated because similar ATRA adducts were previously converted into their corresponding epoxides upon treatment with base.[6]

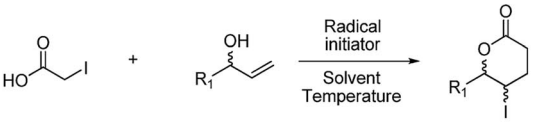


Scheme 3. Initial attempts for iodolactonization by using iodoacetate **6a** as the radical precursor (DCM = dichloromethane).

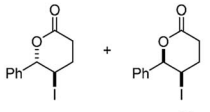
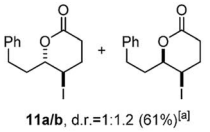
We reasoned that the acid-catalyzed lactonization would be easier by using a carboxylic acid instead of an ester. Therefore, iodoacetic acid was used as the radical precursor. In 2001, Oshima[9] reported the use of this carboxylic acid in radical reactions. We considered that this reagent could serve not only as the radical precursor but also as the acid catalyst for the ionic step. Thus, we proceeded to examine the radical reaction between iodoacetic acid (**6b**) and allylic alcohols **7a** and **7b** under the reaction conditions described in Table 1.

As shown in the Table 1, the reaction between iodoacetic acid (**6b**) and allylic alcohol **7a** with triethylborane/O_2 as the radical initiator afforded a complex mixture of products (Table 1, Entry 1). However, when DLP was used instead, a separable mixture of diastereomeric lactones **10a** and **10b**[10] were isolated in 53 % combined yield without any trace amount of the ATRA adduct (Table 1, Entry 2). When allylic alcohol **7b**[11] was submitted to the same reaction conditions, lactones **11a** and **11b** were obtained in 61 % combined yield (again as a separable mixture of diastereomers). The amount of iodoacetic acid was decreased to 1.2 equiv. (Table 1, Entry 4) and increased to 3 equiv. (Table 1, Entry 5), but in both cases, the yield dropped to 32 and 17 % yield, respectively. In the former case, the reaction did not reach completion, and in the latter one, a series of side products were formed along with the desired lact-

Table 1. Sequential ATRA-lactonization reaction.[a]



6b **7a**, R_1 = Ph; **7b**, R_1 = $PhCH_2CH_2$ **10a/b**, R_1 = Ph; **11a/b**, R_1 = $PhCH_2CH_2$

Entry	Allyl alcohol	**6b** (equiv.)	Radical initiator (equiv.)	Solvent / temperature	Product (yield %)
1	**7a**	2	Et_3B / O_2 (0.6)	DCM / r.t.	Complex mixture
2	**7a**	2	DLP (0.3)	1,2-DCE / reflux	 **10a/b**, d.r.=1:1.1 (53%)[a]
3	**7b**	2	DLP (0.3)	1,2-DCE / reflux	 **11a/b**, d.r.=1:1.2 (61%)[a]
4	**7b**	1.2	DLP (0.3)	1,2-DCE / reflux	**11a/b**, d.r.=1.1 (32%)
5	**7b**	3	DLP (0.3)	1,2-DCE / reflux	**11a/b** , d.r.=1:1 (17%)
6	**7b**	2	DLP (0.3)	AcOEt / reflux	**11a/b** , d.r.=1:1 (35%)
7	**7b**	2	DLP (0.3)	toluene / reflux	**11a/b** , d.r.=1:1 (31%)
8	**7b**	2	DCP (0.1)	chlorobenzene / reflux	Complex mixture
9	**7b**	2	DBP (0.4)	1,2-DCE / reflux	**11a/b** , d.r.=1:1.3 (46%)

[a] The relative stereochemistry was determined by analyzing the vicinal coupling constants. The *trans* diastereomers have $^3J_{H4,H5}$ values of approximately 8 Hz, whereas the *cis* stereoisomers have $^3J_{H4,H5}$ values in the range of 2–3 Hz.

ones. Different solvents and temperatures were employed, but modest yields were observed both at lower (in AcOEt, Table 1, Entry 6) and higher temperatures (in toluene, Table 1, Entry 7). Finally, other radical initiators were examined. Unfortunately, neither dicumyl peroxide (DCP, Table 1, Entry 8) nor benzoyl peroxide (DBP, Table 1, Entry 9) provided better yields. Thus, the best reaction conditions for the iodolactonization involved 1 equiv. of the corresponding allylic alcohol, 2 equiv. of iodoacetic acid, and DLP (substoichiometric amount) in refluxing 1,2-DCE.

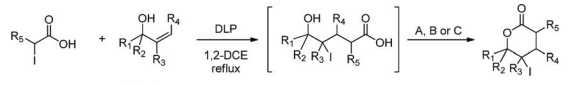
Having determined the optimal reaction conditions, we proceeded to study the scope and limitations of the method. The results are summarized in the Table 2.

Interestingly, secondary allylic alcohols such as **7c**[12] afforded the expected lactones **12a** and **12b** in moderate yield (Table 2, Entry 1). With substrates **7d**[12] and **7e** (Table 2, Entries 2 and 3), rearranged allylic products **13** and **14** were observed. These latter results seem to occur when electron-rich benzylic alcohols are employed as substrates, as the acidic media probably catalyzes the dehydration of the alcohol. Good results were obtained when other secondary alcohols were employed (Table 2, Entry 4). A number of functional groups, such as the acid-sensitive *tert*-butyldimethylsilyl (TBS; i.e., **7g**) and methoxymethyl (MOM; i.e., **7h**) protecting groups, were well tolerated under these reaction conditions. Esters [pivaloyloxy (OPiv); i.e., **7i**] and carbamates (i.e., **7j**) were also suitable protecting groups for the reactions conditions and rendered the corresponding lactones **18a** and **18b** as well as **19a** and **19b** in good yields. A remarkable example involves compound **7f**, which has a free hydroxyl group and formed lactones **15a** and **15b** in 70 % yield. In some experiments (Table 2, Entries 5–10), the reaction afforded a mixture of the expected lactones along with the ATRA adducts, which indicated that the radical step was efficient but the ionic lactonization was not. Thus, in the cases when the lactonization step had not reached completion, 20 mol-% of TFA was added at the end of the radical process (one pot), and the reaction mixture was stirred at room temp. until all of the ATRA adduct was consumed (monitored by TLC analysis). Under these conditions (Method B), other secondary alcohols such as **7k**[13] provided lactones **20a** and **20b** in 54 % yield, and L-proline derivative **7l** allowed for the construction of bicyclic compounds **21a** and **21b** in 71 % yield (Table 2, Entries 5 and 6). The construction of spirocyclic systems is also possible by using this method (Table 2, Entry 7). Alcohols **7m**–**7o**,[14] which are easily prepared by the addition of vinylmagnesium bromide to the corresponding cyclic ketones, provided the [5,6], [6,6], and [6,7] ring systems of spirocyclic lactones **22**, **23**, and **24**, respectively, in good yields. The same substrates **7m**–**7o** were treated with iodopropionic acid[15] (**6c**), a precursor of secondary radicals, to prepare the substituted spirolactones **25a**/**25b**–**27a**/**27b**, respectively, in good yields and variable diastereoselectivities (Table 2, Entry 8). Complex tricyclic structures such as **28a** and **28b** (Table 2, Entry 9) that start from alcohol **7p**[16] as well as lactones **29a** and **29b** that have a sterically congested quaternary center (Table 2, Entry 10) can be easily assembled by using this method. In the latter case, no lactonization occurred after the radical step even with the addition of TFA, but the problem was circumvented by treating the crude reaction mixture with oxalyl chloride (Method C). Disappointingly, substrate **7r**,[17] which also contains a tertiary alcohol, failed to produce the expected products, and **7r** was recovered after several hours of reaction time and the employment of an excess amount of DLP. Next, substituted olefins **7s** and **7t**[18] were studied as the substrates (Table 2, Entries 12 and 13). For these cases, the radical-ionic sequence was successful but afforded moderate yields of product (30 and 47 %, respectively), most likely because of the higher stability of the generated tertiary radical, which causes the iodine transfer to be less efficient.[19] However, the isolation of hydroxylactone **31** suggests that the competitive kinetic lactonization of the respective ATRA adduct is taking place. Interestingly, both lactones **30** and **32** were isolated as single diastereomers, although their relative stereochemistry could not be firmly established. Finally, a control experiment was carried out with iodoacetic acid (**6b**) and allylic alcohol **7b** (Table 2, Entry 14). As expected, no reaction took place in the absence of the radical initiator, and the intact starting materials were recovered after several hours of reaction time, which demonstrates that the process proceeds through a radical pathway.

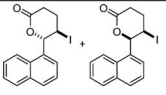
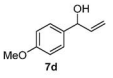
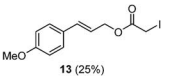
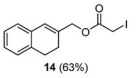
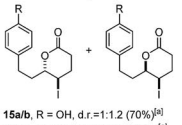
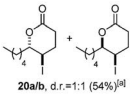
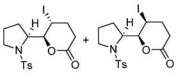
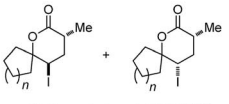
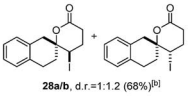
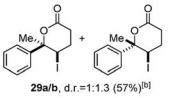
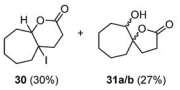
To further demonstrate the synthetic utility of this method, we applied it to the synthesis of (–)-de-*O*-methylcentrolobine (**35**),[20] a tetrahydropirane natural product, which was isolated from some *Centrolobium* species that have significant antileishmanial activity and for which only one racemic[21a] and one asymmetric[21b] synthesis have been reported. Our strategy is based on the use of a lactone such as (*S*)-**33**, which could easily be prepared by applying our method to an enantioenriched allylic alcohol. Thus, the simple addition of **34** to lactone **33** and the subsequent stereoselective reduction of the resulting lactol[22] would provide the total synthesis of **35**, after the removal of the protecting groups (Scheme 4).

Hence, the synthesis of **35** commenced with the preparation of enantiomerically enriched allylic alcohol **38** (Scheme 5). To this end, known epoxide **36**[23] (81 % *ee*) was subjected to mesylation (97 % yield) followed by a substitution reaction with NaI to afford the corresponding iodide, which was treated with Zn dust to provide the desired optically active allylic alcohol **38a** in 62 % yield for the two steps. From this point, the endgame to prepare **35** was straightforward. The treatment of **38** with our developed reaction conditions allowed for the preparation of the expected iodolactones, which were not isolated but directly reduced by switching the solvent to benzene and treating with Bu_3SnH/azobis(isobutyronitrile) (AIBN). Under these conditions, the iodine atom was cleanly removed to render lactone (*S*)-**33a** in 70 % yield (over two steps). When (*S*)-**33a** was added to a preformed solution of the lithium derivative of **34a**,[24] the corresponding lactol was formed and then directly submitted to the reduction with Et_3SiH and $BF_3{\cdot}OEt_2$. To our delight, the addition/reduction sequence worked well, and tetrahydropirane **39** was isolated in 50 % yield (over two steps) as a single *cis* diastereomer. The final double hydrogenolysis of the benzyl groups by using $Pd(OH)_2$ under H_2 in methanol completed the total synthesis of (–)-de-*O*-methylcentrolobine (**35**) in 70 % yield. The spectroscopic and physical data of **35** were in full agreement with those reported in the literature.[21b]

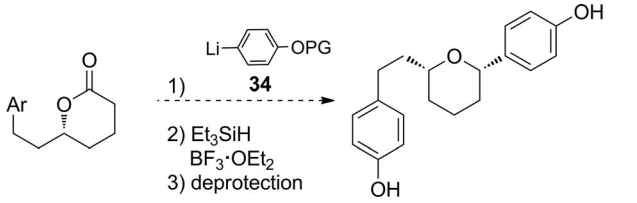
Table 2. Scope and limitations of the intermolecular iodolactonization (Ts = *p*-tolylsulfonyl, n.r.: no reaction). Method A: DLP (0.1 to 0.3 equiv. added portionwise), 1,2-DCE, reflux; Method B: DLP (0.1 to 0.3 equiv. added portionwise), 1,2-DCE, reflux and then TFA (20 mol-%) room temp.; Method C: (i) DLP (0.1 to 0.3 equiv. added portionwise), 1,2-DCE, reflux, (ii) $(COCl)_2$, NEt_3, *N*,*N*-dimethylformamide (DMF, cat.), DCM, 0 °C.



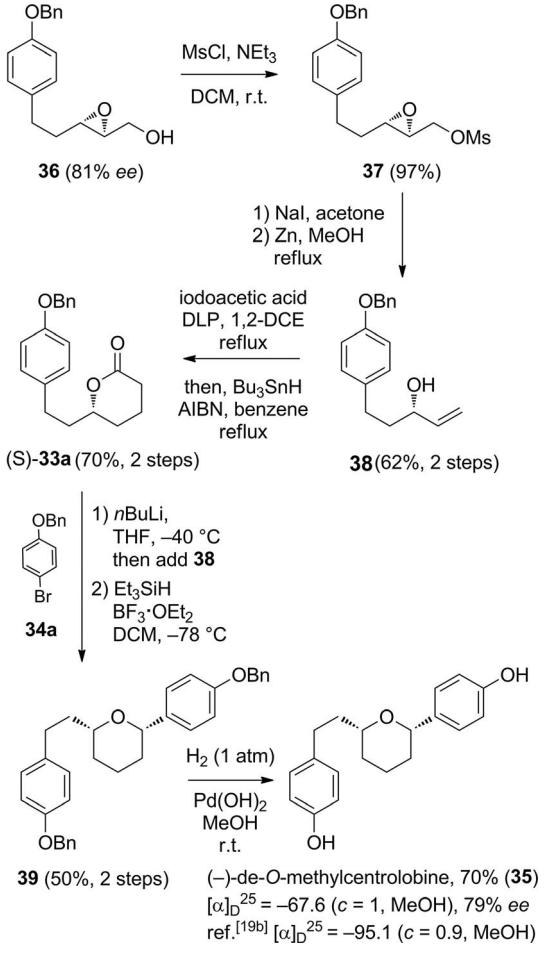
6b–c **7c–t** **12–32**

Entry	Iodoacid	Allylic alcohol	Method	Products (% yield)
1	**6b**	 **7c**	A	 **12a/b** , d.r.=1.5:1 (30%)[a]
2	**6b**	 **7d**	A	 **13** (25%)
3	**6b**	 **7e**	A	 **14** (63%)
4	**6b**	 **7f**, R = OH **7g**, R = OTBS **7h**, R = OMOM **7i**, R = OPiv **7j**, R = N(Cbz)(Me)	A	 **15a/b**, R = OH, d.r.=1:1.2 (70%)[a] **16a/b**, R = OTBS, d.r.=1:1 (66%)[a] **17a/b**, R = OMOM, d.r.=1:1 (64%)[a] **18a/b**, R = OPiv, d.r.=1:1.5 (79%)[a] **19a/b**, R = NMe(Cbz), d.r.=1:1 (64%)[a]
5	**6b**	 **7k**	B	 **20a/b**, d.r.=1:1 (54%)[a]
6	**6b**	 **7l**	B	 **21a/b**, d.r.=1:1.6 (71%)[b]
7	**6b**	 **7m**, *n* = 1 **7n**, *n* = 2 **7o**, *n* = 3	B	 **22**, *n* = 1 (85%) **23**, *n* = 2 (64%) **24**, *n* = 3 (77%)
8	 **6c**	**7m** **7n** **7o**	B	 **25a/b**, *n* = 1, d.r. = 1.2:1 (79%)[b] **26a/b**, *n* = 2, d.r. = 1.3:1 (81%)[b] **27a/b**, *n* = 3, d.r. = 1:1 (80%)[b]
9	**6b**	 **7p**	B	 **28a/b**, d.r.=1:1.2 (68%)[b]
10	**6b**	 **7q**	C	 **29a/b**, d.r.=1:1.3 (57%)[b]
11	**6b**	 **7r**	A	n.r.
12	**6b**	 **7s**	A	 **30** (30%) **31a/b** (27%)
13	**6b**	 **7t**	A	 **32** (47%)
14	**6b**	**7b**	–	n.r.

[a] The stereochemistry was determined by the H4-H5 coupling constant values. [b] The stereochemistry was determined by NOESY experiments (see Supporting Information).



Scheme 4. Strategy for the synthesis of (–)-de-*O*-methylcentrolobine (PG = protecting group).



Scheme 5. Enantioselective total synthesis of (–)-de-*O*-methylcentrolobine (**35**, Ms = methylsulfonyl, THF = tetrahydrofuran).

Conclusions

Herein, we have reported a method based on a radical-ionic sequence between an allylic alcohol and an α-iodo acid in the presence of substoichiometric amounts of lauroyl peroxide to produce the ATRA adduct that subsequently underwent an acid-mediated lactonization reaction. This chemical transformation can be described as the first intermolecular iodolactonization. The scope of the reaction was evaluated by 22 experiments, which afforded a wide variety of iodolactones with diverse functionalities. Carbobenzyloxy (Cbz), TBS, MOM, and Piv protecting groups as well as unprotected hydroxyl groups tolerated the reaction conditions. Mono-, di-, and trisubstituted olefins rendered the expected lactones in variable yields, but the diversely obtained structures, such as fused bicycles or spirocycles of different ring sizes, give this method wide potential for the synthesis of complex molecules. Additionally, the utility of this strategy was demonstrated in the synthesis of (–)-de-*O*-methylcentrolobine (**35**). Efforts to take advantage of the iodine atom in further chemical manipulations and applications to total synthesis are currently under progress and will be reported in due course.

Experimental Section

General Methods: All operations were carried out under argon. Anhydrous solvents were obtained by distillation under an inert atmosphere. Column chromatography was performed with 70e230 mesh silica gel. All reagents and solvents were obtained from commercial suppliers and used without further purification. All compounds were characterized by IR spectra that were recorded on a Bruker Tensor 27 spectrophotometer using film and KBr techniques. All IR data are expressed in wavenumbers [cm^{-1}], and the signals are described by intensity as weak (w), medium (m), or strong (s). Melting points were obtained on a Melt-Temp II apparatus. Specific rotations were measured on a Perkin–Elmer 343 polarimeter by using a sodium lamp (589 nm) and a 1 dM quartz cell. The NMR spectroscopic data were recorded with a JEOL Eclipse þ300 (300 MHz), a Bruker Avance III (400 MHz), or a Varian Unity Inova (500 MHz), and the appropriates deuterated solvents were employed. Chemical shifts are reported parts per million (δ) relative to TMS. COSY, NOESY, and heteronuclear single quantum correlation (HSQC) experiments were carried out to confirm the assignments and relative stereochemistry of the compounds. The MS-FABþ and mass spectrometry-direct analysis in real time (MS-DART) spectra were obtained on a JEOL SX 102A and a JEOL DART AccuTOF JMS-T100CC, respectively. The values of the signals are expressed in mass/charge units (*m*/*z*) followed by the relative intensity relative to a 100 % base peak.

General Procedures for the Radical-Ionic Iodolactonization Reaction

Method A: A solution of the corresponding allylic alcohol (1 mmol) and the iodocarboxylic acid (2 mmol) in 1,2-dichloroethane (5 mL) was heated at reflux under argon for 5 min. Then, lauroyl peroxide (10 mol-%) was added every 1.5 h until the starting material was completely consumed (monitored by TLC analysis). The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel and a short pad of basic alumina on the top).

Method B: A solution of the corresponding allylic alcohol (1 mmol) and the iodocarboxylic acid (2 mmol) in 1,2-dichloroethane (5 mL) was heated at reflux under argon for 5 min. Then, lauroyl peroxide (10 mol-%) was added every 1.5 h until the allylic alcohol was completely consumed (monitored by TLC analysis). Then, the mixture was cooled to room temperature, diluted with 1,2-DCE (5 mL), and covered from light. Trifluoroacetic acid (20 mol-%) was added to the reaction mixture, which was then stirred for an additional 3 h at room temp. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel and a short pad of basic alumina on the top).

Method C: A solution of the corresponding allylic alcohol (1 mmol) and the iodocarboxylic acid (2 mmol) in 1,2-dichloroethane (5 mL) was heated at reflux under argon for 5 min. Then, lauroyl peroxide (10 mol-%) was added every 1.5 h until the allylic alcohol was completely consumed (monitored by TLC analysis). Then, the mixture was cooled to 0 °C, diluted with 1,2-DCE (5 mL), and covered from light. Triethylamine (6 mmol), oxalyl chloride (2.5 mmol), and DMF (1 drop) were successively added to the reaction mixture, which was then stirred at 0 °C for an additional 2 h. Finally, the reaction was quenched with water, and the resulting mixture was extracted with CH_2Cl_2. The organic layer was dried and purified by flash column chromatography (silica gel and a short pad of basic alumina on the top).

5-Iodo-6-phenyltetrahydro-2*H*-pyran-2-one (10a and 10b): Iodoacetic acid (**6b**) and alcohol **7a**[8] were used in the general procedure for Method A to give a separable mixture of diastereomers *trans*-**10a** and *cis*-**10b** (53 % yield).

(5*R,6*S**)-5-Iodo-6-phenyltetrahydro-2*H*-pyran-2-one (10a):** White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.46–7.29 (m, 5 H), 5.55 (d, *J* = 7.9 Hz, 1 H), 4.42 (td, *J* = 7.9, 4.8 Hz, 1 H), 2.85 (dt, *J* = 18.1, 7.0 Hz, 1 H), 2.71 (ddd, *J* = 18.1, 7.3, 6.4 Hz, 1 H), 2.51–2.32 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.3, 137.8, 129.3, 128.9 (2 C), 127.0 (2 C), 87.3, 30.8, 30.7, 24.5 ppm. The analytical data are in full agreement with those reported by Gao.[10]

(5*R,6*R**)-5-Iodo-6-phenyltetrahydro-2*H*-pyran-2-one (10b):** White needles; m.p. 110 °C. IR (KBr): $\tilde{\nu}$ = 3431 (w), 2961 (w), 2930 (w), 1718 (s), 1454 (m), 1310 (m), 1234 (m), 1058 (m), 699 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.31 (m, 5 H), 4.88 (d, *J* = 2.0 Hz, 1 H), 4.66 (dd, *J* = 5.7, 2.7 Hz, 1 H), 3.04 (ddd, *J* = 18.8, 10.6, 8.1 Hz, 1 H), 2.82 (dddd, *J* = 18.7, 6.8, 2.4, 0.7 Hz, 1 H), 2.60–2.43 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7, 138.8, 128.7, 128.5 (2 C), 125.4 (2 C), 82.4, 32.8, 31.0, 28.5 ppm. HRMS (FAB+): calcd. for $C_{11}H_{12}IO_2$ [M + H]$^+$ 302.9882; found 302.9889.

5-Iodo-6-phenethyltetrahydro-2*H*-pyran-2-one (11a and 11b): Iodoacetic acid (**6b**) and allylic alcohol **7b**[11] were used in the general procedure for Method A to give a separable mixture of diastereomers *trans*-**11a** and *cis*-**11b** (61 % yield).

(5*R,6*S**)-5-Iodo-6-phenethyltetrahydro-2*H*-pyran-2-one (11a):** White solid; m.p. 82–83 °C. IR (KCl): $\tilde{\nu}$ = 3025 (w), 2927 (w), 2855 (w), 1769 (s), 1450 (m), 1193 (m), 986 (m), 749 (m), 699 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.16 (m, 5 H), 4.39 (td, *J* = 8.0, 6.3 Hz, 1 H), 4.02 (ddd, *J* = 10.2, 7.9, 3.3 Hz, 1 H), 2.97 (ddd, *J* = 13.7, 8.8, 4.7 Hz, 1 H), 2.72 (ddd, *J* = 13.8, 8.9, 7.5 Hz, 1 H), 2.62–2.43 (m, 3 H), 2.29–2.17 (m, 1 H), 2.16–2.06 (m, 1 H), 2.06–1.94 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.3, 140.1, 128.73 (2 C), 128.69 (2 C), 126.5, 82.3, 38.7, 37.6, 35.1, 29.1, 28.8 ppm. HRMS (DART): calcd. for $C_{13}H_{16}IO_2$ [M + H]$^+$ 331.01950; found 331.02086.

(5*R,6*R**)-5-Iodo-6-phenethyltetrahydro-2*H*-pyran-2-one (11b):** Orange needles; m.p. 104–105 °C. IR (KBr): $\tilde{\nu}$ = 3027 (w), 2942 (m), 2854 (w), 1725 (s), 1497 (m), 1238 (m), 1057 (m), 737 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.18 (m, 5 H), 4.44 (qd, *J* = 3.4, 1.4 Hz, 1 H), 3.42 (ddd, *J* = 8.1, 4.7, 2.0 Hz, 1 H), 2.90 (ddd, *J* = 18.7, 10.7, 8.0 Hz, 1 H), 2.82–2.72 (m, 2 H), 2.66 (dddd, *J* = 18.7, 6.5, 2.7, 0.9 Hz, 1 H), 2.37–2.23 (m, 2 H), 2.17 (dtd, *J* = 14.2, 8.2, 6.1 Hz, 1 H), 1.82 (dddd, *J* = 14.1, 8.7, 7.6, 4.7 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.9, 140.5, 128.8 (2 C), 128.6 (2 C), 126.5, 80.5, 39.6, 31.0, 30.6, 30.3, 28.4 ppm. HRMS (FAB+): calcd. for $C_{13}H_{16}IO_2$ [M + H]$^+$ 331.0195; found 331.0195.

5-Iodo-6-(naphthalen-1-yl)tetrahydro-2*H*-pyran-2-one (12a and 12b): Iodoacetic acid (**6b**) and allylic alcohol **7c**[12] were used in the general procedure for Method A to give a separable mixture of diastereomers *trans*-**12a** and *cis*-**12b** (30 % yield).

(5*R,6*S**)-5-Iodo-6-(naphthalen-1-yl)tetrahydro-2*H*-pyran-2-one (12a):** White solid; m.p. 123–125 °C, decomposes). IR (film): $\tilde{\nu}$ = 2952 (s), 2918 (s), 2850 (s), 1702 (s), 1598 (w), 1513 (w), 1466 (m), 1410 (m), 1350 (w), 1331 (w), 1298 (m), 1244 (m), 1195 (m), 1133 (w), 1065 (w), 1011 (m), 962 (m), 939 (m), 911 (m), 777 (m), 731 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94–7.85 (m, 3 H), 7.61 (ddd, *J* = 8.5, 6.8, 1.5 Hz, 1 H), 7.54 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1 H), 7.49 (dd, *J* = 8.1, 7.2 Hz, 1 H), 7.43 (dt, *J* = 7.2, 1.0 Hz, 1 H), 6.45 (d, *J* = 4.6 Hz, 1 H), 4.79 (q, *J* = 4.9 Hz, 1 H), 3.02 (dt, *J* = 18.5, 8.2 Hz, 1 H), 2.83 (dtd, *J* = 18.4, 5.1, 0.5 Hz, 1 H), 2.19 (ddd, *J* = 8.6, 5.4, 4.5 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.1, 134.0, 133.8, 129.9 (2 C), 129.5, 127.3, 126.3, 125.3, 124.4, 122.5, 85.6, 29.8, 28.3, 24.0 ppm. HRMS (DART) *m/z* calcd. for $C_{15}H_{14}IO_2$ [M + H]$^+$: 353.00385, found 353.00431.

(5*R,6*R**)-5-Iodo-6-(naphthalen-1-yl)tetrahydro-2*H*-pyran-2-one (12b):** Yellow solid; m.p. 109–111 °C (decomposes). IR (film): $\tilde{\nu}$ = 2919 (m), 2850 (m), 1740 (s), 1598 (w), 1511 (w), 1445 (w), 1410 (w), 1334 (m), 1304 (m), 1242 (m), 1228 (m), 1193 (m), 1164 (m), 1133 (w), 1095 (m), 1059 (m), 1015 (w), 953 (w), 915 (m), 901 (w), 798 (m), 786 (m), 774 (m), 732 (w) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 7.4 Hz, 1 H), 7.86 (d, *J* = 8.3 Hz, 1 H), 7.74 (dd, *J* = 7.3, 1.4 Hz, 1 H), 7.67 (d, *J* = 8.6 Hz, 1 H), 7.58–7.47 (m, 3 H), 5.50 (s, 1 H), 4.99 (q, *J* = 2.7 Hz, 1 H), 3.18–3.05 (m, 1 H), 2.91 (ddd, *J* = 18.9, 7.3, 1.9 Hz, 1 H), 2.73 (dddd, *J* = 14.5, 10.9, 7.4, 3.7 Hz, 1 H), 2.52 (dddd, *J* = 14.9, 8.0, 3.7, 1.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.1, 133.6, 133.3, 129.8, 129.3, 128.9, 126.8, 125.7, 125.4, 125.3, 120.9, 79.6, 32.3, 31.1, 28.7 ppm. HRMS (DART): calcd. for $C_{15}H_{14}IO_2$ [M + H]$^+$ 353.00385; found 353.00429.

(*E*)-3-(4-Methoxyphenyl)allyl 2-Iodoacetate (13): Iodoacetic acid (**6b**) and allylic alcohol **7d**[12] were used in the general procedure for Method A to give **13** (25 % yield) as a colorless oil. IR (film): $\tilde{\nu}$ = 3037 (w), 3003 (w), 2955 (m), 2933 (m), 2836 (w), 1730 (s), 1655 (w), 1607 (s), 1576 (w), 1511 (s), 1461 (m), 1442 (m), 1417 (m), 1374 (w), 1302 (m), 1250 (s), 1175 (s), 1118 (m), 1089 (s), 1032 (s), 965 (s), 917 (w), 839 (m), 802 (w), 757 (w), 659 (w) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 8.4 Hz, 2 H), 6.86 (d, *J* = 8.8 Hz, 2 H), 6.65 (d, *J* = 16.4 Hz, 1 H), 6.15 (dt, *J* = 15.8, 6.7 Hz, 1 H), 4.77 (dd, *J* = 6.7, 1.3 Hz, 2 H), 3.81 (s, 3 H), 3.73 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7, 159.9, 135.0, 128.9, 128.1 (2 C), 120.0, 114.2 (2 C), 67.1, 55.5, –5.3 ppm. HRMS (DART): calcd. for $C_{12}H_{13}IO_3$ [M]$^+$ 331.99094; found 331.99157.

(3,4-Dihydronaphthalen-2-yl)methyl 2-Iodoacetate (14): Iodoacetic acid (**6b**) and allylic alcohol **7e** were used in the general procedure for Method A to give **14** (63 % yield). IR (film): $\tilde{\nu}$ = 3058 (m), 3015 (m), 2930 (s), 2885 (m), 2830 (m), 1733 (s), 1485 (w), 1452 (w), 1436 (w), 1415 (w), 1264 (s), 1153 (w), 1087 (m), 966 (m), 885 (w), 856 (w), 757 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15–7.03 (m, 4 H), 6.51 (s, 1 H), 4.74 (s, 2 H), 3.74 (s, 2 H), 2.86 (t, *J* = 8.2 Hz, 2 H), 2.32 (t, *J* = 8.0 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7, 135.0, 134.4, 133.5, 127.55, 127.50, 126.7, 126.5, 126.4, 68.9, 27.8, 24.7, –5.5 ppm. HRMS (DART): calcd. for $C_{13}H_{17}INO_2$ [M + NH$_4$]$^+$ 346.03040; found 346.03052.

6-(4-Hydroxyphenethyl)-5-iodotetrahydro-2*H*-pyran-2-one (15a and 15b): Iodoacetic acid (**6b**) and allylic alcohol **7f** were used in the general procedure for Method A to give a separable mixture of diastereomers *trans*-**15a** and *cis*-**15b** (70 % yield).

(5*R,6*S**)-6-(4-Hydroxyphenethyl)-5-iodotetrahydro-2*H*-pyran-2-one (15a):** White solid; m.p. 143–144 °C. IR (film): $\tilde{\nu}$ = 3368 (br. m), 3018 (w), 2923 (s), 2852 (m), 1716 (s), 1613 (m), 1596 (w), 1514

(s), 1450 (m), 1360 (m), 1228 (s), 1173 (m), 1057 (m), 1025 (m), 986 (w), 923 (w), 883 (w), 829 (m), 759 (w), 716 (w) cm^{-1}. ^1H NMR (400 MHz, [D_6]acetone): δ = 8.13 (s, 1 H), 7.06 (d, J = 8.8 Hz, 2 H), 6.77 (d, J = 8.5 Hz), 4.53 (td, J = 8.5, 2.9 Hz, 1 H), 4.45 (td, J = 8.5, 4.7 Hz, 1 H), 2.77 (ddd, J = 14.5, 10.1, 4.9 Hz, 1 H), 2.70–2.59 (m, 3 H), 2.57–2.49 (m, 1 H), 2.47–2.36 (m, 1 H), 2.28 (dddd, J = 14.2, 9.9, 6.9, 2.9 Hz, 1 H), 2.03–1.94 (m, 1 H) ppm. ^{13}C NMR (100 MHz, [D_6]acetone): δ = 169.5, 156.5, 132.5, 130.2 (2 C), 116.1 (2 C), 84.4, 37.8, 32.5, 31.2, 30.6, 25.3 ppm. HRMS (DART): calcd. for $C_{13}H_{16}IO_3$ $[M + H]^+$ 347.01441; found 347.01476.

(5*R,6*R**)-6-(4-Hydroxyphenethyl)-5-iodotetrahydro-2*H*-pyran-2-one (15b):** Yellow solid; m.p. 139–140 °C. IR (film): $\tilde{\nu}$ = 3349 (br. m), 3018 (m), 2924 (s), 2853 (m), 1712 (s), 1612 (w), 1595 (w), 1514 (s), 1447 (m), 1357 (m), 1243 (s), 1173 (m), 1116 (w), 1090 (w), 1056 (m), 922 (w), 887 (w), 830 (m), 760 (w) cm^{-1}. ^1H NMR (400 MHz, [D_6]acetone): δ = 8.14 (s, 1 H), 7.06 (d, J = 8.4 Hz, 2 H), 6.76 (d, J = 8.5 Hz, 2 H), 4.82 (td, J = 3.4, 2.0 Hz, 1 H), 3.58 (ddd, J = 7.2, 5.2, 1.9 Hz, 1 H), 2.76–2.60 (m, 4 H), 2.57–2.47 (m, 1 H), 2.30 (ddt, J = 14.9, 7.2, 3.1 Hz, 1 H), 1.96 (dddd, J = 13.9, 9.0, 7.8, 6.2 Hz, 1 H), 1.80 (dddd, J = 13.7, 9.2, 7.2, 5.1 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, [D_6]acetone): δ = 168.8, 156.6, 132.5, 130.2 (2 C), 116.1, 116.0, 80.8, 40.9, 34.1, 31.6, 30.3, 28.9 ppm. HRMS (DART): calcd. for $C_{13}H_{16}IO_3$ $[M + H]^+$ 347.01441; found 347.01447.

6-{4-[(*tert*-Butyldimethylsilyl)oxy]phenethyl}-5-iodotetrahydro-2*H*-pyran-2-one (16a and 16b): Iodoacetic acid (**6b**) and allylic alcohol **7g** were used in the general procedure for Method A to give a separable mixture of diastereomers *trans*-**16a** and *cis*-**16b** (66 % yield).

(5*R,6*S**)-6-{4-[(*tert*-Butyldimethylsilyl)oxy]phenethyl}-5-iodotetrahydro-2*H*-pyran-2-one (16a):** Green oil. IR (film): $\tilde{\nu}$ = 2955 (m), 2929 (m), 2895 (m), 2857 (m), 1742 (s), 1609 (m), 1510 (s), 1471 (w), 1462 (w), 1387 (w), 1361 (w), 1334 (w), 1254 (s), 1202 (m), 1170 (m), 1053 (w), 1028 (m), 914 (s), 839 (s), 780 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.06 (d, J = 8.4 Hz, 2 H), 6.77 (d, J = 8.4 Hz, 2 H), 4.45 (td, J = 8.9, 2.7 Hz), 4.09 (td, J = 8.9, 5.1 Hz, 1 H), 2.83 (ddd, J = 14.3, 9.9, 4.9 Hz, 1 H), 2.73–2.62 (m, 2 H), 2.57 (dd, J = 8.2, 6.1 Hz, 1 H), 2.54–2.44 (m, 1 H), 2.42–2.27 (m, 2 H), 2.00 (dddd, J = 14.3, 9.3, 8.6, 4.8 Hz, 1 H), 0.98 (s, 9 H), 0.19 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.0, 154.1, 133.2, 129.5 (2 C), 120.2 (2 C), 84.1, 36.7, 32.1, 30.9, 30.0, 25.8 (3 C), 22.7, 18.3, –4.3 (2 C) ppm. HRMS (DART): calcd. for $C_{19}H_{30}IO_3Si$ $[M + H]^+$ 461.10089; found 461.10163.

(5*R,6*R**)-6-{4-[(*tert*-Butyldimethylsilyl)oxy]phenethyl}-5-iodotetrahydro-2*H*-pyran-2-one (16b):** Green oil. IR (film): $\tilde{\nu}$ = 2954 (m), 2929 (m), 2895 (m), 2857 (m), 1740 (s), 1608 (w), 1510 (s), 1471 (w), 1462 (w), 1448 (w), 1359 (w), 1254 (s), 1207 (w), 1170 (w), 1092 (w), 1055 (m), 1010 (w), 916 (s), 839 (s), 781 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.04 (d, J = 8.4 Hz, 2 H), 6.76 (d, J = 8.5 Hz, 2 H), 4.43 (dddd, J = 4.0, 3.3, 2.1, 0.8 Hz, 1 H), 3.39 (ddd, J = 8.0, 4.8, 2.0 Hz, 1 H), 2.90 (ddd, J = 18.7, 10.8, 7.9 Hz, 1 H), 2.76–2.60 (m, 3 H), 2.38–2.21 (m, 2 H), 2.18–2.06 (m, 1 H), 1.78 (dddd, J = 14.1, 8.5, 7.7, 4.8 Hz, 1 H), 0.98 (s, 9 H), 0.19 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 154.0, 132.9, 129.3 (2 C), 120.1 (2 C), 80.4, 39.6, 30.8, 30.2, 29.6, 28.3, 25.7 (3 C), 18.1, –4.4 (2 C) ppm. HRMS (DART): calcd. for $C_{19}H_{30}IO_3Si$ $[M + H]^+$ 461.10089; found 461.10212.

5-Iodo-6-[4-(methoxymethoxy)phenethyl]tetrahydro-2*H*-pyran-2-one (17a and 17b): Iodoacetic acid (**6b**) and allylic alcohol **7h** were used in the general procedure for Method A to give a separable mixture of diastereomers *trans*-**17a** and *cis*-**17b** (64 % combined yield).

(5*R,6*S**)-5-Iodo-6-[4-(methoxymethoxy)phenethyl]tetrahydro-2*H*-pyran-2-one (17a):** Colorless oil. IR (film): $\tilde{\nu}$ = 3445 (m), 2951 (m), 2925 (m), 2852 (w), 1733 (s), 1611 (w), 1510 (s), 1452 (w), 1232 (s), 1199 (m), 1151 (s), 1077 (m), 1004 (s), 921 (w), 831 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.15–7.05 (m, 2 H), 7.02–6.92 (m, 2 H), 5.15 (s, J = 2.4 Hz, 2 H), 4.47 (td, J = 8.9, 2.7 Hz, 1 H), 4.12–4.06 (m, 1 H), 3.48 (s, J = 1.6 Hz, 3 H), 2.88–2.79 (m, 1 H), 2.73–2.30 (m, 5 H), 2.13–1.84 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.9, 155.7, 133.9, 129.6 (2 C), 116.5 (2 C), 94.6, 83.9, 56.1, 36.8, 32.1, 30.9, 30.0, 22.6 ppm. HRMS (DART): calcd. for $C_{15}H_{20}IO_4$ $[M + H]^+$ 391.04063; found 391.04137.

(5*R,6*R**)-5-Iodo-6-[4-(methoxymethoxy)phenethyl]tetrahydro-2*H*-pyran-2-one (17b):** Colorless oil. IR (film): $\tilde{\nu}$ = 3446 (m), 2951 (s), 2826 (m), 1736 (w), 1510 (s), 1446 (w), 1353 (w), 1234 (s), 1198 (m), 1151 (s), 1078 (m), 1056 (m), 1003 (s), 920 (m), 829 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.11 (d, J = 8.8 Hz, 2 H), 6.96 (d, J = 8.8 Hz, 2 H), 5.15 (s, 2 H), 4.43 (dd, J = 5.4, 2.8 Hz, 1 H), 3.48 (s, 3 H), 3.41 (ddd, J = 8.0, 4.4, 2.0 Hz, 1 H), 2.90 (ddd, J = 18.7, 10.6, 8.1 Hz, 1 H), 2.78–2.60 (m, 3 H), 2.36–2.23 (m, 2 H), 2.17–2.08 (m, 1 H), 1.82–1.73 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.9, 155.8, 133.8, 129.5 (2 C), 116.6 (2 C), 94.6, 80.4, 56.1, 39.8, 30.9, 30.4, 29.7, 28.4 ppm. HRMS (DART): calcd. for $C_{15}H_{20}IO_4$ 391.04063 $[M + H]^+$; found 391.04027.

4-[2-(3-Iodo-6-oxotetrahydro-2*H*-pyran-2-yl)ethyl]phenyl Pivalate (18a and 18b): Iodoacetic acid (**6b**) and allylic alcohol **7i** were used in the general procedure for Method A to give the separable mixture of diastereomers *trans*-**18a** and *cis*-**18b** (79 % yield).

4-{2-[(2*R,3*S**)-3-Iodo-6-oxotetrahydro-2*H*-pyran-2-yl]ethyl}-phenyl Pivalate (18a):** Pale yellow solid; m.p. 73–74 °C. IR (film): $\tilde{\nu}$ = 3034 (w), 2970 (m), 2929 (m), 2872 (w), 1745 (s), 1605 (w), 1507 (m), 1479 (m), 1456 (m), 1417 (w), 1395 (w), 1366 (w), 1335 (w), 1278 (m), 1244 (m), 1199 (s), 1166 (s), 1100 (s), 1054 (m), 1028 (m), 985 (w), 941 (w), 896 (w), 854 (w), 794 (w), 759 (w) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.22 (d, J = 8.4 Hz, 2 H), 6.99 (d, J = 8.4 Hz, 2 H), 4.46 (td, J = 9.0, 2.6 Hz, 1 H), 4.09 (td, J = 9.1, 4.9 Hz, 1 H), 2.89 (ddd, J = 14.3, 10.0, 4.7 Hz, 1 H), 2.79–2.71 (m, 1 H), 2.71–2.63 (m, 1 H), 2.59–2.46 (m, 2 H), 2.43–2.31 (m, 2 H), 2.01 (dtd, J = 14.1, 9.2, 4.7 Hz, 1 H), 1.35 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.3, 169.8, 149.5, 137.8, 129.5 (2 C), 121.6 (2 C), 83.8, 39.1, 36.6, 32.1, 31.0, 30.2, 27.2 (3 C), 22.5 ppm. HRMS (DART): calcd. for $C_{18}H_{24}IO_4$ $[M + H]^+$ 431.07193; found 431.07196.

4-{2-[(2*R,3*R**)-3-Iodo-6-oxotetrahydro-2*H*-pyran-2-yl]ethyl}-phenyl Pivalate (18b):** Green oil. IR (film): $\tilde{\nu}$ = 3033 (w), 2971 (m), 2932 (m), 2871 (w), 1744 (s), 1605 (w), 1507 (m), 1479 (m), 1451 (m), 1415 (w), 1396 (m), 1350 (m), 1278 (m), 1237 (s), 1199 (s), 1166 (s), 1122 (s), 1056 (m), 1029 (m), 1018 (m), 922 (w), 896 (m), 853 (w), 794 (w), 759 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.20 (d, J = 8.4 Hz, 2 H), 6.98 (d, J = 8.5 Hz, 2 H), 4.43 (q, J = 3.0 Hz, 1 H), 3.41 (ddd, J = 8.4, 4.3, 1.9 Hz, 1 H), 2.90 (ddd, J = 18.7, 10.6, 8.1 Hz, 1 H), 2.85–2.73 (m, 2 H), 2.67 (ddd, J = 18.9, 6.6, 3.0 Hz, 1 H), 2.38–2.23 (m, 2 H), 2.16 (dtd, J = 14.1, 8.1, 5.9 Hz, 1 H), 1.79 (dtd, J = 14.2, 8.2, 4.2 Hz, 1 H), 1.35 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.4, 168.9, 149.7, 137.8, 129.5 (2 C), 121.7 (2 C), 80.3, 39.7, 39.2, 30.9, 30.3, 30.0, 28.4, 27.3 (3 C) ppm. HRMS (DART): calcd. for $C_{18}H_{24}IO_4$ $[M + H]^+$ 431.07193; found 431.07199.

Benzyl {4-[2-(3-Iodo-6-oxotetrahydro-2*H*-pyran-2-yl)ethyl]-phenyl}(methyl)carbamate (19a and 19b): Iodoacetic acid (**6b**) and allylic alcohol **7j** were used in the general procedure for Method A to give a separable mixture of diastereomers *trans*-**19a** and *cis*-**19b** (64 % yield).

Benzyl (4-{2-[(2*R,3*S**)-3-Iodo-6-oxotetrahydro-2*H*-pyran-2-yl]ethyl}phenyl)(methyl)carbamate (19a):** Colorless oil. IR (film): $\tilde{\nu}$ = 3458 (br. w), 3032 (m), 2952 (s), 2925 (s), 1734 (s), 1696 (s), 1513

(m), 1451 (m), 1385 (m), 1345 (s), 1246 (m), 1149 (s), 1110 (w), 1025 (m), 841 (w), 732 (s), 696 (s), 598 (m), 573 (m), 528 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.28 (m, 5 H), 7.23–7.16 (m, 4 H), 5.16 (s, 2 H), 4.47 (td, *J* = 9.0, 2.7 Hz, 1 H), 4.09 (td, *J* = 8.8, 5.2 Hz, 1 H), 3.31 (s, 3 H), 2.90 (ddd, *J* = 13.8, 10.1, 4.8 Hz, 1 H), 2.77–2.47 (m, 4 H), 2.43–2.31 (m, 2 H), 2.10–1.95 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.9, 155.5, 141.5, 138.5, 136.7, 129.0 (2 C), 128.5 (2 C), 128.0 (2 C), 127.8, 125.9 (2 C), 83.9, 67.4, 37.9, 36.5, 32.2, 31.0, 30.3, 22.5 ppm. HRMS (DART): calcd. for $C_{22}H_{25}INO_4$ $[M + H]^+$ 494.08283; found 494.08284.

Benzyl (4-{2-[(2*R,3*R**)-3-Iodo-6-oxotetrahydro-2*H*-pyran-2-yl]ethyl}phenyl)(methyl)carbamate (19b):** Colorless oil. IR (film): $\tilde{\nu}$ = 3458 (br. w), 3032 (m), 2949 (s), 2927 (s), 2861 (m), 1735 (s), 1609 (w), 1513 (s), 1445 (m), 1386 (m), 1345 (s), 1237 (m), 1207 (w), 1149 (s), 1111 (w), 1053 (s), 1010 (m), 920 (w), 840 (m), 762 (m), 733 (s), 696 (s), 598 (w), 574 (w), 537 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.27 (m, 5 H), 7.21–7.16 (m, 4 H), 5.16 (s, 2 H), 4.44 (q, *J* = 3.0 Hz, 1 H), 3.42 (ddd, *J* = 8.3, 4.5, 2.0 Hz), 3.30 (s, 3 H), 2.90 (ddd, *J* = 18.8, 10.8, 8.0 Hz, 1 H), 2.83–2.59 (m, 3 H), 2.36–2.10 (m, 3 H), 1.84–1.76 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.9, 155.5, 141.6, 138.4, 136.7, 129.0 (2 C), 128.5 (2 C), 128.0 (2 C), 127.8, 126.0 (2 C), 80.4, 67.4, 39.6, 37.9, 30.9, 30.3, 30.0, 28.4 ppm. HRMS (DART): calcd. for $C_{22}H_{25}INO_4$ $[M + H]^+$ 494.08283; found 494.08289.

5-Iodo-6-pentyltetrahydro-2*H*-pyran-2-one (20a and 20b): Iodoacetic acid (**6b**) and allylic alcohol **7k** were used in the general procedure for Method B to give a separable mixture of iodolactone diastereomers *trans*-**20a** and *cis*-**20b** (54 % yield).

(5*R,6*S**)-5-Iodo-6-pentyltetrahydro-2*H*-pyran-2-one (20a):** Volatile colorless oil. IR (film): $\tilde{\nu}$ = 2954 (s), 2926 (s), 2857 (m), 1738 (s), 1457 (m), 1415 (w), 1381 (m), 1335 (m), 1246 (m), 1198 (m), 1172 (m), 1142 (m), 1114 (m), 1053 (m), 1020 (m), 942 (w), 912 (w), 884 (w), 732 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.51 (td, *J* = 8.4, 3.1 Hz, 1 H), 4.12 (td, *J* = 8.7, 5.1 Hz, 1 H), 2.76–2.64 (m, 1 H), 2.61–2.45 (m, 2 H), 2.43–2.29 (m, 1 H), 2.01 (dddd, *J* = 13.9, 10.6, 5.6, 3.0 Hz, 1 H), 1.75 (dddd, *J* = 14.3, 10.3, 8.1, 4.8 Hz, 1 H), 1.59–1.50 (m, 1 H), 1.48–1.24 (m, 5 H), 0.90 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.0, 85.0, 34.8, 31.9, 31.4, 30.8, 24.2, 22.9, 22.5, 14.0 ppm. HRMS (DART): calcd. for $C_{10}H_{18}IO_2$ $[M + H]^+$ 297.03515; found 297.03546.

(5*R,6*R**)-5-Iodo-6-pentyltetrahydro-2*H*-pyran-2-one (20b):** Volatile yellow oil. IR (film): $\tilde{\nu}$ = 2955 (s), 2926 (s), 2857 (m), 1736 (s), 1447 (m), 1411 (m), 1378 (m), 1352 (m), 1240 (s), 1200 (m), 1113 (m), 1045 (s), 921 (w), 762 (w) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.49 (q, *J* = 2.9 Hz, 1 H), 3.45 (ddd, *J* = 7.5, 5.7, 1.9 Hz, 1 H), 2.90 (ddd, *J* = 18.7, 10.1, 8.6 Hz, 1 H), 2.68 (ddd, *J* = 18.8, 5.7, 3.7 Hz, 1 H), 2.41–2.28 (m, 2 H), 1.86–1.71 (m, 1 H), 1.64–1.48 (m, 1 H), 1.47–1.24 (m, 6 H), 0.90 (t, *J* = 6.5 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.2, 81.9, 37.7, 31.5, 30.9, 30.6, 28.4, 24.2, 22.5, 14.0 ppm. HRMS (DART): calcd. for $C_{10}H_{18}IO_2$ $[M + H]^+$ 297.03515; found 297.03596.

5-Iodo-6-[(*S*)-1-tosylpyrrolidin-2-yl]tetrahydro-2*H*-pyran-2-one (21a and 21b): Iodoacetic acid (**6b**) and allylic alcohol **7l** were used in the general procedure for Method B to give a separable mixture of diastereomers *trans*-**21a** and *cis*-**21b** (71 % yield).

(–)-(5*S*,6*R*)-5-Iodo-6-[(*S*)-1-tosylpyrrolidin-2-yl]tetrahydro-2*H*-pyran-2-one (21a): Yellow solid; m.p. 127–129 °C. $[\alpha]_D^{25}$ = –42.0 (*c* = 0.59, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3421 (w), 2956 (w), 2924 (m), 2885 (w), 1744 (s), 1597 (w), 1451 (w), 1343 (m), 1195 (m), 1159 (s), 1091 (m), 1051 (m), 988 (w), 817 (w), 666 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.4 Hz, 2 H), 7.36 (d, *J* = 7.6 Hz, 2 H), 5.11 (dt, *J* = 3.2, 1.6 Hz, 1 H), 3.77–3.71 (m, 1 H), 3.57 (dd, *J* = 6.5, 1.6 Hz, 1 H), 3.50–3.42 (m, 1 H), 3.27–3.18 (m, 1 H), 2.93 (ddd, *J* = 18.7, 10.0, 8.5 Hz, 1 H), 2.70 (ddd, *J* = 18.4, 7.5, 2.7 Hz, 1 H), 2.45 (s, 3 H), 2.44–2.31 (m, 2 H), 2.29–2.14 (m, 1 H), 1.86–1.69 (m, 1 H), 1.57 (dtt, *J* = 12.8, 7.4, 3.9 Hz, 1 H), 1.48–1.29 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 144.3, 133.8, 130.1 (2 C), 127.9 (2 C), 82.2, 64.4, 50.0, 31.3, 30.0, 28.8, 26.7, 24.4, 21.7 ppm. HRMS (FAB+): calcd. for $C_{16}H_{21}NSO_4I$ 450.02360; found 450.02480.

(–)-(5*R*,6*R*)-5-Iodo-6-[(*S*)-1-tosylpyrrolidin-2-yl]tetrahydro-2*H*-pyran-2-one (21b): White-yellow solid; m.p. 168–169 °C. $[\alpha]_D^{25}$ = –58.4 (*c* = 0.68, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3421 (w), 2956 (m), 2924 (m), 1740 (s), 1455 (w), 1341 (s), 1203 (m), 1158 (s), 1090 (s), 1022 (m), 817 (w), 665 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.3 Hz, 2 H), 7.35 (d, *J* = 7.8 Hz, 2 H), 4.88 (dd, *J* = 8.1, 4.4 Hz, 1 H), 4.34–4.27 (m, 1 H), 4.12–4.05 (m, 1 H), 3.53–3.42 (m, 1 H), 3.27 (dt, *J* = 10.9, 6.8 Hz, 1 H), 2.85–2.74 (m, 1 H), 2.65–2.57 (m, 1 H), 2.57–2.49 (m, 1 H), 2.45 (s, 3 H), 2.44–2.36 (m, 1 H), 1.92–1.81 (m, 2 H), 1.59–1.39 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.3, 144.1, 134.1, 130.0 (2 C), 127.8 (2 C), 85.9, 61.8, 49.7, 30.9, 30.5, 26.2, 24.4, 21.7, 19.1 ppm. HRMS (FAB+): calcd. for $C_{16}H_{21}NSO_4I$ 450.0236; found 450.0237.

10-Iodo-6-oxaspiro[4.5]decan-7-one (22): Highly photosensitive oil. IR (film): $\tilde{\nu}$ = 2955 (m), 2923 (m), 2870 (m), 1730 (s), 1626 (m), 1434 (m), 1344 (m), 1251 (m), 1205 (m), 1163 (s), 1062 (m), 1028 (s), 991 (m), 913 (w), 884 (w), 765 (w) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.49 (t, *J* = 4.4 Hz, 1 H), 2.90 (ddd, *J* = 18.8, 9.3, 8.1 Hz, 1 H), 2.65 (dddd, *J* = 18.8, 7.3, 3.2, 0.7 Hz, 1 H), 2.45–2.35 (m, 1 H), 2.34–2.26 (m, 1 H), 2.13–1.99 (m, 3 H), 1.97–1.77 (m, 4 H), 1.75–1.61 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.2, 94.6, 42.1, 38.4, 32.4, 29.9, 28.4, 25.6, 23.4 ppm. HRMS (DART): calcd. for $C_9H_{14}IO_2$ $[M + H]^+$ 281.00385; found 281.00322.

5-Iodo-1-oxaspiro[5.5]undecan-2-one (23): Highly photosensitive oil. IR (film): $\tilde{\nu}$ = 2927 (s), 2859 (m), 1716 (s), 1447 (m), 1332 (m), 1274 (m), 1209 (s), 1142 (s), 1097 (m), 1039 (m), 1009 (m), 987 (s), 913 (m), 892 (w), 867 (w), 760 (m), 658 (w), 589 (m), 520 (m), 486 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.48 (dd, *J* = 6.0, 3.9 Hz, 1 H), 2.85 (dt, *J* = 18.1, 7.9 Hz, 1 H), 2.69–2.50 (m, 2 H), 2.42–2.30 (m, 1 H), 2.03–1.87 (m, 2 H), 1.83–1.65 (m, 4 H), 1.64–1.45 (m, 3 H), 1.37–1.19 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.3, 83.3, 38.6, 35.5, 34.6, 28.81, 28.76, 25.0, 21.9, 21.5 ppm. HRMS (FAB+): calcd. for $C_{10}H_{16}IO_2$ $[M + H]^+$ 295.0195; found 295.0193.

5-Iodo-1-oxaspiro[5.6]dodecan-2-one (24): Highly photosensitive oil. IR (film): $\tilde{\nu}$ = 2925 (s), 2856 (m), 1732 (s), 1455 (m), 1346 (w), 1331 (w), 1247 (m), 1200 (w), 1165 (m), 1023 (m), 918 (w), 881 (w), 834 (w), 768 (w) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.48 (dd, *J* = 6.5, 4.0 Hz, 1 H), 2.83 (dt, *J* = 18.4, 8.4 Hz, 1 H), 2.66–2.58 (m, 1 H), 2.51 (dtd, *J* = 15.2, 7.6, 4.0 Hz, 1 H), 2.38 (dddd, *J* = 14.9, 8.2, 6.5, 4.5 Hz, 1 H), 2.13–1.94 (m, 4 H), 1.83–1.59 (m, 4 H), 1.60–1.42 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.4, 87.6, 41.7, 38.9, 34.4, 29.3, 29.2, 28.9 (2 C), 22.6, 22.4 ppm. HRMS (DART): calcd. for $C_{11}H_{18}IO_2$ $[M + H]^+$ 309.03515; found 309.03595.

10-Iodo-8-methyl-6-oxaspiro[4.5]decan-7-one (25a and 25b): 2-Iodopropionic acid (**6c**) and allylic alcohol **7m** were used in the general procedure for Method B to give a separable mixture of diastereomers *trans*-**25a** and *cis*-**25b** (79 % combined yield).

(8*R,10*R**)-10-Iodo-8-methyl-6-oxaspiro[4.5]decan-7-one (25a):** White solid; m.p. 47–48 °C. IR (film): $\tilde{\nu}$ = 2958 (m), 2926 (m), 2874 (m), 2853 (m), 1731 (s), 1453 (m), 1378 (m), 1344 (m), 1303 (w), 1237 (m), 1208 (m), 1157 (m), 1053 (m), 1010 (m), 982 (w), 925 (w), 747 (w) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.51 (t, *J* = 4.0 Hz, 1 H), 3.05 (dq, *J* = 10.8, 7.2 Hz, 1 H), 2.42–2.33 (m, 1 H), 2.14–1.99 (m, 4 H), 1.97–1.78 (m, 4 H), 1.72–1.61 (m, 1 H), 1.36 (d, *J* = 7.2 Hz, 3

H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.0, 94.8, 43.7, 39.0, 38.3, 34.0, 33.3, 25.8, 23.4, 17.0 ppm. HRMS (DART): calcd. for $C_{10}H_{16}IO_2$ $[M + H]^+$ 295.01950; found 295.01933.

(8*R,10*S**)-10-Iodo-8-methyl-6-oxaspiro[4.5]decan-7-one (25b):** Yellow solid; m.p. 48–49 °C. IR (film): $\tilde{\nu}$ = 2962 (m), 2934 (m), 2873 (m), 1731 (s), 1452 (m), 1434 (m), 1376 (w), 1340 (m), 1238 (m), 1160 (m), 1088 (w), 1047 (w), 1008 (m), 975 (m), 919 (w), 775 (w), 748 (w) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.54 (dd, *J* = 10.8, 3.9 Hz, 1 H), 2.75–2.59 (m, 2 H), 2.31–2.16 (m, 2 H), 2.15–2.06 (m, 1 H), 2.04–1.88 (m, 4 H), 1.77–1.68 (m, 2 H), 1.33 (d, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.1, 95.0, 40.0, 39.4, 38.2, 37.2, 29.5, 25.0, 24.5, 17.6 ppm. HRMS (DART): calcd. for $C_{10}H_{16}IO_2$ $[M + H]^+$ 295.01950; found 295.01996.

5-Iodo-3-methyl-1-oxaspiro[5.5]undecan-2-one (26a and 26b): 2-Iodopropionic acid (**6c**) and allylic alcohol **7n** were used in the general procedure for Method B to give a separable mixture of diastereomers *trans*-**26a** and *cis*-**26b** (81 % combined yield).

(3*R,5*R**)-5-Iodo-3-methyl-1-oxaspiro[5.5]undecan-2-one (26a):** White solid; m.p. 58–59 °C. IR (film): $\tilde{\nu}$ = 2935 (s), 2862 (m), 1733 (s), 1450 (m), 1376 (w), 1354 (w), 1327 (w), 1277 (w), 1224 (m), 1207 (m), 1144 (m), 1096 (w), 1064 (m), 1022 (w), 1064 (m), 983 (w), 936 (w), 748 (w) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.56 (t, *J* = 4.2 Hz, 1 H), 3.08–2.97 (m, 1 H), 2.41 (ddd, *J* = 15.2, 7.2, 4.4 Hz, 1 H), 2.26 (ddd, *J* = 15.1, 10.2, 3.8 Hz, 1 H), 2.06–1.98 (m, 1 H), 1.95–1.89 (m, 1 H), 1.78–1.68 (m, 3 H), 1.63–1.44 (m, 4 H), 1.36 (d, *J* = 7.2 Hz, 3 H), 1.32–1.25 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.1, 83.4, 40.4, 37.0, 35.9, 35.8, 34.0, 25.0, 22.2, 21.7, 17.1 ppm. HRMS (DART): calcd. for $C_{11}H_{18}IO_2$ $[M + H]^+$ 309.03515; found 309.03621.

(3*R,5*S**)-5-Iodo-3-methyl-1-oxaspiro[5.5]undecan-2-one (26b):** Yellow solid; m.p. 75–76 °C. IR (film): $\tilde{\nu}$ = 2934 (s), 2863 (m), 1732 (s), 1447 (m), 1374 (w), 1333 (w), 1207 (s), 1150 (m), 1118 (s), 1085 (m), 1032 (m), 970 (m), 926 (w), 871 (w), 695 (w) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.32 (dd, *J* = 12.1, 3.8 Hz, 1 H), 2.67–2.54 (m, 2 H), 2.43–2.32 (m, 1 H), 2.05–1.96 (m, 2 H), 1.84–1.67 (m, 5 H), 1.65–1.51 (m, 2 H), 1.30 (d, *J* = 6.8 Hz, 3 H), 1.24–1.16 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.1, 84.4, 38.5, 38.0, 37.0, 33.2, 31.5, 25.2, 21.2 (2 C), 17.2 ppm. HRMS (DART): calcd. for $C_{11}H_{18}IO_2$ $[M + H]^+$ 309.03515; found 309.03647.

5-Iodo-3-methyl-1-oxaspiro[5.6]dodecan-2-one (27a and 27b): 2-Iodopropionic acid (**6c**) and allylic alcohol **7o** were used in the general procedure for Method B to give a separable mixture of diastereomers *trans*-**27a** and *cis*-**27b** (80 % combined yield).

(3*R,5*R**)-5-Iodo-3-methyl-1-oxaspiro[5.6]dodecan-2-one (27a):** White oil. IR (film): $\tilde{\nu}$ = 2925 (s), 2854 (m), 1732 (s), 1458 (m), 1378 (w), 1329 (w), 1232 (m), 1148 (m), 1061 (m), 1012 (m), 930 (w) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.58 (t, *J* = 4.8 Hz, 1 H), 3.06–2.96 (m, 1 H), 2.45 (ddd, *J* = 15.1, 7.5, 5.0 Hz, 1 H), 2.21 (ddd, *J* = 15.1, 9.9, 4.0 Hz, 1 H), 2.08–1.93 (m, 4 H), 1.79–1.40 (m, 8 H), 1.35 (d, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.3, 87.9, 43.3, 39.1, 37.6, 35.3, 34.1, 29.5, 29.1, 22.8, 22.4, 17.1 ppm. HRMS (DART): calcd. for $C_{12}H_{20}IO_2$ $[M + H]^+$ 323.05080; found 323.05152.

(3*R,5*S**)-5-Iodo-3-methyl-1-oxaspiro[5.6]dodecan-2-one (27b):** Yellow oil. IR (film): $\tilde{\nu}$ = 2927 (s), 2857 (m), 1733 (s), 1458 (m), 1377 (w), 1337 (w), 1224 (m), 1160 (m), 1106 (w), 1065 (w), 1020 (m), 1006 (m), 952 (w), 936 (w), 905 (w), 756 (w) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.32 (dd, *J* = 12.3, 3.8 Hz, 1 H), 2.65–2.53 (m, 2 H), 2.39–2.29 (m, 1 H), 2.23 (ddd, *J* = 15.1, 9.9, 1.9 Hz, 1 H), 2.16 (ddd, *J* = 14.7, 10.2, 1.6 Hz, 1 H), 1.94–1.85 (m, 2 H), 1.83–1.70 (m, 2 H), 1.69–1.48 (m, 6 H), 1.29 (d, *J* = 6.7 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.2, 87.9, 41.8, 39.2, 38.0, 37.1, 32.4, 29.0, 29.0, 23.2, 22.8, 17.1 ppm. HRMS (DART): calcd. for $C_{12}H_{20}IO_2$ $[M + H]^+$ 323.05080; found 323.05166.

3′-Iodo-3,4,4′,5′-tetrahydro-1*H*-spiro[naphthalene-2,2′-pyran]-6′(3′*H*)-one (28a and 28b): Iodoacetic acid (**6b**) and allylic alcohol **7p** were used in the general procedure for Method B to give a separable mixture of diastereomers *trans*-**28a** and *cis*-**28b** (68 % combined yield).

(2*R,3′*S**)-3′-Iodo-3,4,4′,5′-tetrahydro-1*H*-spiro[naphthalene-2,2′-pyran]-6′(3′*H*)-one (28a):** Yellow oil. IR (film): $\tilde{\nu}$ = 3060 (w), 3019 (w), 2924 (s), 2852 (m), 1733 (s), 1583 (w), 1496 (m), 1453 (s), 1412 (m), 1371 (m), 1331 (m), 1281 (s), 1258 (s), 1230 (s), 1201 (s), 1180 (s), 1142 (m), 1113 (m), 1098 (m), 1098 (m), 1053 (s), 1020 (m), 975 (m), 956 (w), 927 (w), 882 (w), 838 (w), 811 (w), 751 (m), 678 (w) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18–7.04 (m, 4 H), 4.51 (dd, *J* = 6.0, 4.0 Hz, 1 H), 3.25 (d, *J* = 16.9 Hz, 1 H), 3.16 (d, *J* = 17.4 Hz, 1 H), 3.12–3.05 (m, 1 H), 2.94 (dt, *J* = 18.7, 8.2 Hz, 1 H), 2.80 (dt, *J* = 17.0, 5.8 Hz, 1 H), 2.71 (ddd, *J* = 18.7, 7.5, 3.8 Hz, 1 H), 2.60 (dtd, *J* = 15.8, 8.1, 3.9 Hz, 1 H), 2.43 (dddd, *J* = 15.0, 8.3, 5.8, 3.8 Hz, 1 H), 2.28–2.21 (m, 1 H), 2.17–2.09 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.1, 134.4, 132.5, 129.6, 128.5, 126.6, 126.5, 82.9, 43.3, 32.7, 32.4, 28.85, 28.81, 26.2 ppm. HRMS (DART): calcd. for $C_{14}H_{19}INO_2$ $[M + NH_4]^+$ 360.04605; found 360.04514.

(2*R,3′*R**)-3′-Iodo-3,4,4′,5′-tetrahydro-1*H*-spiro[naphthalene-2,2′-pyran]-6′(3′H)-one (28b):** White solid; m.p. 86–88 °C (decomposes). IR (film): $\tilde{\nu}$ = 3060 (w), 3020 (w), 2923 (m), 2850 (m), 1735 (s), 1538 (w), 1495 (m), 1453 (m), 1372 (w), 1348 (m), 1331 (m), 1279 (m), 1243 (m), 1203 (s), 1136 (m), 1099 (m), 1044 (s), 1017 (m), 974 (m), 942 (w), 919 (w), 900 (w), 881 (w), 750 (s) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19–7.11 (m, 3 H), 7.05–6.99 (m, 1 H), 4.53 (dd, *J* = 5.2, 3.8 Hz, 1 H), 3.25 (d, *J* = 16.8 Hz, 1 H), 3.14 (d, *J* = 16.6 Hz, 1 H), 3.08–2.85 (m, 3 H), 2.72 (dddd, *J* = 18.7, 7.2, 3.5, 0.7 Hz, 1 H), 2.57 (dddd, *J* = 15.2, 9.2, 7.2, 3.8 Hz, 1 H), 2.36 (dddd, *J* = 15.2, 8.0, 5.2, 3.4 Hz, 1 H), 2.31–2.17 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.0, 134.7, 132.1, 129.1, 128.9, 126.9, 126.4, 83.2, 39.0, 36.6, 31.7, 28.8 (2 C), 25.8 ppm. HRMS (DART): calcd. for $C_{14}H_{19}INO_2$ $[M + NH_4]^+$ 360.04605; found 360.04657.

5-Iodo-6-methyl-6-phenyltetrahydro-2*H*-pyran-2-one (29a and 29b): Iodoacetic acid (**6b**) and allylic alcohol **7q**[25] were used in the general procedure for Method C to give a separable mixture of *trans*-**29a** and *cis*-**29b** diastereomers (57 % combined yield).

(5*R,6*S**)-5-Iodo-6-methyl-6-phenyltetrahydro-2*H*-pyran-2-one (29a):** Photosensitive colorless oil. IR (film): $\tilde{\nu}$ = 3446 (br. w), 2983 (m), 2922 (m), 1733 (s), 1612 (m), 1495 (w), 1442 (m), 1377 (w), 1347 (w), 1329 (w), 1237 (s), 1146 (s), 1076 (m), 1043 (s), 930 (w), 905 (w), 884 (w), 762 (s), 699 (s) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.28 (m, 5 H), 4.94 (ddt, *J* = 3.4, 0.6 Hz, 1 H), 2.94 (dddd, *J* = 19.0, 10.4, 8.2, 0.4 Hz, 1 H), 2.53 (dddd, *J* = 19.1, 7.2, 2.1, 0.8 Hz, 1 H), 2.07 (dddd, *J* = 15.0, 8.2, 3.8, 2.0 Hz, 1 H), 1.95 (dddd, *J* = 15.0, 10.4, 7.2, 3.4 Hz, 1 H), 1.82 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.7, 141.3, 129.3 (2 C), 128.2, 124.5 (2 C), 86.7, 35.3, 34.2, 28.5, 27.9 ppm. HRMS (DART): calcd. for $C_{12}H_{14}IO_2$ $[M + H]^+$ 317.00385; found 317.00470.

(5*R,6*R**)-5-Iodo-6-methyl-6-phenyltetrahydro-2*H*-pyran-2-one (29b):** Photosensitive clear oil. IR (film): $\tilde{\nu}$ = 3059 (w), 2989 (m), 2926 (m), 2854 (m), 1741 (s), 1600 (w), 1494 (m), 1445 (s), 1409 (w), 2377 (m), 1345 (m), 1328 (m), 1252 (s), 1202 (s), 1162 (s), 1142 (m), 1097 (m), 1060 (s), 1029 (w), 992 (m), 921 (m), 885 (w), 803 (w), 766 (m), 701 (m), 681 (w) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.28 (m,

5 H), 4.75 (t, *J* = 3.6 Hz, 1 H), 3.02 (dddd, *J* = 18.9, 9.6, 8.3, 0.4 Hz, 1 H), 2.77 (dddd, *J* = 18.9, 7.4, 2.6, 0.7 Hz, 1 H), 2.60 (dddd, *J* = 15.1, 9.6, 7.4, 3.7 Hz, 1 H), 2.38 (dddd, *J* = 15.0, 8.3, 4.6, 2.6 Hz, 1 H), 1.86 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 168.9, 144.9, 128.4 (2 C), 128.0 (2 C), 124.3, 86.1, 34.5, 28.6, 28.5, 27.7 ppm. HRMS (DART): calcd. for $C_{12}H_{14}IO_2$ $[M + H]^+$ 317.00385; found 317.00447.

4a-Iodooctahydrocyclohepta[*b*]pyran-2(3*H*)-one (30): Iodoacetic acid (**6b**) and allylic alcohol **7s** were used in the general procedure for Method A to give compound **30** (30 % yield, single diastereomer) as a yellow solid; m.p. 68 °C. IR (film): $\tilde{\nu}$ = 3439 (w), 3324 (w), 2925 (s), 2859 (m), 1720 (s), 1447 (m), 1352 (m), 1342 (m), 1250 (m), 1204 (s), 1148 (w), 1090 (w), 1044 (s), 1010 (s), 918 (m), 873 (m), 829 (s), 770 (m), 683 (m), 591 (s), 476 (s), 456 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.03–2.93 (m, 2 H), 2.71 (ddd, *J* = 18.9, 7.6, 1.7 Hz, 1 H), 2.41–2.28 (m, 2 H), 2.10–1.43 (m, 10 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.4, 88.1, 60.2, 42.5, 40.9, 35.5, 30.2, 25.8, 25.4, 21.8 ppm. HRMS (DART): calcd. for $C_{10}H_{16}IO_2$ $[M + H]^+$ 295.01950; found 295.01956.

6-Hydroxy-1-oxaspiro[4.6]undecan-2-one (31a and 31b): Yellow solid (27 % yield, mixture of diastereomers); m.p. 65 °C. IR (film): $\tilde{\nu}$ = 3398 (s), 3936 (s), 2856 (m), 1724 (s), 1457 (w), 1407 (w), 1314 (s), 1271 (m), 1251 (m), 1176 (m), 1160 (m), 1035 (m), 1001 (m), 975 (m), 932 (w), 874 (m), 805 (w), 680 (w), 566 (m), 534 (m), 468 (w), 439 (w) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.87 (dd, *J* = 9.9, 2.8 Hz, 1 H, 6-H), 3.55 (dd, *J* = 9.5, 2.4 Hz, 1 H, 6*-H), 2.78–2.32 (m, 6 H, 3ab-H, 3ab*-H, 4a-H, 4a*-H), 2.10 (br. s, 2 H, OH, OH*), 1.99–1.36 (m, 22 H, 4b-H, 4b*-H, 7-H, 7*-H, 8-H, 8*-H, 9-H, 9*-H, 10-H, 10*-H, 11-H, 11*-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.7 (C-2), 177.5 (C-2*), 92.3 (C-5), 90.5 (C-5*), 77.7 (C-6), 77.2 (C-6*), 37.2 (C-11), 36.1 (C-11*), 31.5 (C9), 31.4 (C-8), 31.3 (C-4), 30.0 (C-3), 29.1 (C-3*), 26.9 (C-9*), 26.8 (C-8*), 26.3 (C-4*), 23.3 (C-10), 22.8 (C-7), 20.9 (C-10*), 20.5 (C-7*) ppm. HRMS (DART): calcd. for $C_{10}H_{17}O_3$ $[M + H]^+$ 185.11777; found 185.11770.

8a-Iodooctahydro-3*H*-isochromen-3-one (32): Iodoacetic acid **6b** and allylic alcohol **7t** were used in the general procedure for Method A to give **32** (47 % yield, single diastereomer) as a yellow oil . IR (film): $\tilde{\nu}$ = 3439 (w), 3033 (s), 2987 (w), 2940 (m), 2861 (w), 1733 (s), 1461 (w), 1445 (w), 1374 (m), 1342 (m), 1248 (s), 1236 (s), 1211 (w), 1192 (w), 1046 (m), 919 (w), 850 (w) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.62 (d, *J* = 12.5 Hz, 1 H), 4.26 (d, *J* = 12.5 Hz, 1 H), 2.65 (dd, *J* = 18.8, 6.0 Hz, 1 H), 2.29 (dd, *J* = 18.4, 12.0 Hz, 1 H), 2.24–2.19 (m, 1 H), 2.02–1.93 (m, 1 H), 1.86–1.76 (m, 2 H), 1.61–1.53 (m, 1 H), 1.42–1.13 (m, 3 H), 0.36 (dddd, *J* = 12.0, 10.8, 5.8, 3.4 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5, 82.0, 58.9, 42.7, 38.1, 37.6, 30.1, 24.5, 22.8 ppm. HRMS (DART): calcd. for $C_9H_{14}IO_2$ $[M + H]^+$ 281.00385; found 281.00411.

(–)-{(2*S*,3*S*)-3-[4-(Benzyloxy)phenethyl]oxiran-2-yl}methyl Methanesulfonate (37): To a solution of of **36**[23] (0.42 g, 1.492 mmol) in dry CH_2Cl_2 (15 mL) at 0 °C were added triethylamine (0.416 mL, 2.984 mmol) and methanesulfonyl chloride (0.172 mL, 2.238 mmol), and the resulting mixture was stirred at 0 °C for 2 h. The reaction was quenched with water, and the mixture was extracted with CH_2Cl_2. The organic layer was dried with Na_2SO_4, concentrated, and purified by flash chromatography (hexane/ethyl acetate, 4:1) to give **37** (0.525 g, 97 % yield) as a white solid; m.p. 77–78 °C. $[\alpha]_D^{25}$ = –16.6 (*c* = 0.53, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3028 (w), 2982 (w), 2983 (w), 2855 (w), 1610 (m), 1582 (w), 1511 (s), 1476 (w), 1452 (m), 1385 (w), 1344 (s), 1296 (w), 1253 (s), 1238 (s), 1165 (s), 1115 (w), 1088 (w), 1040 (m), 1011 (m), 980 (s), 965 (s), 925 (m), 884 (m), 830 (s), 806 (s), 781 (m), 736 (s), 695 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.29 (m, 5 H), 7.10 (d, *J* = 8.6 Hz, 2 H), 6.91 (d, *J* = 8.6 Hz, 2 H), 5.05 (s, 2 H), 4.39 (dd, *J* = 11.9, 2.9 Hz, 1 H), 4.05 (dd, *J* = 11.9, 6.4 Hz, 1 H), 3.05 (s, 3 H), 2.97 (dt, *J* = 6.4, 2.2 Hz, 1 H), 2.91 (td, *J* = 6.0, 2.1 Hz, 1 H), 2.77 (ddd, *J* = 14.2, 8.3, 6.0 Hz, 1 H), 2.67 (dt, *J* = 14.0, 8.0 Hz, 1 H), 1.96–1.77 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.4, 137.2, 133.1, 129.4 (2 C), 128.7 (2 C), 128.1, 127.6 (2 C), 115.1 (2 C), 70.2, 69.9, 56.1, 55.3, 38.0, 33.4, 31.2 ppm. HRMS (DART): calcd. for $C_{19}H_{26}NO_5S$ $[M + NH_4]^+$ 380.15317; found 380.15308.

(–)-(*S*)-5-[4-(Benzyloxy)phenyl]pent-1-en-3-ol (38): To a solution of **37** (0.137 g, 0.378 mmol) in THF (1.5 mL) was added NaI (0.113 g, 0.756 mmol), and the mixture was heated at reflux for 2 h. The reaction was cooled to room temp., and the THF was removed by evaporation. The crude residue was partitioned between water and ethyl acetate. The organic phase was dried with Na_2SO_4, and the solvents were evaporated. The residue was dissolved in MeOH (1.5 mL), and then zinc dust (0.124 g, 1.890 mmol) and iodine (0.010 g, 0.038 mmol) were added. The resulting mixture was heated at reflux for 1 h and then cooled to room temperature. The mixture was filtered through Celite, and the filter cake was washed with ethyl acetate. The solvent was removed by evaporation, and the crude product was purified by flash chromatography (hexane/ethyl acetate, 9:1) to give **38** (0.063 g, 62 % yield) as a white solid; m.p. 53–54 °C. $[\alpha]_D^{25}$ = –3.8 (*c* = 0.54, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3298 (br. m), 3062 (w), 3031 (w), 2925 (w), 2892 (w), 2858 (w), 1611 (m), 1580 (w), 1511 (s), 1451 (m), 1383 (m), 1312 (w), 1296 (w), 1255 (s), 1241 (s), 1174 (m), 1118 (w), 1098 (w), 1043 (s), 1014 (s), 984 (s), 916 (s), 857 (w), 821 (m), 785 (w), 734 (s), 694 (s), 636 (w), 611 (m), 560 (m), 512 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.28 (m, 5 H), 7.12 (d, *J* = 8.4 Hz, 2 H), 6.90 (d, *J* = 8.8 Hz, 2 H), 5.90 (ddd, *J* = 17.2, 10.4, 6.1 Hz, 1 H), 5.24 (dt, *J* = 17.2, 1.4 Hz, 1 H), 5.13 (dt, *J* = 10.4, 1.3 Hz, 1 H), 5.04 (s, 2 H), 4.11 (qt, *J* = 6.2, 1.1 Hz, 1 H), 2.75–2.57 (m, 2 H), 1.89–1.74 (m, 2 H, 4-H), 1.56 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2, 141.2, 137.3, 134.3, 129.5 (2 C), 128.7 (2 C), 128.0, 127.6 (2 C), 115.0, 114.9 (2 C), 72.6, 70.2, 38.8, 30.9 ppm. HRMS (DART): calcd. for $C_{18}H_{24}NO_2$ $[M + NH_4]^+$ 286.18070; found 286.18077.

(–)-(*R*)-6-[4-(Benzyloxy)phenethyl]tetrahydro-2*H*-pyran-2-one [(*S*)-33a]: By following the general procedure for Method A of the iodolactonization sequence, **38** (0.062 g, 0.231 mmol) and iodoacetic acid (**6b**, 86 mg, 0.462 mmol) in 1,2-DCE (1.5 mL) were treated with DLP (four additions of 0.018 g, 0.046 mmol). When the iodolactonization step was complete (monitored by TLC analysis), the solvent was removed under reduced pressure, and the residue was dissolved in benzene (3 mL). Then, azobis(isobutyronitrile) (AIBN, 0.005 g, 0.057 mmol) and tributyltin hydride (0.155 mL, 0.577 mmol) were added. The mixture was degassed with argon for 5 min and then heated at reflux for 1 h. Then, the reaction was cooled to room temperature, and the solvent removed by evaporation. The crude residue was purified by flash chromatography (hexane/ethyl acetate/acetic acid, 94.5:5:0.5 to 84.5:15:0.5) to give of (*S*)-**33a** (49 mg, 70 % yield) as a white solid; m.p. 79–80 °C. $[\alpha]_D^{25}$ = –41.8 (*c* = 0.39, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3026 (w), 2953 (w), 2926 (w), 2857 (w), 1724 (s), 1608 (w), 1579 (w), 1510 (m), 1453 (m), 1416 (w), 1382 (m), 1363 (w), 1329 (w), 1298 (w), 1230 (s), 1194 (m), 1173 (m), 1152 (m), 1104 (w), 1052 (s), 1016 (s), 983 (m), 929 (m), 858 (w), 831 (m), 814 (m), 783 (w), 745 (s), 698 (m), 640 (w), 613 (w), 546 (w), 528 (w), 514 (w) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.29 (m, 5 H), 7.11 (d, *J* = 8.6 Hz, 2 H), 6.91 (d, *J* = 8.6 Hz, 2 H), 5.04 (s, 2 H), 4.25 (dddd, *J* = 11.1, 8.3, 4.3, 2.8 Hz, 1 H), 2.80 (ddd, *J* = 14.5, 9.4, 5.5 Hz, 1 H), 2.69 (ddd, *J* = 13.9, 9.1, 7.2 Hz, 1 H), 2.63–2.53 (m, 1 H), 2.51–2.39 (m, 1 H), 2.06–1.95 (m, 1 H), 1.94–1.78 (m, 4 H), 1.63–1.51 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.0, 157.3, 137.3, 133.5,

129.6 (2 C), 128.7 (2 C), 128.0, 127.6 (2 C), 115.0 (2 C), 79.5, 70.2, 37.8, 30.3, 29.6, 28.0, 18.6 ppm. HRMS (DART): calcd. for $C_{20}H_{23}O_3$ $[M + H]^+$ 311.16472; found 311.16483.

(–)-(2*R*,6*S*)-2-[4-(Benzyloxy)phenethyl]-6-[4-(benzyloxy)phenyl]tetrahydro-2*H*-pyran (39): To a solution of *p*-bromobenzyloxybenzene (**34a**,[24] 0.083 g, 0.315 mmol) in dry THF (1 mL) at –78 °C under argon was added *n*-butyllithium (2.5 M solution in THF, 0.118 mL, 0.295 mmol). After the resulting mixture was stirring at –78 °C for 1 h, a solution of lactone (*S*)-**33a** (0.061 g, 0.197 mmol) in of dry THF (1 mL) was transferred by cannula into the reaction flask, and the reaction mixture was stirred at –78 °C until there was complete consumption of the starting material (monitored by TLC analysis). The reaction was quenched with a saturated aqueous NH_4Cl solution, and the mixture was extracted with CH_2Cl_2. The organic layer was dried with Na_2SO_4, filtered, and concentrated. The crude lactol was used directly in the reduction step without further purification. To a solution of the crude lactol in dry CH_2Cl_2 (2 mL) at –78 °C was added triethylsilane (0.126 mL, 0.788 mmol) followed by the dropwise addition of $BF_3{\cdot}OEt_2$ (0.097 mL, 0.788 mmol). The temperature was increased to –40 °C, and the reaction was stirred for 1.5 h and then quenched with water. The mixture was neutralized with triethylamine and then extracted with CH_2Cl_2. The organic extract was dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude residue. Purification by flash chromatography (hexane/ethyl acetate, 99:1 to 95:5) gave **39** (0.041 g, 44 % yield) as a white solid along with the recovered starting material (5.4 mg, 48 % yield based on recovered starting material), m.p. 68–69 °C. $[\alpha]_D^{25} = -44.7$ (*c* = 1.02, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3061 (w), 3031 (w), 2927 (m), 2857 (m), 1736 (w), 1610 (m), 1583 (m), 1510 (s), 1452 (m), 1381 (m), 1349 (w), 1312 (m), 1296 (m), 1243 (s), 1207 (m), 1173 (m), 1140 (w), 1113 (w), 1080 (m), 1039 (s), 1025 (s), 994 (m), 945 (w), 919 (w), 904 (w), 834 (m), 809 (m), 783 (m), 729 (s), 693 (s), 673 (w), 614 (w), 574 (w), 539 (m), 461 (w) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.28 (m, 12 H), 7.11 (d, *J* = 8.6 Hz, 2 H), 6.95 (d, *J* = 8.7 Hz, 2 H), 6.89 (d, *J* = 8.6 Hz, 2 H), 5.06 (s, 2 H), 5.03 (s, 2 H), 4.29 (dd, *J* = 11.1, 2.4 Hz, 1 H), 3.44 (dddd, *J* = 11.1, 7.9, 4.7, 2.0 Hz, 1 H), 2.77–263 (m, 2 H), 1.96–1.86 (m, 2 H), 1.82 (dd, *J* = 14.8, 2.7 Hz, 1 H), 1.72 (dddd, *J* = 18.1, 8.8, 4.4, 2.5 Hz, 1 H), 1.66–1.57 (m, 2 H), 1.49 (tdd, *J* = 12.9, 11.0, 3.7 Hz, 1 H), 1.37–1.29 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.1, 157.0, 137.4, 137.3, 136.3, 135.0, 129.5 (2 C), 128.7 (4 C), 128.0 (2 C), 127.62 (2 C), 127.58 (2 C), 127.2 (2 C), 114.8 (2 C), 114.7 (2 C), 79.1, 77.3, 70.19, 70.16, 38.4, 33.5, 31.4, 30.9, 24.2 ppm. HRMS (DART): calcd. for $C_{33}H_{35}O_3$ $[M + H]^+$ 479.25862; found 479.25884.

(–)-De-*O*-methylcentrolobine (35): To a solution of **39** (0.041 g, 0.085 mmol) in MeOH (5 mL) were added $Pd(OH)_2$ (20 wt-% over charcoal, 0.008 g). The reaction flask was charged with H_2 and then stirred vigorously for 24 h. The reaction was filtered through Celite, and the filter cake was washed with MeOH and acetone. The solvent was removed by evaporation, and the crude product was purified by flash chromatography (hexanes/ethyl acetate, 7:3) to give **35** (0.018 g, 70 % yield) as a white solid; m.p. 170 °C. $[\alpha]_D^{25} = -67.6$ (*c* = 1.07, MeOH). IR (KBr): $\tilde{\nu}$ = 3360 (br. s), 3065 (w), 3024 (w), 2974 (m), 2919 (m), 2842 (m), 1887 (w), 1701 (w), 1653 (w), 1613 (m), 1600 (m), 1512 (s), 1441 (m), 1367 (m), 1311 (w), 1292 (w), 1267 (m), 1228 (s), 1173 (m), 1152 (w), 1121 (w), 1087 (m), 1022 (m), 982 (w), 956 (w), 940 (w), 919 (w), 900 (w), 863 (w), 825 (s), 785 (w), 752 (w), 617 (w), 574 (w), 548 (w), 536 (w), 523 (w), 508 (w), 444 (w) cm^{-1}. ^1H NMR (400 MHz, $[D_6]$acetone): δ = 8.19 (s, 1 H), 8.04 (s, 1 H), 7.23–7.18 (m, 2 H), 7.05–6.98 (m, 2 H), 6.81–6.77 (m, 2 H), 6.75–6.71 (m, 2 H), 4.26 (dd, *J* = 11.2, 2.1 Hz, 1 H), 3.42 (dddd, *J* = 9.8, 7.9, 4.5, 1.8 Hz, 1 H), 2.71–2.56 (m, 2 H), 1.92–1.85 (m, 1 H), 1.82–1.59 (m, 5 H), 1.47–1.36 (m, 1 H), 1.32–1.25 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2, 156.2, 136.0, 134.0, 130.1 (2 C), 127.8 (2 C), 115.9 (2 C), 115.6 (2 C), 79.9, 77.7, 39.5, 34.6, 32.1, 31.5, 24.8 ppm. HRMS (EI): calcd. for $C_{19}H_{22}O_3$ $[M]^+$ 298.1569; found 298.1553.

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