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Studies on the factors controlling the stereoselectivity in electrophilic iodocyclization of alkylidenecyclopropyl ketones

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ABSTRACT

An efficient electrophilic iodocyclization of alkylidenecyclopropyl ketones with *N*-iodosuccinimide (NIS) or I_2 in aqueous CH_3CN affording 3-oxabicyclo[3.1.0]hexan-2-ols is described. NIS is a better electrophilic iodocyclization reagent than I_2. Four chiral centers were formed within one step. The stereochemistry was established by the X-ray diffraction studies of compounds **2e**–**2h**, **2n**, and **2c**. It is quite interesting to observe that the substituent of the cyclopropane ring plays an important role in determining the relative stereochemistry at the 4-position: with R^2 being an acyl or ester group a mixture of (1*S**,2*R**,4*S**,5*R**)-**2** (major) and (1*R**,2*R**,4*R**,5*R**)-**2** (minor) was formed with moderate selectivity while the reaction of the substrates with R^2 being sulfonyl and *p*-methylphenylsulfonyl or R^1 being phenyl afforded (1*R**,2*R**,4*S**,5*S**)-**2** or (1*S**,2*R**,4*S**,5*R**)-**2f** as the only product. The reaction is general for a range of different substrates to afford the products in moderate to high yields.

1. Introduction

3-Oxabicyclo[3.1.0]hexan-2-ols are important units frequently found in numerous biologically active natural products or pharmacologically interesting unnatural compounds.[1] Compounds containing this unit can also serve as key intermediates for the preparation of the stereoisomeric chrysanthemic acids,[2] norcaradienes,[3] 3-oxabicyclo[3.1.0]hexan-2-ones,[4] and substituted cyclopropanes.[5] There are some known methods available for their preparations.[6] However, most of these methods suffer from their long synthetic routes or poor yields.[7] Thus, developing an efficient methodology for synthesis of 3-oxabicyclo[3.1.0]hexan-2-ols is highly desirable.

Alkylidenecyclopropanes (ACPs) are highly strained but readily accessible molecules, which may serve as useful building blocks in organic synthesis.[8] ACPs readily undergo a variety of ring-opening reactions to relief the ring strain, which comes from the copresence of *exo*-cyclic double bond and the three-membered carbocycle.[9] Numerous efforts have been devoted to the research in this area, such as 1,3-dipolar cycloaddition,[10] Diels–Alder reaction,[11] and the reactions via proximal or distal cleavage under the catalysis of transition metal complexes or Lewis acids.[12] Furthermore, the C–C double bond in ACPs is also very reactive. Thus, an attractive but troublesome feature of ACPs is their multi-reaction sites that may lead to the formation of a variety of different products (Scheme 1). Therefore, it is attractive to develop the reactions of ACPs, which proceed in a selective fashion leading to the synthesis of different products by choice of different catalysts or reagents.

In our previous reports, different ring-opening reactions of ACPs were observed under the catalysis of Pd(II), Pd(0), or I^-, based on the nature of the catalyst and reaction conditions.[13] Besides the selective cleavage of the σ-bonds (proximal and distal bonds) in the cyclopropane ring, we have also observed the iodolactonization of the alkylidenecyclopropyl esters.[14] Herein, we wish to report our recent observation on the factors determining the diastereoselectivity in the iodocyclization of alkylidenecyclopropyl ketones with *N*-iodosuccinimide (NIS) to form 3-oxabicyclo[3.1.0]hexan-2-ols.

2. Results and discussion

Initially, the reaction of 1-(ethoxycarbonyl)-2-(octylidene)cyclopropyl methyl ketone (**1a**) with NIS was carried out in CH_3CN/H_2O=2:1 at room temperature. To our delight, the reaction smoothly led to the formation of a diastereomeric mixture of product **2a** with a ratio of 33:67 in 73% yield (entry 1, Table 1). When 2 equiv of I_2 were used, the combined yield of **2a** was only 39% (entry 2, Table 1), much inferior to the reaction of **1a** with NIS. Thus, we chose NIS as the iodocyclization reagent to optimize the reaction conditions. As we have demonstrated the important role of water in the reaction of alkylidenecyclopropyl carboxylic acid esters with iodine or NIS,[11] further screening of the solvent system was conducted (Table 1). In most cases, the reaction proceeded smoothly to afford moderate yields of a diastereomeric mixture of **2a** in a mixed solvent of CH_3CN/H_2O (1:1 to 8:1 by volume) (entries

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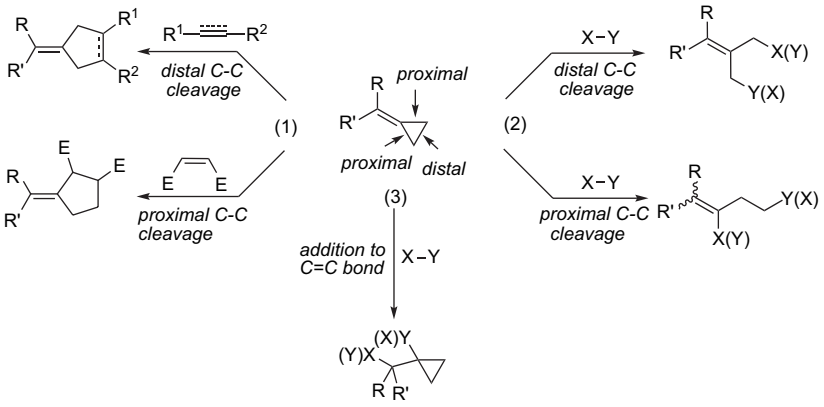


Scheme 1.

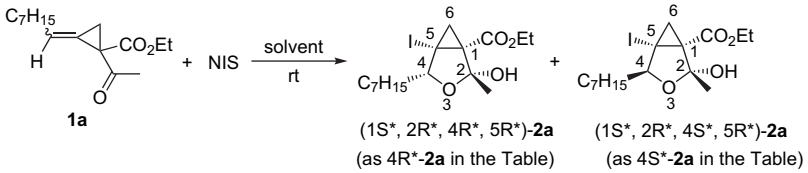
3–5, Table 1). The best results were obtained when a mixed solvent of CH_3CN/H_2O (10:1) was used affording **2a** in 85% yield (entry 6, Table 1). Further studies showed that the yield decreased with a further increased ratio of CH_3CN/H_2O (entry 7, Table 1). Although there are four new chiral centers formed in the reaction, only two diastereomers, i.e., (1*S**,2*R**,4*R**,5*R**)-**2a** and (1*S**,2*R**,4*S**,5*R**)-**2a**, were formed in a ratio of 41:59 to 32:68. The difference is the relative configuration at the 4-position. The two diastereomers can be readily separated by column chromatography on silica gel.

With the optimized reaction conditions in hand, the scope of the reaction was studied with the typical results summarized in Table 2. R^1 may be alkyl, Bn, or Ph; R^2 may be CO_2Et and $COCH_3$; R^3 may be Me or Ph. The diastereomeric ratios of the products of (1*S**,2*R**,4*R**,5*R**)-**2** and (1*S**,2*R**,4*S**,5*R**)-**2** do not seem to have direct correlation with the *E*/*Z* ratios of the starting materials. Under the current reaction conditions, (1*S**,2*R**,4*S**,5*R**)-**2** is more favored than (1*S**,2*R**,4*R**,5*R**)-**2**. However, it is interesting to note that only (1*S**,2*R**,4*S**,5*R**)-**2f** was obtained when R^1 is the phenyl group (entry 6, Table 2). With this result in hand, we next started to look into the steric effect of R^2 on the diastereoselectivity of this cyclization.

In fact, we observed that the reaction of the starting materials with R^2 being bulkier substituent, such as SO_2Ph and Ts, also proceeded smoothly to afford the (1*R**,2*R**,4*S**,5*S**)-**2g**–**2m** as the only products with R^1 being 1-alkyl or *c*-hexyl in moderate to good yields (Table 3). The relative stereochemistry in terms of the orientation of all the substituents here is the same as what observed in the major products (1*S**,2*R**,4*S**,5*R**)-**2a**–**2d**, (1*R**,2*R**,4*S**,5*R**)-**2e**, or (1*S**,2*R**,4*S**,5*R**)-**2f**. With R^1 being $TBSOCH_2CH_2$, the iodocyclization products underwent further desilylation to afford (1*R**,2*R**,4*S**,5*S**)-**2l** and (1*R**,2*R**,4*S**,5*S**)-**2m** (entries 6 and 7, Table 3). The stereochemistry of these major products **2** was established by the X-ray diffraction study of (1*R**,2*R**,4*S**,5*R**)-**2e**,[15] (1*S**,2*R**,4*S**,5*R**)-**2f**,[16] (1*S**,2*R**,4*S**,5*R**)-**2g**,[17] and (1*S**,2*R**,4*S**,5*R**)-**2h**[18] (Fig. 1). In addition, the stereochemistry of these minor products **2** was also established by the X-ray diffraction study of (1*S**,2*R**,4*R**,5*R**)-**2c**[19] (Fig. 1). The structures of other products were tentatively assigned based on the comparison of the chemical shift of the hydrogen atom at 4-position in the ^1H NMR spectra of **2e**–**2h** and **2c**. A conclusion may be made by comparison of the results of Tables 2 and 3 that the diastereoselectivities of the reaction is determined by the nature of R^1 and R^2.

Furthermore, the tricyclic products **2n** and **2o** were formed as the only diastereomers in 73% and 61% yields when 2-(cyclohexylidene)cyclopropyl ketones **1n** and **1o** were submitted to the standard reaction conditions (Scheme 2). It should be noted with interest that here again the same type of products (1*S**,2*R**,5*R**)-**2n** and (1*R**,2*R**,5*S**)-**2o** were formed. The structure of the two products were established by the X-ray diffraction study of (1*S**,2*R**,5*R**)-**2n** (Fig. 2),[20] indicating the highly selective formation of the same type of chiral centers at 1-, 2-, and 5-positions.

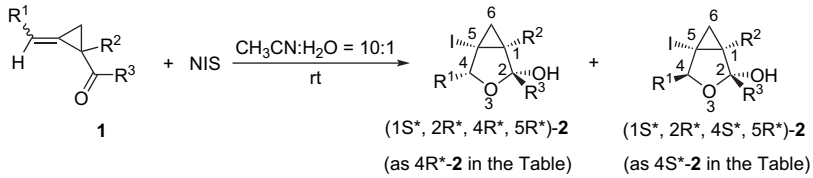
Table 1
Iodocyclization of 1-(ethoxycarbonyl)-2-(octylidene)cyclopropyl methyl ketone (**1a**) with NIS under different conditions[a]



Entry	$MeCN/H_2O$	Time (h)	Isolated yield of **2a** (%)		$4R^*$-**2a**/$4S^*$-**2a**
			$4R^*$-**2a**	$4S^*$-**2a**	
1	2:1	0.75	24	49	33:67
2[b]	2:1	0.5	16	23	41:59
3	1:1	6.25	26	46	36:64
4	4:1	5	27	45	38:62
5	8:1	5	23	49	32:68
6	10:1	3.25	34	51	40:60
7	20:1	2.25	23	43	35:65

[a] The reaction was carried out using 0.25–0.5 mmol of **1a** and 0.3–0.6 mmol of NIS (1.2 equiv) in 1.5–3 mL of solvent at rt.
[b] I_2 (2 equiv) was used instead of NIS.

Table 2
Iodocyclization of alkylidenecyclopropyl ketones **1** with NIS[a]



Entry	**1**			*E*/*Z* ratio of **1**	Time (h)	Yield of 4*R**-**2** (%)	Yield of 4*S**-**2** (%)
	R^1	R^2	R^3				
1	C_7H_{15}	CO_2Et	Me (**1a**)	2.5:1	3	34 (4*R**-**2a**)	51 (4*S**-**2a**)
2	C_4H_9	CO_2Et	Me (**1b**)	2.1:1	3	22 (4*R**-**2b**)	54 (4*S**-**2b**)
3	Bn	CO_2Et	Me (**1c**)	1:1	12	21 (4*R**-**2c**)	43 (4*S**-**2c**)
4[b]	C_7H_{15}	CO_2Et	Ph (**1d**)	—	4	17 (4*R**-**2d**)	67 (4*S**-**2d**)
5	C_7H_{15}	COMe	Me (**1e**)	2.5:1	2	21 (4*R**-**2e**)[c]	51 (4*S**-**2e**)[c]
6	Ph	CO_2Et	Me (**1f**)	100:0	2	—	76 (4*S**-**2f**)

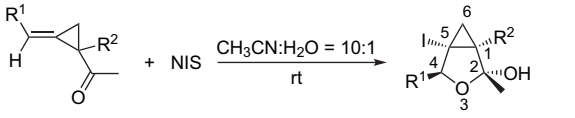
[a] The reaction was carried out using 0.25–0.5 mmol of **1** and 1.2 equiv of NIS in 1.5–3 mL of the mixed solvent (CH_3CN/H_2O=10:1) at rt.
[b] *E*/*Z* ratio of **1** is not detected.
[c] According to the sequence rule, the relative configuration of the chiral center at 1-position in **2e** should be read as *R**.

A possible mechanism for this iodocyclization reaction is depicted in Scheme 3. Firstly, electrophilic interaction of I^+ with the C=C bond would form the intermediate **3**, which would undergo a ring-opening reaction to generate a carbocationic intermediate **3A**. Due to the steric interaction between group R^1 and I, the subsequent intramolecular nucleophilic attack of the carbonyl oxygen at the positively charged carbon center would lead to the formation of the intermediate **4C** as the major or only diastereomer. Subsequent stereoselective attack of **4B** or **4C** by water could finally lead to the formation of different diastereomer of product **2**, depending on the steric bulkiness of R^1 and R^2 groups.

3. Conclusion

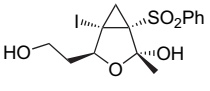
In conclusion, we have developed an iodocyclization reaction of alkylidenecyclopropyl ketones with NIS under aqueous conditions leading to the formation of 3-oxabicyclo[3.1.0]hexan-2-ols in moderate to good yields. The stereoselectivity of the products might be influenced by the steric effects of the substituent group R^1 and R^2 of the starting materials. With R^1 being phenyl or R^2 being bulkier substituents, such as SO_2Ph and Ts, only the (1*S**,2*R**,4*S**,5*R**)-**2f** or (1*R**,2*R**,4*S**,5*S**)-**2g–2m** were obtained. In this reaction, H_2O may act as a nucleophile, leading to the generation of hydroxyl group in the product. Further investigations in this area are being carried out in our laboratory.

Table 3
Iodocyclization of alkylidenecyclopropyl ketones **1** with NIS[a]

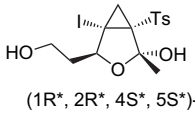


Entry	**1**		Time (h)	Yield of (1*R**,2*R**,4*S**,5*S**)-**2** (%)
	R^1	R^2		
1	C_4H_9	SO_2Ph (**1g**)	15	83 (**2g**)
2	C_7H_{15}	SO_2Ph (**1h**)	14.5	80 (**2h**)
3[b]	C_8H_{15}	SO_2Ph (**1i**)	85	71 (**2i**)
4[c]	C_7H_{15}	Ts (**1j**)	40	62 (**2j**)
5[c]	*c*-Hexyl	SO_2Ph (**1k**)	36	65 (**2k**)
6[c]	$TBSOCH_2CH_2$	SO_2Ph (**1l**)	11	83 (**2l**)[d]
7[c]	$TBSOCH_2CH_2$	Ts (**1m**)	11	68 (**2m**)[d]

[a] The reaction was carried out using 0.1–0.5 mmol of **1** and 1.2 equiv of NIS in 1.5–3 mL of solvent at rt.
[b] NIS (1.7 equiv) was used.
[c] NIS (1.5 equiv) was used.
[d] The iodocyclization products underwent subsequent desilylation to afford **2l** and **2m**.



(1R*, 2R*, 4S*, 5S*)-**2l**



(1R*, 2R*, 4S*, 5S*)-**2m**

4. Experimental section

4.1. Synthesis of alkylidenecyclopropyl ketones (1a–1o)

Alkylidenecyclopropyl ketones **1a–1e**, **1g–h**, and **1n** used in this study were easily prepared via the $Rh_2(OAc)_4$-catalyzed cyclopropanation of the corresponding 1,2-allenes[21] with the corresponding diazo compounds[22] according to known procedure.[23,13b]

*4.1.1. 1-(Ethoxycarbonyl)-2-(benzylidene)cyclopropyl methyl ketone (E-**1f**)*

A solution of 2-diazo-3-oxobutyric acid ethyl ester **6a** (935 mg, 6 mmol) in 10 mL of CH_2Cl_2 was added with a syringe to a solution of phenylpropadiene (2.162 g, 19 mmol) and $Rh_2(OAc)_4$ (7 mg, 0.016 mmol) in 5 mL of CH_2Cl_2 under reflux. After the addition was over, the mixture was stirred for 5 h under reflux. Evaporation and chromatography on silica gel (eluent: petroleum ether; petroleum ether/Et_2O=20:1) gave *E*-**1f** (418 mg, 29%) as a liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J*=7.2 Hz, 2H), 7.36 (t, *J*=6.6 Hz, 2H), 7.28 (t, *J*=6.6 Hz, 1H), 6.86 (t, *J*=2.7 Hz, 1H), 4.27–4.16 (m, 2H), 2.54 (dd, *J*=2.7, 9.6 Hz, 1H), 2.47 (dd, *J*=2.7, 9.6 Hz, 1H), 2.39 (s, 3H), 1.27 (t, *J*=6.9 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 200.1, 168.8, 135.5, 128.6, 128.1, 127.3, 124.0, 119.1, 61.6, 37.8, 28.2, 18.7, 14.0; MS (EI) *m*/*z* 244 (M^+, 34.77), 215 (69.44), 199 (64.62), 43 (100); IR (neat) 1709, 1600, 1454, 1292, 1257 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{16}O_3^+$ (M^+): 244.1099. Found: 244.1106. The stereochemistry of this product was determined by the ^1H–^1H NOESY spectra (300 MHz).

*4.1.2. 1-(Phenylsulfonyl)-2-(nonylidene)cyclopropyl methyl ketone (E-**1i**)*

The reaction of 1-(phenylsulfonyl)-1-diazopropan-2-one **6b** (672 mg, 3.0 mmol) with undeca-1,2-diene (3.38 g, 22 mmol) and $Rh_2(OAc)_4$ (5 mg, 0.01 mmol) in CH_2Cl_2 (15 mL) afforded *E*-**1i** (132 mg, 13%) as a liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, *J*=7.8 Hz, 2H), 7.63 (t, *J*=7.5 Hz, 1H), 7.53 (t, *J*=7.8 Hz, 2H), 6.14–6.07

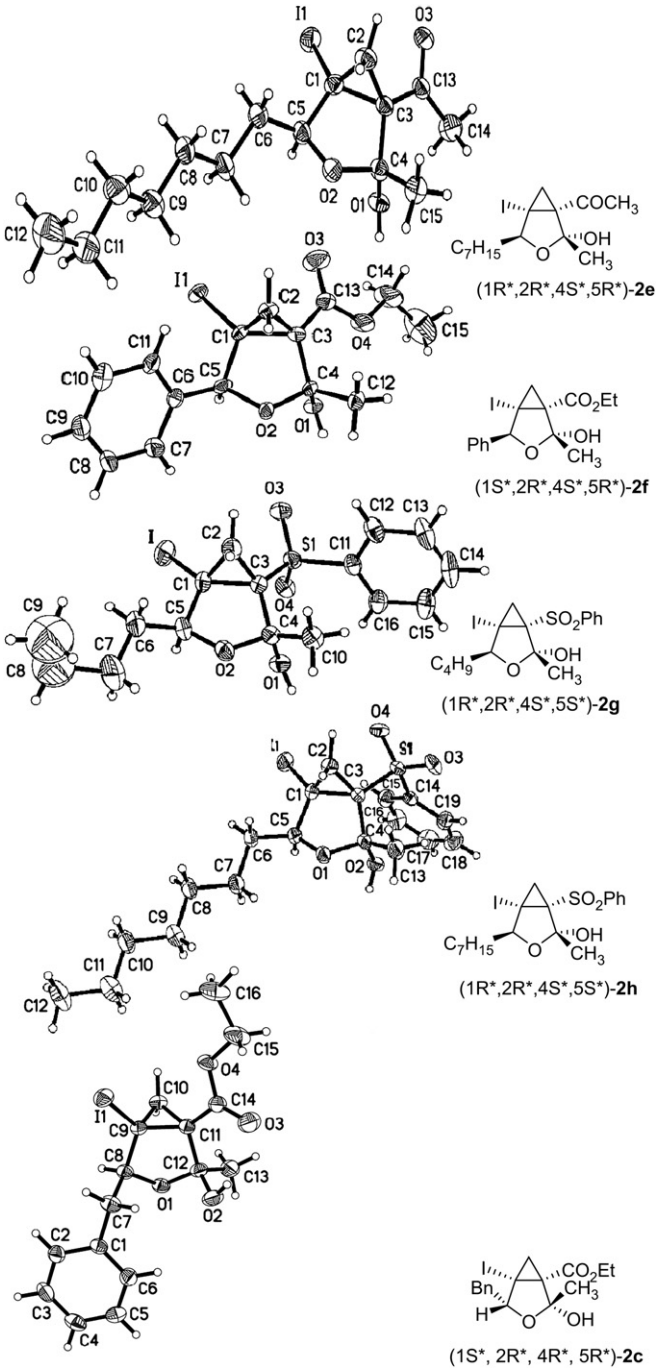
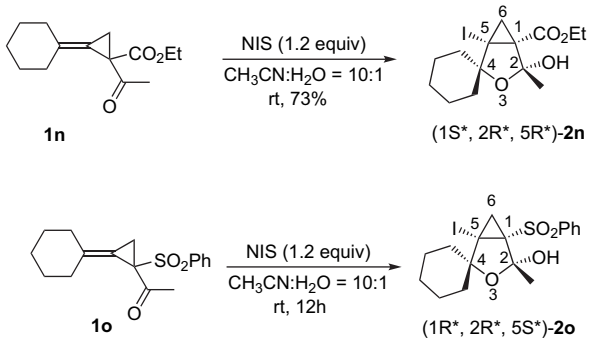


Figure 1. ORTEP representations of **2e**–**2h** and **2c**.



Scheme 2.

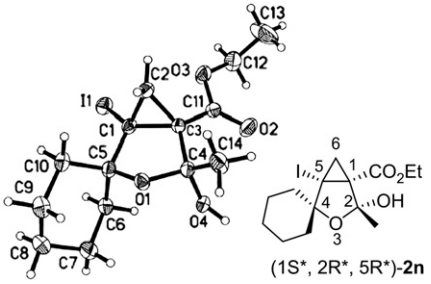


Figure 2. ORTEP representation of **2n**.

(m, 1H), 2.68–2.64 (m, 1H), 2.33–2.27 (m, 3H), 2.08 (s, 3H), 1.54–1.46 (m, 2H), 1.35–1.27 (m, 10H), 0.88 (t, J=6.3 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 196.9, 139.2, 133.6, 129.1, 128.6, 125.2, 118.3, 53.6, 31.7, 31.3, 29.2, 29.14, 29.08, 28.2, 26.3, 22.5, 17.5, 14.0; MS (EI) m/z 348 (M^+, 2.46), 249 (56.33), 43 (100); IR (neat) 2927, 1706, 1568, 1447, 1320, 1157 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{28}O_3S^+$ (M+Na^+): 348.1759. Found: 348.1765.

4.1.3. 1-(p-Methylphenylsulfonyl)-2-(octylidene)cyclopropyl methyl ketone (E-**1j**)

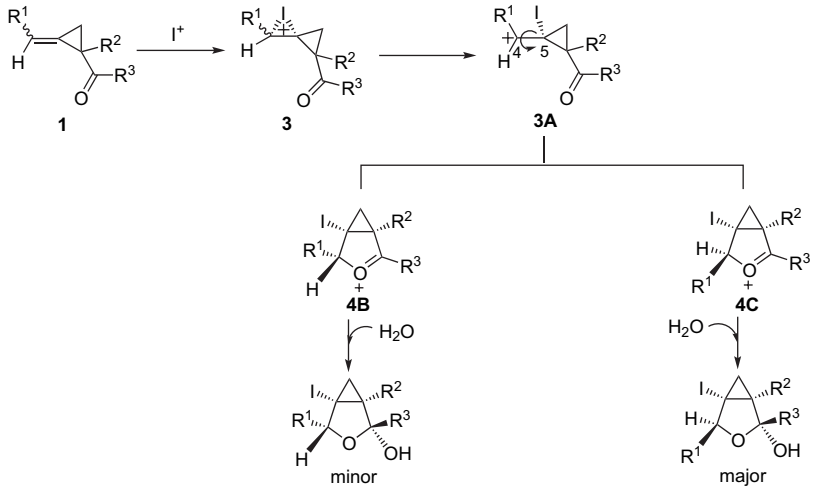
The reaction of 1-(*p*-methylbenzenesulfonyl)-1-diazopropan-2-one **6c** (951 mg, 4 mmol) with deca-1,2-diene (2.007 g, 0.145 mmol) and $Rh_2(OAc)_4$ (5 mg, 0.011 mmol) in CH_2Cl_2 (15 mL) afforded *E*-**1j** (209 mg, 15%) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (d, J=8.4 Hz, 2H), 7.30 (d, J=8.4 Hz, 2H), 6.11–6.07 (m, 1H), 2.63–2.59 (m, 1H), 2.42 (s, 3H), 2.30–2.25 (m, 3H), 2.07 (s, 3H), 1.52–1.47 (m, 2H), 1.29–1.28 (m, 8H), 0.87 (t, J=6.0 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 197.0, 144.6, 136.2, 129.3, 129.2, 124.9, 118.5, 53.7, 31.7, 31.3, 29.04, 28.96, 28.3, 26.4, 22.5, 21.6, 17.4, 14.0; MS (EI) m/z 348 (M^+, 0.67), 263 (12.28), 43 (100); IR (neat) 2927, 1706, 1597, 1319, 1156 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{28}O_3S^+$ (M^+): 348.1759. Found: 348.1754. The stereochemistry of this product was determined by the ^{1}H–^{1}H NOESY spectra (300 MHz).

4.1.4. 1-(Phenylsulfonyl)-2-(cyclohexylmethylene)cyclopropyl methyl ketone (E-**1k**)

The reaction of 1-(phenylsulfonyl)-1-diazopropan-2-one **6b** (770 mg, 3.4 mmol) with propa-1,2-dienylcyclohexane (4.4 g, 36 mmol) and $Rh_2(OAc)_4$ (7 mg, 0.016 mmol) in CH_2Cl_2 (15 mL) afforded *E*-**1k** (255 mg, 23%) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, J=7.5 Hz, 2H), 7.62 (t, J=7.5 Hz, 1H), 7.52 (t, J=7.8 Hz, 2H), 6.01 (dt, J=2.7, 6.3 Hz, 1H), 2.72–2.67 (m, 1H), 2.38–2.33 (m, 2H), 2.07 (s, 3H), 1.86–1.65 (m, 6H),1.37–1.16 (m, 4H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 197.0, 139.1, 133.6, 129.9, 129.2, 128.7, 117.0, 52.7, 39.9, 31.9, 31.8, 26.3, 25.9, 25.6, 18.0; MS (EI) m/z 318 (M^+, 1.86), 236 (24.03), 43 (100); IR (neat) 2926, 1704, 1585, 1447, 1318, 1157 cm^{-1}, HRMS (EI) calcd for $C_{18}H_{22}O_3S^+$ (M^+): 318.1290. Found: 318.1276.

4.1.5. 1-(Phenylsulfonyl)-2-((2-tert-butyldimethyloxysilane)-amylidene)cyclopropyl methyl ketone (E-**1l**)

The reaction of 1-(phenylsulfonyl)-1-diazopropan-2-one **6b** (670 mg, 3 mmol) with 5-*tert*-butyldimethylsiloxylpenta-1,2-diene (1.828 g, 9 mmol) and $Rh_2(OAc)_4$ (8+8 mg, 0.036 mmol) in CH_2Cl_2 (10 mL) afforded *E*-**1l** (221 mg, 19%) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, J=7.2 Hz, 2H), 7.62 (t, J=7.5 Hz, 1H), 7.51 (t, J=7.8 Hz, 2H), 6.17–6.12 (m, 1H), 3.80–3.72 (m, 2H), 2.68–2.64 (m, 1H), 2.54–2.48 (m, 2H), 2.34–2.29 (m, 1H), 2.05 (s, 3H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 196.8, 139.2, 133.6, 129.1, 128.7, 122.1, 119.9, 61.6, 53.8, 34.9, 26.3, 25.8, 18.2, 17.3, −5.4; MS (ESI) m/z 395 (M+H^+); IR (neat) 2954, 1705, 1568, 1320, 1447, 1157, 1098 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{30}NaO_4SSi^+$ (M+Na^+): 417.1526. Found: 417.1522.



Scheme 3.

*4.1.6. 1-(p-Methylphenylsulfonyl)-2-((2-tert-butyldimethyl-oxysilane)amylidene)-cyclopropyl methyl ketone (E-**1m**)*

The reaction of 1-(*p*-methylbenzenesulfonyl)-1-diazopropan-2-one **6c** (721 mg, 3 mmol) with 5-*tert*-butyldimethylsiloxylpenta-1,2-diene (1.786 g, 9 mmol) and $Rh_2(OAc)_4$ (8 mg, 0.018 mmol) in CH_2Cl_2 (10 mL) afforded *E*-**1m** (143 mg, 12%) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J=8.7 Hz, 2H), 7.32 (t, J=7.8 Hz, 2H), 6.17–6.11 (m, 1H), 3.80–3.72 (m, 2H), 2.65–2.61 (m, 1H), 2.54–2.48 (m, 2H), 2.43 (s, 3H), 2.31–2.27 (m, 1H), 2.08 (s, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 196.9, 144.7, 136.2, 129.4, 129.2, 121.9, 120.1, 61.7, 54.0, 34.9, 26.5, 25.8, 21.6, 18.2, 17.3, −5.4; MS (ESI) m/z 409 ($M+H^+$); IR (neat) 2954, 1706, 1599, 1470, 1319, 1157, 1095 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{32}NaO_4SSi^+$ ($M+Na^+$): 431.1683. Found: 431.1674.

*4.1.7. 1-(Phenylsulfonyl)-2-(cyclohexylidene)cyclopropyl methyl ketone (**1o**)*

The reaction of 1-(phenylsulfonyl)-1-diazopropan-2-one **6b** (1.796 g, 8 mmol) with vinylidenecyclohexane (3.439 g, 32 mmol) and $Rh_2(OAc)_4$ (20 mg+17 mg, 0.086 mmol) afforded **1o** (0.824 g, 34%) as a solid, mp 93–94 °C (Et_2O/petroleum ether). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, J=7.2 Hz, 2H), 7.61 (t, J=7.8 Hz, 1H), 7.52 (t, J=7.8 Hz, 2H), 2.61 (d, J=8.7 Hz, 1H), 2.39–2.35 (m, 2H), 2.26 (d, J=9.0 Hz, 1H), 2.19–2.09 (m, 2H), 2.04 (s, 3H), 1.73–1.45 (m, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 197.8, 139.7, 137.7, 133.5, 129.3, 128.6, 109.8, 54.9, 33.6, 33.5, 27.3, 27.1, 26.1, 25.8, 18.4; MS (EI) m/z 304 (0.97, M^+), 262 (9.44), 43 (100); IR (neat) 2934, 1702, 1568, 1447, 1308, 1150 cm^{-1}. Anal. Calcd for $C_{17}H_{20}O_3S$: C, 67.08; H, 6.62. Found: C, 67.18; H, 6.62.

4.2. Typical procedure for iodocyclization of alkylidenecyclopropyl ketones with NIS

4.2.1. Synthesis of (1S,2R*,5R*)-1-(ethoxycarbonyl)-2-methyl-4-heptyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol (**2a**)*

A solution of **1a** (68 mg, 0.25 mmol) and NIS (68 mg, 0.3 mmol) in 1 mL of CH_3CN and 0.1 mL of H_2O was stirred in a flask for 3.25 h at room temperature as monitored by TLC. The reaction was quenched with a saturated aqueous $Na_2S_2O_3$ solution, extracted with ether, and dried over anhydrous $MgSO_4$. Evaporation and column chromatography on silica gel (eluent: petroleum ether/Et_2O=8:1) afforded (1S*,2R*,4R*,5R*)-**2a** (35 mg, 34%) and (1S*,2R*,4S*,5R*)-**2a** (52 mg, 51%).

4.2.1.1. (1S,2R*,4R*,5R*)-1-(Ethoxycarbonyl)-2-methyl-4-heptyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1S*,2R*,4R*,5R*)-**2a**).* Oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.01 (s, 1H), 4.38–4.21 (m, 2H), 3.98 (dd, J=11.1, 4.2 Hz, 1H), 1.91–1.80 (m, 2H), 1.83 (d, J=5.4 Hz, 1H), 1.58–1.55 (m, 2H), 1.46 (s, 3H), 1.45 (d, J=5.4 Hz, 1H), 1.35 (t, J=7.2 Hz, 3H), 1.29–1.26 (m, 8H), 0.86 (t, J=6.0 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.1, 103.3, 84.7, 62.1, 42.4, 37.8, 31.8, 29.27, 29.26, 27.1, 26.8, 24.3, 22.6, 14.2, 14.1, 12.9; MS (ESI) m/z 433 ($M+Na^+$), 393 ($M+H^+$)−H_2O; IR (neat) 3467, 2926, 1722 (sh), 1699, 1466, 1376, 1080, 1210 cm^{-1}; HRMS (MALDI) calcd for $C_{16}H_{27}O_4INa^+$ ($M+Na^+$): 433.0846. Found: 433.0846.

4.2.1.2. (1S,2R*,4S*,5R*)-1-(Ethoxycarbonyl)-2-methyl-4-heptyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1S*,2R*,4S*,5R*)-**2a**).* Oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.97 (s, 1H), 4.41–4.19 (m, 3H), 1.84–1.75 (m, 1H), 1.71 (d, J=6.3 Hz, 1H), 1.54–1.20 (m, 18H), 0.86 (t, J=6.0 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.1, 102.6, 84.2, 62.0, 41.7, 31.7, 29.63, 29.60, 29.1, 26.2, 23.4, 22.8, 22.6, 14.3, 14.1, 12.8; MS (ESI) m/z 433 ($M+Na^+$), 393 ($M+H^+$)−H_2O; IR (neat) 3468, 2928, 1722, 1699, 1376, 1211 cm^{-1}; HRMS (MALDI) calcd for $C_{16}H_{27}O_4INa^+$ ($M+Na^+$): 433.0846. Found: 433.0836.

4.2.2. (1S,2R*,5R*)-1-(Ethoxycarbonyl)-2-methyl-4-butyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol (**2b**)*

The reaction of **1b** (113 mg, 0.5 mmol) and NIS (135 mg, 0.6 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1S*,2R*,4R*,5R*)-**2b** (40 mg, 22%) and (1S*,2R*,4S*,5R*)-**2b** (99 mg, 54%).

4.2.2.1. (1S,2R*,4R*,5R*)-1-(Ethoxycarbonyl)-2-methyl-4-butyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1S*,2R*,4R*,5R*)-**2b**).* Oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.00 (s, 1H), 4.37–4.20 (m, 2H), 3.97 (dd, J=11.1, 3.9 Hz, 1H), 1.93–1.81 (m, 2H), 1.82 (d, J=5.7 Hz, 1H), 1.59–1.51 (m, 1H), 1.48–1.44 (m, 4H), 1.40–1.23 (m, 6H), 0.89 (t, J=6.9 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.0, 103.3, 84.7, 62.1, 42.4, 37.5, 28.9, 27.1, 24.3, 22.3, 14.2, 14.0, 12.8; MS (ESI) m/z 391 ($M+Na^+$), 351 ($M+H^+$)−H_2O; IR (neat) 3457, 2956, 1722 (sh), 1697, 1376, 1209 cm^{-1}; HRMS (MALDI) calcd for $C_{13}H_{21}O_4INa^+$ ($M+Na^+$): 391.0377. Found: 391.0393.

4.2.2.2. (1S,2R*,4S*,5R*)-1-(Ethoxycarbonyl)-2-methyl-4-butyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1S*,2R*,4S*,5R*)-**2b**).* Oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.96 (s, 1H), 4.40–4.18 (m, 3H), 1.81–1.77 (m, 1H), 1.69 (d, J=6.0 Hz, 1H), 1.49–1.27 (m, 12H), 0.88 (t, J=6.9 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.0, 102.6, 84.1, 61.9, 41.7, 29.3, 28.3, 23.3, 22.8, 22.7, 14.2, 13.9, 12.8; MS (ESI) m/z 391 ($M+Na^+$), 351

($M+H^+$)$-H_2O$; IR (neat) 3469, 2935, 1722, 1698, 1376, 1208 cm^{-1}; HRMS (MALDI) calcd for $C_{13}H_{21}O_4INa^+$ ($M+Na^+$): 391.0377. Found: 391.0377.

4.2.3. (1S,2R*,5R*)-1-(Ethoxycarbonyl)-2-methyl-4-benzyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol (**2c**)*

The reaction of **1c** (130 mg, 0.5 mmol) and NIS (135 mg, 0.6 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1*S**,2*R**,4*R**,5*R**)-**2c** (42 mg, 21%) and (1*S**,2*R**,4*S**,5*R**)-**2c** (87 mg, 43%).

4.2.3.1. (1S,2R*,4R*,5R*)-1-(Ethoxycarbonyl)-2-methyl-4-benzyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1S*,2R*,4R*,5R*)-**2c**).* Oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.21 (m, 5H), 5.17 (s, 1H), 4.43–4.20 (m, 3H), 3.35 (dd, *J*=13.5, 3.0 Hz, 1H), 3.21 (dd, *J*=13.5, 11.1 Hz, 1H), 1.89 (d, *J*=5.7 Hz, 1H), 1.48 (d, *J*=5.7 Hz, 1H), 1.47 (s, 3H), 1.39 (t, *J*=5.7 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.0, 138.9, 129.8, 128.2, 126.2, 103.6, 85.4, 62.2, 43.6, 42.7, 27.2, 24.4, 14.2, 11.8; MS (ESI) *m*/*z* 425 ($M+Na^+$), 385 ($M+H^+$)$-H_2O$; IR (neat) 3457, 2985, 1720 (sh), 1696, 1377, 1214 cm^{-1}; HRMS (MALDI) calcd for $C_{16}H_{19}O_4INa^+$ ($M+Na^+$): 425.0220. Found: 425.0214.

4.2.3.2. (1S,2R*,4S*,5R*)-1-(Ethoxycarbonyl)-2-methyl-4-benzyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1S*,2R*,4S*,5R*)-**2c**).* Oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.29–7.21 (m, 5H), 4.95 (s, 1H), 4.70 (dd, *J*=7.5, 3.0 Hz, 1H), 4.36–4.19 (m, 2H), 3.13 (dd, *J*=14.7, 3.0 Hz, 1H), 2.84 (dd, *J*=14.1, 7.2 Hz, 1H), 1.65 (d, *J*=6.0 Hz, 1H), 1.45 (s, 3H), 1.33 (t, *J*=7.5 Hz, 3H), 1.25 (d, *J*=6.3 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 169.9, 137.0, 129.5, 128.1, 126.4, 102.7, 84.1, 61.9, 41.2, 35.5, 23.2, 22.8, 14.2, 11.9; MS (ESI) *m*/*z* 425 ($M+Na^+$), 385 ($M+H^+$)$-H_2O$; IR (neat) 3464, 2985, 1720, 1697, 1376, 1213 cm^{-1}; HRMS (MALDI) calcd for $C_{16}H_{19}O_4INa^+$ ($M+Na^+$): 425.0220. Found: 425.0225.

4.2.4. (1S,2R*,5R*)-1-(Ethoxycarbonyl)-2-phenyl-4-heptyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol (**2d**)*

The reaction of **1d** (165 mg, 0.5 mmol) and NIS (135 mg, 0.6 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1*S**,2*R**,4*R**,5*R**)-**2d** (41 mg, 17%) and (1*S**,2*R**,4*S**,5*R**)-**2d** (157 mg, 67%).

4.2.4.1. (1S,2R*,4R*,5R*)-1-(Ethoxycarbonyl)-2-phenyl-4-heptyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1S*,2R*,4R*,5R*)-**2d**).* Oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.51–7.48 (m, 2H), 7.35–7.30 (m, 3H), 6.15 (s, 1H), 4.39–4.21 (m, 3H), 2.04–1.96 (m, 2H), 1.86 (d, *J*=6.3 Hz, 1H), 1.68–1.63 (m, 2H), 1.55 (d, *J*=6.6 Hz, 1H), 1.36 (t, *J*=6.3 Hz, 3H), 1.45–1.26 (m, 8H), 0.88 (t, *J*=6.6 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.3, 141.0, 128.4, 128.1, 125.7, 103.9, 85.1, 62.3, 43.4, 38.2, 31.9, 29.32, 29.27, 26.9, 26.8, 22.6, 14.2, 14.1, 13.1; MS (ESI) *m*/*z* 495 ($M+Na^+$), 455 ($M+H^+$)$-H_2O$; IR (neat) 3428, 2925, 1735, 1697, 1600, 1449, 1375, 1177 cm^{-1}; HRMS (MALDI) calcd for $C_{21}H_{29}O_4INa^+$ ($M+Na^+$): 495.1003. Found: 495.1000.

4.2.4.2. (1S,2R*,4S*,5R*)-1-(Ethoxycarbonyl)-2-phenyl-4-heptyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1S*,2R*,4S*,5R*)-**2d**).* Oil. ^1H NMR (300 MHz, $CDCl_3$) δ 7.53–7.50 (m, 2H), 7.36–7.32 (m, 3H), 6.11 (s, 1H), 4.64 (dd, *J*=8.4, 2.4 Hz, 1H), 4.38–4.20 (m, 2H), 1.95–1.88 (m, 1H), 1.78 (d, *J*=6.3 Hz, 1H), 1.64–1.48 (m, 4H), 1.41–1.25 (m, 11H), 0.89 (t, *J*=6.3 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.3, 140.0, 128.5, 128.1, 125.6, 103.2, 84.6, 62.2, 42.7, 31.7, 29.64, 29.58, 29.1, 26.2, 22.6, 22.5, 14.2, 14.1, 12.7; MS (ESI) *m*/*z* 495 ($M+Na^+$), 455 ($M+H^+$)$-H_2O$; IR (neat) 3433, 2928, 1735 (sh), 1696, 1449, 1375, 1174 cm^{-1}; HRMS (MALDI) calcd for $C_{21}H_{29}O_4INa^+$ ($M+Na^+$): 495.1003. Found: 495.1012.

4.2.5. (1R,2R*,5R*)-1-Acetyl-2-methyl-4-heptyl-5-iodo-3-oxabicyclo[3.1.0]-hexan-2-ol (**2e**)*

The reaction of **1e** (119 mg, 0.5 mmol) and NIS (135 mg, 0.6 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1*R**,2*R**,4*R**,5*R**)-**2e** (40 mg, 21%) and (1*R**,2*R**,4*S**,5*R**)-**2e** (97 mg, 51%).

4.2.5.1. (1R,2R*,4R*,5R*)-1-Acetyl-2-methyl-4-heptyl-5-iodo-3-oxabicyclo[3.1.0]-hexan-2-ol ((1R*,2R*,4R*,5R*)-**2e**).* Oil. ^1H NMR (300 MHz, $CDCl_3$) δ 4.39 (s, 1H), 3.98 (dd, *J*=11.1, 3.6 Hz, 1H), 2.39 (s, 3H), 1.92–1.73 (m, 2H), 1.77 (d, *J*=5.7 Hz, 1H), 1.63–1.40 (m, 1H), 1.53 (d, *J*=6.6 Hz, 1H), 1.45 (s, 3H), 1.40–1.26 (m, 9H), 0.86 (t, *J*=6.0 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 205.6, 104.0, 84.5, 48.5, 37.6, 31.8, 29.6, 29.3, 29.2, 27.8, 26.8, 24.6, 22.6, 14.1, 13.3; MS (ESI) *m*/*z* 403 ($M+Na^+$), 363 ($M+H^+$)$-H_2O$; IR (neat) 3435, 2925, 1679, 1456, 1363, 1192 cm^{-1}; HRMS calcd for $C_{15}H_{25}O_3INa^+$ ($M+Na^+$): 403.0741. Found: 403.0751.

4.2.5.2. (1R,2R*,4S*,5R*)-1-Acetyl-2-methyl-4-heptyl-5-iodo-3-oxabicyclo[3.1.0]-hexan-2-ol ((1R*,2R*,4S*,5R*)-**2e**).* Solid, mp 55–58 °C (petroleum ether/ether). ^1H NMR (300 MHz, $CDCl_3$) δ 4.65 (s, 1H), 4.36 (m, 1H), 2.34 (s, 3H), 1.88–1.75 (m, 1H), 1.67 (d, *J*=6.3 Hz, 1H), 1.48 (d, *J*=6.3 Hz, 1H), 1.44 (s, 3H), 1.40–1.25 (m, 11H), 0.85 (t, *J*=6.6 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 205.8, 103.3, 83.9, 48.0, 31.7, 29.55, 29.53, 29.2, 29.1, 26.2, 23.7, 23.5, 22.6, 14.1, 13.8; MS (ESI) *m*/*z* 403 ($M+Na^+$), 363 ($M+H^+$)$-H_2O$; IR (neat) 3418, 2927, 1674, 1363, 1199 cm^{-1}; HRMS calcd for $C_{15}H_{25}O_3INa^+$ ($M+Na^+$): 403.0741. Found: 403.0744.

4.2.6. (1S,2R*,4S*,5R*)-1-(Ethoxycarbonyl)-4-phenyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-one ((1S*,2R*,4S*,5R*)-**2f**)*

The reaction of **1f** (122 mg, 0.5 mmol) and NIS (135 mg, 0.6 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1*S**,2*R**,4*S**,5*R**)-**2f** (148 mg, 76%) as a solid, mp 108–110 °C (petroleum ether/ether). ^1H NMR (300 MHz, $CDCl_3$) δ 7.50–7.47 (m, 2H), 7.40–7.36 (m, 3H), 5.53 (s, 1H), 5.19 (s, 1H), 4.41–4.25 (m, 2H), 1.79 (d, *J*=6.3 Hz, 1H), 1.76 (d, *J*=6.3 Hz, 1H), 1.60 (s, 3H), 1.37 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 169.9, 135.0, 128.6, 128.2, 127.4, 103.0. 84.8, 62.1, 42.2, 23.3, 22.4, 14.2, 13.6; MS (ESI) *m*/*z* 411 ($M+Na^+$), 371 ($M+H^+$)$-H_2O$; IR (neat) 3453, 2984, 1719, 1696, 1376, 1214 cm^{-1}. Anal. Calcd for $C_{15}H_{17}O_4I$: C, 46.71; H, 4.41. Found: C, 46.40; H, 4.39.

4.2.7. (1R,2R*,4S*,5S*)-1-Phenylsulfonyl-2-methyl-4-butyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1R*,2R*,4S*,5S*)-**2g**)*

The reaction of **1g** (144 mg, 0.5 mmol) and NIS (135 mg, 0.6 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1*R**,2*R**,4*S**,5*S**)-**2g** (180 mg, 83%) as a solid, mp 123–126 °C (Et_2O/hexane). ^1H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, *J*=7.5 Hz, 2H), 7.66 (t, *J*=6.9 Hz, 1H), 7.54 (d, *J*=6.9 Hz, 2H), 4.22 (d, *J*=7.2 Hz, 1H), 3.75 (s, 1H), 2.11 (d, *J*=6.6 Hz, 1H), 1.91–1.85 (m, 1H), 1.56 (d, *J*=6.3 Hz, 1H), 1.43–1.24 (m, 5H), 1.02 (s, 3H), 0.87 (t, *J*=5.4 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 138.9, 134.1, 129.8, 128.8, 102.6, 82.3, 55.1, 28.7, 28.0, 23.4, 22.6, 22.5, 13.8, 8.4; MS (ESI) *m*/*z* 459 ($M+Na^+$), 419 ($M+H^+$)$-H_2O$; IR (neat) 3471, 2933, 1447, 1391, 1307, 1151 cm^{-1}. Anal. Calcd for $C_{16}H_{21}O_4SI$: C, 44.05; H, 4.85. Found: C, 44.29; H, 4.70.

4.2.8. (1R,2R*,4S*,5S*)-1-Phenylsulfonyl-2-methyl-4-heptyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1R*,2R*,4S*,5S*)-**2h**)*

The reaction of **1h** (167 mg, 0.5 mmol) and NIS (136 mg, 0.6 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1*R**,2*R**,4*S**,5*S**)-**2h** (151 mg, 80%) as a solid, mp 85–87 °C (ether/hexane). ^1H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, *J*=8.1 Hz, 2H), 7.67 (t, *J*=5.4 Hz, 1H), 7.54 (t, *J*=8.1 Hz, 2H), 4.23–4.21 (m, 1H), 3.66 (br s, 1H), 2.10 (d, *J*=6.6 Hz, 1H), 1.90–1.83 (m, 1H), 1.56 (d, *J*=6.0 Hz, 1H), 1.47–1.16 (m, 11H), 1.02 (s, 3H), 0.84 (m, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 138.9, 134.1, 129.8, 128.8, 102.6, 82.3, 55.1, 31.7, 29.4, 29.1, 29.0, 25.9, 23.4, 22.6, 22.5, 14.0, 8.4; MS (ESI) *m*/*z* 501 ($M+Na^+$), 461 ($M+H^+$)$-H_2O$; IR (neat) 3465, 2928, 1449, 1391, 1303, 1153 cm^{-1}. Anal. Calcd for $C_{19}H_{27}O_4SI$: C, 47.70; H, 5.69. Found: C, 48.07; H, 5.62.

4.2.9. (1R,2R*,4S*,5S*)-1-Phenylsulfonyl-2-methyl-4-octyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1R*,2R*,4S*,5S*)-**2i**)*

The reaction of **1i** (52 mg, 0.15 mmol) and NIS (41+17 mg, 0.26 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1*R**,2*R**,4*S**,5*S**)-**2i** (55 mg, 72%) as a liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J=7.5 Hz, 2H), 7.68 (t, J=7.2 Hz, 1H), 7.56 (t, J=8.4 Hz, 2H), 4.22 (d, J=6.3 Hz, 1H), 3.76 (s, 1H), 2.10 (d, J=6.3 Hz, 1H), 1.91–1.84 (m, 1H), 1.57 (d, J=6.3 Hz, 1H), 1.44–1.25 (m, 13H), 1.01 (s, 3H), 0.86 (t, J=6.3 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 138.8, 134.2, 129.8, 128.9, 102.6, 82.4, 55.1, 31.8, 29.5, 29.3, 29.2, 29.1, 26.0, 23.5, 22.59, 22.56, 14.1, 8.3; MS (ESI) m/z 515 ($M+Na^+$), 475 ($M+H^+$)$-H_2O$; IR (neat) 3457, 2922, 1448, 1390, 1305, 1156 cm^{-1}; HRMS (MALDI) calcd for $C_{20}H_{29}O_4SINa^+$: 515.0724. Found: 515.0745.

4.2.10. (1R,2R*,4S*,5S*)-1-p-Methylphenylsulfonyl-2-methyl-4-octyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1R*,2R*,4S*,5S*)-**2j**)*

The reaction of **1j** (39 mg, 0.12 mmol) and NIS (39 mg, 0.18 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1*R**,2*R**,4*S**,5*S**)-**2j** (34 mg, 62%) as a liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J=8.1 Hz, 2H), 7.36 (t, J=8.1 Hz, 2H), 4.25–4.22 (m, 1H), 3.78 (s, 1H), 2.46 (s, 3H), 2.10 (d, J=6.3 Hz, 1H), 1.91–1.85 (m, 1H), 1.56 (d, J=6.6 Hz, 1H), 1.44–1.26 (m, 11H), 1.01 (s, 3H), 0.86 (t, J=6.6 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 145.3, 135.9, 129.8, 129.6, 102.6, 82.4, 55.0, 31.7, 29.5, 29.09, 29.06, 25.98, 23.5, 22.60, 22.58, 21.7, 14.1, 8.4; MS (ESI) m/z 515 ($M+Na^+$), 475 ($M+H^+$)$-H_2O$; IR (neat) 3454, 2928, 1596, 1466, 1402, 1302, 1175 cm^{-1}; HRMS (MALDI) calcd for $C_{20}H_{29}O_4SINa^+$: 515.0724. Found: 515.0727.

4.2.11. (1R,2R*,4S*,5S*)-1-Phenylsulfonyl-2-methyl-4-cyclohexyl-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1R*,2R*,4S*,5S*)-**2k**)*

The reaction of **1k** (38 mg, 0.12 mmol) and NIS (42 mg, 0.18 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1*R**,2*R**,4*S**,5*S**)-**2k** (36 mg, 65%) as a solid, mp 118–119 °C (petroleum ether/ethyl acetate). ^1H NMR (300 MHz, $CDCl_3$) δ 8.07 (d, J=8.4 Hz, 2H), 7.68 (t, J=7.2 Hz, 1H), 7.56 (t, J=7.8 Hz, 2H), 4.10 (d, J=3.3 Hz, 1H), 3.84 (s, 1H), 2.21 (d, J=6.3 Hz, 1H), 1.95–1.86 (m, 1H), 1.75–1.62 (m, 5H), 1.32–1.10 (m, 6H), 1.01 (s, 3H); ^{13}C NMR (75.4 MHz, DMSO) δ 139.6, 133.7, 129.9, 128.4, 102.0, 83.4, 54.4, 37.4, 30.2, 26.1, 26.0, 25.7, 25.6, 22.7, 22.6, 7.01; MS (ESI) m/z 485 ($M+Na^+$), 445 ($M+H^+$)$-H_2O$; IR (neat) 3427, 2852, 1450, 1387, 1312, 1153 cm^{-1}. Anal. Calcd for $C_{18}H_{23}O_4SI$: C, 46.76; H, 5.01. Found: C, 46.94; H, 5.11.

4.2.12. (1R,2R*,4S*,5S*)-1-Phenylsulfonyl-2-methyl-4-(2-hydroxyethyl)-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1R*,2R*,4S*,5S*)-**2l**)*

The reaction of **1l** (62 mg, 0.16 mmol) and NIS (55 mg, 0.24 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1*R**,2*R**,4*S**,5*S**)-**2l** (55 mg, 83%) as a liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J=8.4 Hz, 2H), 7.68 (t, J=7.5 Hz 1H), 7.56 (t, J=8.1 Hz, 2H), 4.52 (s, 1H), 4.42 (dd, J=10.2, 2.1 Hz, 1H), 3.76–3.71 (m, 2H), 2.22–2.11 (m, 2H), 2.12 (d, J=6.9 Hz, 1H), 1.56 (d, J=6.6 Hz, 1H), 1.57–1.47 (m, 1H), 1.02 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 138.7, 134.2, 129.9, 128.9, 103.1, 80.8, 59.8, 55.0, 31.5, 23.4, 22.5, 7.6; MS (ESI) m/z 442 ($M+NH_4^+$), 407 ($M+H^+$)$-H_2O$; IR (neat) 3474, 2926, 1447, 1307, 1150 cm^{-1}; HRMS (MALDI) calcd for $C_{14}H_{17}O_5SINa^+$ ($M+Na$) $^+$: 446.9734. Found: 446.9725.

4.2.13. (1R,2R*,4S*,5S*)-1-p-Methylphenylsulfonyl-2-methyl-4-(2-hydroxyethyl)-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1R*,2R*,4S*,5S*)-**2m**)*

The reaction of **1m** (41 mg, 0.10 mmol) and NIS (35 mg, 0.15 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1*R**,2*R**,4*S**,5*S**)-**2m** (30 mg, 68%) as a liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J=8.1 Hz, 2H), 7.36 (d, J=8.1 Hz, 2H), 4.42 (dd, J=1.8, 10.2 Hz, 1H), 4.19 (s, 1H), 3.79–3.76 (m, 2H), 2.45 (s, 3H), 2.23–2.10 (m, 2H), 2.12 (d, J=6.3 Hz, 1H), 1.59–1.49 (m, 1H), 1.57 (d, J=6.6 Hz, 1H), 1.00 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 145.5, 135.7, 129.9, 129.6, 103.1, 81.2, 60.1, 54.9, 31.5, 23.5, 22.5, 21.7, 7.5; MS (ESI) m/z 456 ($M+NH_4^+$), 421 ($M+H^+$)$-H_2O$; IR (neat) 3477, 2923, 1597, 1303, 1147 cm^{-1}; HRMS (MALDI) calcd for $C_{15}H_{19}O_5SINa^+$ ($M+Na$)$^+$: 460.9890. Found: 460.9898.

4.2.14. (1S,2R*,5R*) -1-(Ethoxycarbonyl)-2-methyl-4,4-pentamethylene-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1S*,2R*,5R*)-**2n**)*

The reaction of **1n** (103 mg, 0.44 mmol) and NIS (118 mg, 0.52 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1*S**,2*R**,5*R**)-**2n** (121 mg, 73%) as a solid, mp 56–57 °C (petroleum ether). ^1H NMR (300 MHz, $CDCl_3$) δ 5.08 (s, 1H), 4.39–4.18 (m, 2H), 2.20–2.16 (m, 1H), 1.89–1.79 (m, 1H), 1.72–1.39 (m, 12H), 1.34 (t, J=7.2 Hz, 3H), 1.24–1.12 (m, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.1, 102.8, 85.7, 61.9, 42.0, 37.8, 31.8, 25.6, 25.4, 24.9, 22.40, 22.36, 20.5, 14.2; MS (ESI) m/z 403 ($M+Na^+$), 363 ($M+H^+$)$-H_2O$; IR (neat) 3454, 2936, 1697, 1447, 1376, 1203 cm^{-1}; HRMS (MALDI) calcd for $C_{14}H_{21}O_4INa^+$ ($M+Na^+$): 403.0377. Found: 403.0375. Anal. Calcd for $C_{14}H_{21}O_4I$: C, 44.22; H, 5.71. Found: C, 44.17; H, 5.71.

4.2.15. (1R,2R*,5R*)-1-Phenylsulfonyl -2-methyl-4,4-pentamethylene-5-iodo-3-oxabicyclo[3.1.0]hexan-2-ol ((1R*,2R*,5S*)-**2o**)*

The reaction of **1o** (31 mg, 0.1 mmol) and NIS (27 mg, 0.12 mmol) in 2 mL of CH_3CN and 0.2 mL of H_2O afforded (1*R**,2*R**,5*S**)-**2o** (28 mg, 61%) as a solid, mp 102–104 °C (decomposition). ^1H NMR (300 MHz, $CDCl_3$) δ 8.12 (d, J=7.2 Hz, 2H), 7.66 (t, J=7.5 Hz, 1H), 7.54 (t, J=7.5 Hz, 2H), 3.26 (s, 1H), 2.10 (d, J=6.3 Hz, 1H), 1.96–1.86 (m, 1H), 1.75–1.35 (m, 9H), 1.14 (s, 4H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 139.0, 133.9, 130.0, 128.6, 102.7, 84.4, 55.9, 38.0, 31.1, 26.1, 25.1, 24.5, 22.2, 22.1, 16.2; MS (EI) m/z 448 (M^+, 21.61), 321 (100); IR (neat) 3479, 2936, 1577, 1447, 1307, 1150 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{21}O_4ISNa^+$ ($M+Na^+$): 471.0097. Found: 471.0095.

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Supplementary data

The $^1H/^{13}C$ NMR spectra of all the products. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.06.060.

References and notes

1. (a) Koft, E. R.; Smith, A. B., III. *J. Am. Chem. Soc.* **1982**, *104*, 2659; (b) Smith, A. B., III; Huryn, D. M. *J. Org. Chem.* **1985**, *50*, 1342; (c) Smith, A. B., III; Yokoyama, Y.; Dunlap, N. K. *Tetrahedron Lett.* **1987**, *28*, 3663.
2. Mann, J.; Thomas, A. *Tetrahedron Lett.* **1986**, *27*, 3533.
3. Kohmoto, S. K.; Koyano, I.; Funabashi, T.; Kishikawa, K.; Yamamoto, M.; Yamada, K. *Tetrahedron Lett.* **1995**, *36*, 553.
4. Epe, B.; Trautmann, D.; Mondon, A. *Tetrahedron Lett.* **1979**, *20*, 1365.
5. Martin, S. F.; Hom, R. K. *Tetrahedron Lett.* **1999**, *40*, 2887.
6. Tanaka, K.; Matsuura, H.; Funaki, I.; Suzuki, H. *J. Chem. Soc., Chem. Commun.* **1991**, 1145.
7. Baird, M. S.; Huber, F. A.; Tverezovsky, V. V.; Bolesov, I. G. *Tetrahedron* **2000**, *56*, 4799.
8. For reviews, see: (a) Binger, P.; Büch, H. M. *Top. Curr. Chem.* **1987**, *135*, 77; (b) Ohta, T.; Takaya, H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol. 5, p 1185; (c) *Carbocyclic Three-Membered Ring Compounds: Methods of Organic Chemistry (Houben-Weyl)*, 4th ed.; de Meijere, A., Ed.; 1997; Vol. E17, p 2217; (d) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49; (e) Brandi, A.; Goti, A. *Chem. Rev.* **1998**, *98*, 589;

(f) Nakamura, I.; Yammamoto, Y. *Adv. Synth. Catal.* **2002**, *344*, 111; (g) Brandi, A.; Cicchi, S.; Cordero, F. M.; Goti, A. *Chem. Rev.* **2003**, *103*, 1213.
9. (a) Noyori, R.; Hayashi, N.; Katô, M. *J. Am. Chem. Soc.* **1971**, *93*, 4948; (b) Yamago, S.; Nakamura, E. *J. Am. Chem. Soc.* **1989**, *111*, 7285; (c) Lautens, M.; Han, W. *J. Am. Chem. Soc.* **2002**, *124*, 6312; (d) Nötzel, M. W.; Rauch, K.; Labahn, T.; Meijere, A. *Org. Lett.* **2002**, *4*, 839; (e) Lautens, M.; Han, W.; Liu, J. H.-C. *J. Am. Chem. Soc.* **2003**, *125*, 4028; (f) Lu, L.; Chen, G.; Ma, S. *Org. Lett.* **2006**, *8*, 835; (g) Taillier, C.; Lautens, M. *Org. Lett.* **2007**, *9*, 591; (h) Huang, X.; Yang, Y. *Org. Lett.* **2007**, *9*, 1667.
10. Goti, A.; Anichini, B.; Brandi, A.; Kozhushkov, S.; Gratkowski, C.; Meijere, A. *J. Org. Chem.* **1996**, *61*, 1665.
11. Bottini, A. T.; Cabral, L. J. *Tetrahedron* **1978**, *34*, 3187.
12. (a) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1; (b) Suginome, M.; Matsuda, T.; Ito, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11015; (c) Nakamura, I.; Oh, B. H.; Saito, S.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 1298; (d) Camacho, D. H.; Nakamura, I.; Saito, S.; Yamamoto, Y. *J. Org. Chem.* **2001**, *66*, 270; (e) Shi, M.; Xu, B. *Org. Lett.* **2002**, *4*, 2145; (f) Huang, X.; Zhou, H. *Org. Lett.* **2002**, *4*, 4419; (g) Delgado, A.; Rodriguez, J. R.; Castedo, L.; Mascareñas, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 9282; (h) Krafft, M. E.; Boñaga, L. V. R.; Felts, A. S.; Hirosawa, C.; Kerrigan, S. *J. Org. Chem.* **2003**, *68*, 6039.
13. (a) Ma, S.; Zhang, J. *Angew. Chem., Int. Ed.* **2003**, *42*, 183; (b) Ma, S.; Lu, L.; Zhang, J. *J. Am. Chem. Soc.* **2004**, *126*, 9645.
14. Ma, S.; Lu, L. *J. Org. Chem.* **2005**, *70*, 7629.
15. Crystal data for compound **2e**: $C_{15}H_{25}O_3I$, MW=380.25, monoclinic, space group $P2(1)/n$, final R indices [$I>2\sigma(I)$], $R1$=0.0480, $wR2$=0.0945, R indices (all data), $R1$=0.0699, $wR2$=0.1032, a=5.5873(7) Å, b=23.713(3) Å, c=12.9064(17) Å, α=90°, β=100.286(6)°, γ=90°, V=1682.5(4) Å^3, T=293(2) K, Z=4, reflections collected/unique: 9918/3646 (R(int)=0.0854), parameters 176. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center. CCDC: 675216.
16. Crystal data for compound **2f**: $C_{15}H_{17}O_4I$, MW=388.19, orthorhombic, space group $Pca2(1)$, final R indices [$I>2\sigma(I)$], $R1$=0.0430, $wR2$=0.1009, R indices (all data), $R1$=0.0594, $wR2$=0.1114, a=24.413(4) Å, b=5.5093(9) Å, c=23.070(4) Å, α=90°, β=90°, γ=90°, V=3148.5(9) Å^3, T=293(2) K, Z=8, reflections collected/unique: 17,364/6890 (R(int)=0.0803), parameters 367. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center. CCDC: 675219.
17. Crystal data for compound **2g**: $C_{16}H_{21}O_4IS$, MW=436.29, monoclinic, space group $P2(1)/n$, final R indices [$I>2\sigma(I)$], $R1$=0.0602, $wR2$=0.1665, R indices (all data), $R1$=0.0925, $wR2$=0.1838, a=5.8129(7) Å, b=23.903(3) Å, c=13.1603(15) Å, α=90°, β=94.138(2)°, γ=90°, V=1823.8(4) Å^3, T=293(2) K, Z=4, reflections collected/unique: 10,734/3964 (R(int)=0.0746), parameters 192. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center. CCDC: 609200.
18. Crystal data for compound **2h**: $C_{19}H_{27}O_4IS$, MW=478.37, monoclinic, space group $P2(1)/c$, final R indices [$I>2\sigma(I)$], $R1$=0.0523, $wR2$=0.1251, R indices (all data), $R1$=0.0648, $wR2$=0.1324, a=18.310(2) Å, b=8.3333(11) Å, c=13.8883(18) Å, α=90°, β=90.091(2)°, γ=90°, V=2119.2(5) Å^3, T=293(2) K, Z=4, reflections collected/unique: 12,017/4625 (R(int)=0.0958), parameters 230. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center. CCDC: 675218.
19. Crystal data for compound **2c**: $C_{16}H_{19}O_4I$, MW=402.21, triclinic, space group $P\bar{1}$, final R indices [$I>2\sigma(I)$], $R1$=0.0306, $wR2$=0.0878, R indices (all data), $R1$=0.0354, $wR2$=0.1033, a=9.2595(11) Å, b=10.4975(12) Å, c=10.5681(12) Å, α=115.660(5)°, β=112.581(6)°, γ=92.261(6)°, V=828.41(17) Å^3, T=296(2) K, Z=2, reflections collected/unique: 6008/2806 (R(int)=0.0198), parameters 190. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center. CCDC: 690548.
20. Crystal data for compound **2n**: $C_{14}H_{21}O_4I$, MW=380.21, triclinic, space group $P\bar{1}$, final R indices [$I>2\sigma(I)$], $R1$=0.0693, $wR2$=0.1869, R indices (all data), $R1$=0.0857, $wR2$=2046, a=13.4652(11) Å, b=15.2074(12) Å, c=16.2382(13) Å, α=74.6950(10)°, β=71.977(2)°, γ=81.322(2)°, V=3041.1(4) Å^3, T=293(2) K, Z=8, reflections collected/unique: 16,151/11,183 (R(int)=0.1319), parameters 703. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center. CCDC: 675217.
21. Taherirastgar, F.; Brandsma, L. *Synth. Commun.* **1997**, *27*, 4035.
22. Regitz, M.; Hocher, J. *Org. Synth. Coll.* **1973**, *V*, 179.
23. Cheng, C.; Shimo, T.; Somekawa, K.; Baba, M. *Tetrahedron* **1998**, *54*, 2031.