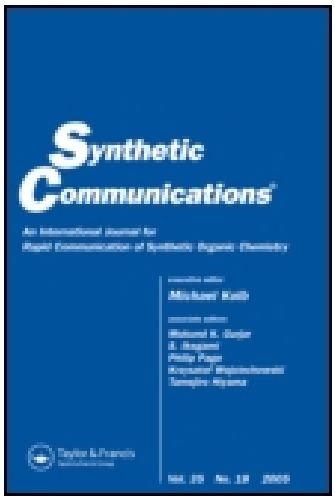

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Christopher J. Nichols [a]

[a] Department of Chemistry , California State University , Chico, California, USA

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The Formation of 7-Oxabicyclo[4.2.0]octanes and 6-Oxabicyclo[3.2.1]octanes via Cationic Iodocyclization

Christopher J. Nichols*

Department of Chemistry, California State University, Chico, California, USA

ABSTRACT

Several 2-cyclohexenemethanol derivatives were subjected to cationic iodocyclization. Two product types were formed: the fused 7-oxabicyclo[4.2.0]octane, and the bridged 6-oxabicyclo[3.2.1]octane. The degree of substitution in the alkenol determined the ratio of the products, with aromatic substituents leading to the formation of the fused system as the major product.

Key Words: Oxabicyclooctane; Etherification; Oxetane.

*Correspondence: Christopher J. Nichols, Assistant Professor of Chemistry, Department of Chemistry, California State University, 400 W. 1st St., Chico, CA, USA 95929-0210; Fax: 1-530-898-5234; E-mail: cjnichols@csuchico.edu.

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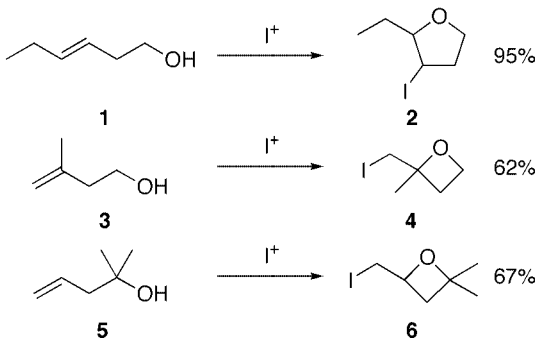
INTRODUCTION

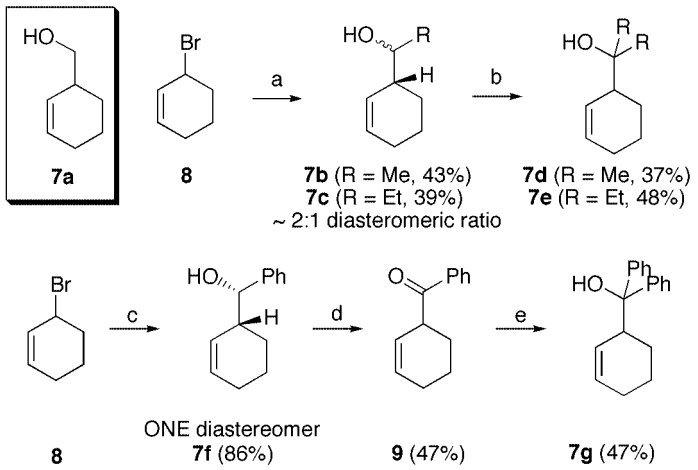
The use of iodonium species to convert an alkenol to a cyclic iodoether has been extensively studied.[1] Schauble and others have shown that when homoallylic alcohols are treated with a source of I^+ (either $I(coll)_2ClO_4$ or $I_2/NaHCO_3$), the major product is generally the less strained 5-membered tetrahydrofuran ring, such as the compound **2** (Sch. 1).[2] This 5-*endo* cyclization is particularly favored in the case of a 1,2-disubstituted alkene. An oxetane (compounds **4** or **6**, formed via a 4-*exo* cyclization) can only be obtained if either the proximal carbon is substituted (as in the alcohol **3**), or if extra alkyl groups are added to the system (as in the dimethyl alcohol **5**). This so-called geminal dialkyl effect[3] has demonstrated the ability to greatly affect the course of a cyclization, both in terms of relative reaction rates and regiochemistry.[4] In a continuing investigation of the synthesis of oxetanes through iodocyclization,[5] this research focused on the formation of bicyclic molecules by treating derivatives of 2-cyclohexenemethanol **7a** with a source of I^+, namely iodonium *bis-sym*-collidine perchlorate.[6]

RESULTS AND DISCUSSION

2-Cyclohexenemethanol **7a** itself was made by literature methods in two steps from benzoic acid.[7] The other homoallylic alcohols **7b–g** were made by treating 3-bromocyclohexene **8** with powdered metallic tin and the appropriate aldehyde (Sch. 2). The use of benzaldehyde had been found to lead to the formation of only one diastereomer of the alcohol **7f**, but with aliphatic aldehydes (acetaldehyde and propionaldehyde) the



Scheme 1.

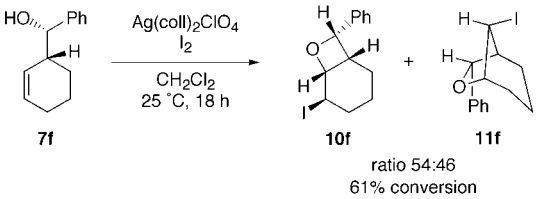


Scheme 2. Reagents and Conditions: (a) Sn, MeCHO or EtCHO, THF/NH_4Cl (aq.) 6:1, 0°C to rt, 2 d; (b) i. TPAP/NMO, CH_2Cl_2, 4 h, ii. MeLi or EtMgBr, THF, −78°C to rt, 20 h; (c) Sn, PhCHO, THF/NH_4Cl (aq.) 6:1, 65°C, 20 h; (d) PCC, CH_2Cl_2; (e) PhBr, Mg, ether, 0°C to rt, 20 h.

diastereoselectivity of the reaction which forms the products **7b** and **7c** is less than 2:1.[8] Attempted direct formation of the geminal dialkyl or diaryl derivatives **7d**, **7e**, and **7g** through the addition of symmetrical ketones to the stannylated bromide was unsuccessful. However, oxidation of the monoalkylated species with either pyridinium chlorochromate (PCC) or tetrapropylammonium perruthenate (TPAP) and *N*-methylmorpholine *N*-oxide,[9] followed by immediate treatment with an appropriate alkyl anion (PhMgBr, CH_3Li or EtMgBr) furnished the disubstituted alcohols **7d**, **7e**, and **7g** in a modest yield.

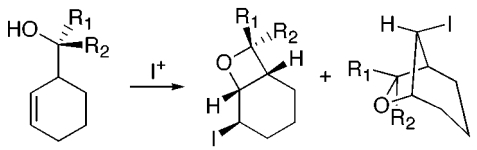
The first alkenol studied, the benzaldehyde derivative **7f**, yielded two different products upon treatment with iodonium *bis-sym*-collidine perchlorate (Sch. 3). These were identified as the 7-oxabicyclo[4.2.0]octane **10f** and the 6-oxabicyclo[3.2.1]octane **11f**, formed in 61% total yield and in a 54:46 ratio. These products were separated by column chromatography, and COSY and NOESY studies established the identity and relative stereochemistry of the two products. This analysis also confirmed the stereochemistry of the alcohol **7f**, which had up to this point been assigned based on literature reports.[8]

When other cyclohexenemethanols were treated in the same fashion the differences in product ratios were striking (Table 1). The



Scheme 3.

Table 1.



Starting material	R_1, R_2	Ration of **10**:**11**	Yield (%)	Time for 90% loss of **7**
7a	H, H	0:100	40[b]	10 min
7d	Me, Me	30:70	60[c]	5 h
7e	Et, Et	26:74	81[c]	1 h
7f	Ph, H	54:46	61[c]	15 min
7g	Ph, Ph	62:38	68[b]	—

[a]Typical procedure is as follows: To a solution of $Ag(coll)_2ClO_4$ (5 equiv.) in CH_2Cl_2 is added I_2 (5 equiv.) and the solution is stirred until the I_2 has completely reacted (typically 20–40 min). Then a CH_2Cl_2 solution of alkenol is added, and the mixture is stirred for 18 h. Filtration of the AgI and washing of the organic layer with aq. sodium thiosulfate, 1 M aq. HCl, and aq. sodium bicarbonate is followed by removal of the solvent in vacuo and column chromatography to isolate the products.
[b]Isolated yield.
[c]Yield and product ratio by NMR.

unsubstituted compound **7a** ($R_1 = R_2 = H$) gave exclusively the bridged bicyclic ether **11a**. Iodocyclization in the presence of two geminal methyl or ethyl groups (in **7d** and **7e**) still resulted in the bridged ethers **11d** and **11e** being predominant but now small amounts of the oxetanes **10d** and **10e** were also isolated. Having aromatic rings in the alkenol changed the identity of the major product: for both the monophenyl (**7f**) and diphenyl

(**7g**) alcohols the fused compounds **10f** and **10g** were the major products. This is a similar effect to prior studies[2] as the addition of geminal dialkyl groups led to a higher proportion of the oxetane product. In **7f**, one benzene ring causes more of the oxetane to be formed than do two methyl or ethyl groups—this can be explained by unfavorable steric interactions in the bicyclic product molecule **11f**, where the large aromatic ring is in an endo position.

Kinetic studies using ^{1}H NMR were also carried out at 21°C on the four alcohols **7a**, **7d**, **7e**, and **7f**. They were each treated with four equivalents of $I(coll)_2ClO_4$ (to ensure complete reaction) in $CDCl_3$ and the formation of products followed by the appearance of characteristic peaks (typically of those hydrogen atoms on carbons α to the oxygen atoms) in the ^{1}H NMR. The more substituents the alcohols possessed, the more slowly the cyclizations occurred, which is in contrast to a typical geminal dialkyl effect in which such substituents enhance the rates of cyclization.[3] This is likely a steric effect, with the reaction slowing as the nucleophilic oxygen is hindered by the extra alkyl groups. The rates of reaction and relative ratios of products are both governed by steric interactions but in different senses: the tertiary alcohols slow the reaction down, but the presence of only one alkyl group in position R_2 (see Table 1) is enough to decrease the amount of bridged compound formed.

EXPERIMENTAL

General

Unless otherwise stated, starting materials were obtained from commercial suppliers (Aldrich Chemical, ACROS, Fisher Scientific) and used without purification. THF was distilled over Na/benzophenone, and CH_2Cl_2 was distilled over CaH_2. NMR spectra were recorded on a Varian Mercury VX300, except for compounds **10f** and **11f**, which were sent to the University of California, Santa Barbara for analysis on their Varian UNITY-INOVA 500 MHz spectrometer. FT-IR spectra were recorded on a Mattson Galaxy Series 3000. 2-Cyclohexenemethanol **7a** was synthesized in two steps from benzoic acid according to the method of Walton.[7] Silver (I) *bis*-collidine perchlorate was synthesized from silver nitrate, collidine, and sodium perchlorate.[8]

(1R*,1′RS*)-1-Cyclohex-2-enylethanol (7b). To a solution of 3-bromocyclohexene (1.20 mL, 10.4 mmol) in THF (17 mL) and saturated aqueous ammonium chloride (3 mL) cooled to 0°C was added

acetaldehyde (3.5 mL, 63 mmol) and powdered tin (1.17 g, 9.86 mmol), and the solution was stirred for 44 h, allowing to warm to room temperature. Brine (10 mL) was added, and the mixture was extracted with ether (3×: 20, 20, 50 mL). The combined extracts were dried over $MgSO_4$ and the solvent removed in vacuo. Column chromatography (SiO_2, 15% ethyl acetate/85% hexane) afforded 535.9 mg of **7b** (4.25 mmol, 43%) as a colorless oil, as a 2:1 mixture of two diastereomers.

^{1}H NMR (300 MHz, $CDCl_3$) δ: mixture of 2 diastereomers, 5.5–5.9 (both isomers, 2H, m), 3.77 (major isomer, 1H, qd, $J = 6.3$, 5.1 Hz), 3.67 (minor isomer, 1H, quin, $J = 6.2$ Hz), 1.30–2.10 (both isomers, 8H, m), 1.22 (minor isomer, 3H, d, $J = 6.3$ Hz), 1.20 (major isomer, 3H, d, $J = 6.3$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: major isomer: 130.5, 128.5, 70.9, 42.99, 25.5, 23.5, 21.5, 20.2; minor isomer: 129.9, 127.2, 71.7, 42.97, 25.7, 25.5, 21.9, 21.2; IR (neat) 3360 (br, s), 3024 (s), 2934 (br, s), 1448 (s), 1374 (s), 1086 (s) cm^{-1}.

(1R*,1′RS*)-1-Cyclohex-2-enyl-propan-1-ol (7c). To a slurry of powdered tin (1.24 g, 10.4 mmol) in THF (17 mL) and saturated aq. NH_4Cl (4 mL), cooled to 0°C, was added 3-bromocyclohexene (1.11 mL, 9.6 mmol), followed by propionaldehyde (4.3 mL, 60 mmol). The solution was stirred for 22 h, allowing to warm to room temperature, and the THF was removed by rotary evaporation. Brine (20 mL) was added, and the mixture was extracted with ether (3×: 40, 40, 100 mL). The combined extracts were dried over $MgSO_4$ and the solvent removed in vacuo. Column chromatography (SiO_2, 10% ethyl acetate/90% hexane) afforded 0.52 g of **7c** (3.71 mmol, 39%) as a 72:28 mixture of two diastereomers.

^{1}H NMR (300 MHz, $CDCl_3$) δ: mixture of two diastereomers, 5.86 (both isomers, 1H, m), 5.70 (minor isomer, 1H, dq, $J = 10.1$, 2.5 Hz), 5.54 (major isomer, 1H, dqd, $J = 10.1$, 2.2, 0.8 Hz), 3.49 (major isomer, 1H, dt, $J = 7.5$, 5.0 Hz), 3.36 (minor isomer, 1H, dt, $J = 8.4$, 4.4 Hz), 2.22 (both isomers, 1H, m), 1.98 (both isomers, 2H, m), 1.74 (both isomers, 2H, m), 1.50 (both isomers, 5H, m), 0.96 (both isomers, 3H, t, $J = 7.5$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ: major isomer: 130.7, 129.1, 76.2, 41.0, 26.8, 25.46, 22.8, 21.6, 10.7; minor isomer: 130.3, 127.1, 76.8, 41.1, 27.7, 26.2, 25.51, 22.0, 10.6; IR (neat) 3358 (br, s), 3023 (m), 2931 (s), 1456 (m), 1113 (m), 966 (s), 725 (m) cm^{-1}.

2-Cyclohex-2-enylpropan-2-ol (7d). To a solution of **7b** (66.0 mg, 0.523 mmol) in CH_2Cl_2 (4 mL) was added solid *N*-methylmorpholine *N*-oxide (195 mg, 1.66 mmol) and powdered molecular sieves (ca. 100 mg, 4Å). Tetrapropylammonium perruthenate (39 mg, 0.111 mmol) was then added, and the mixture stirred for 4 h. The solution was filtered through Celite, and the solvent removed in vacuo. THF (5 mL) was

added, and the solution was cooled to −78°C. Methyllithium (1.4 M, 1.5 mL, 2.1 mmol) was added slowly, and the solution was stirred for 16 h, allowing to warm to room temperature. Ether and water were added, and the layers were separated. The aqueous layer was extracted once more with ether, and the organic layers were combined, washed with brine, dried over $MgSO_4$, and the solvent removed in vacuo. Column chromatography (SiO_2, 10% ethyl acetate/90% hexane) afforded 27.3 mg of **7d** (0.195 mmol, 37%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.84 (1H, dq, $J = 10.6$, 3.1 Hz), 5.74 (1H, dquin, $J = 10.5$, 1.5 Hz), 2.15 (1H, m), 1.98 (2H, m), 1.82 (2H, m), 1.52 (2H, m), 1.32 (1H, td, $J = 11.2$, 2.2 Hz), 1.21 (3H, s), 1.17 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 129.9, 127.7, 73.1, 47.1, 28.1, 26.4, 25.4, 24.7, 22.5; IR (neat): 3377 (br, s), 2973 (m), 2930 (m), 1147 (s), 1124 (s) cm^{-1}.

3-Cyclohex-2-enylpentan-3-ol (7e). To a solution of **7c** (170.5 mg, 1.22 mmol) in CH_2Cl_2 (3 mL) was added solid *N*-methylmorpholine *N*-oxide (210 mg, 1.79 mmol) and powdered molecular sieves (ca. 100 mg, 4Å). Tetrapropylammonium perruthenate (24 mg, 0.068 mmol) was then added, and the mixture stirred for 3 h. The solution was filtered through Celite, and the solvent removed in vacuo. THF (5 mL) was added, and the solution was cooled to −78°C. Ethyl magnesium bromide (1.0 M, 2.5 mL, 2.5 mmol) was added slowly, and the solution was stirred for 16 h, allowing to warm to room temperature. Water (2 mL) and HCl (1 M, 2.5 mL) were added, followed by ether (25 mL), and the layers were separated. The aqueous layer was extracted once more with ether, the organic layers were combined and washed with brine, dried over $MgSO_4$, and the solvent removed in vacuo. Column chromatography (SiO_2, 8% ethyl acetate/92% hexane) afforded 98.8 mg of **7e** (0.587 mmol, 48%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.84 (1H, ddtd, $J = 10.4$, 4.7, 2.4, 0.8 Hz), 5.71 (1H, ddq, $J = 10.4$, 2.2, 1.6 Hz), 2.32 (1H, m), 1.96 (2H, m), 1.77 (2H, m), 1.30–1.60 (7H, m), 0.87 (6H, 2 overlapping t, $J_1 = 7.4$ Hz, $J_2 = 7.6$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 130.2, 127.5, 76.1, 42.3, 28.9, 27.9, 25.4, 23.8, 22.6, 7.9, 7.8; IR (neat): 3476 (br, s), 3028 (m), 2966 (s), 2937 (s), 2881 (s), 1136 (s), 949 (s) cm^{-1}.

(1R*,1′S*)-Cyclohex-2-enylphenylmethanol (7f). To a solution of 3-bromocyclohexene (5.36 g, 33.3 mmol) in THF (35 mL) and saturated aqueous ammonium chloride (6 mL) was added benzaldehyde (2.03 mL, 20.0 mmol) and powdered tin (3.57 g, 30.1 mmol). The solution was heated to 65°C for 20 h, and the THF was removed by rotary evaporation. Brine (40 mL) was added, and the mixture was extracted with ether (3×: 75, 75, 200 mL). The combined extracts were dried over $MgSO_4$ and

the solvent removed in vacuo. Column chromatography (SiO_2, 8% ethyl acetate/92% hexane) afforded 3.231 g of **7f** (17.2 mmol, 86%) as a colorless oil, and as a single diastereomer.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.25–7.36 (5H, m), 5.83 (1H, dq, $J = 10.2$, 3.2 Hz), 5.40 (1H, dq, $J = 10.2$, 1.4 Hz), 4.60 (1H, d, $J = 6.6$ Hz), 2.52 (1H, m), 2.00 (2H, m), 1.85 (1H, br s), 1.75 (2H, m), 1.54 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 143.1, 130.7, 128.5, 128.2, 127.6, 126.7, 77.6, 43.2, 25.5, 24.1, 21.3; IR (neat): 3420 (br, s), 1739 (m), 1726 (m), 1459 (m), 1377 (m), 1240 (s), 1060 (m) cm^{-1}.

2-Cyclohexenyl phenyl ketone (9). To a solution of pyridinium chlorochromate (1.71 g, 7.93 mmol) in CH_2Cl_2 (10 mL) was added solid sodium acetate (130 mg, 1.71 mmol) followed by a solution of **7f** (995 mg, 5.28 mmol) in CH_2Cl_2 (5 mL), and the mixture was stirred for 2 h. The mixture was diluted with ether, filtered through Celite, and the solvent was removed in vacuo. Column chromatography (SiO_2, 2% ethyl acetate/98% hexane) afforded 467.0 mg of **9** (2.51 mmol, 47%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.96 (2H, dd, $J = 8.4$, 1.3 Hz), 7.56 (1H, m), 7.47 (2H, m), 5.93 (1H, dtd, $J = 10.1$, 4.0, 2.2 Hz), 5.74 (1H, dq, $J = 10.1$, 2.3 Hz), 4.09 (1H, m), 1.61–2.12 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 202.1, 136.4, 133.1, 130.4, 128.9, 128.7, 125.0, 44.1, 26.1, 25.0, 21.2); IR (neat): 2937 (m), 1682 (s), 1447 (m), 1212 (s), 961 (m), 697 (s) cm^{-1}.

Cyclohex-2-enyldiphenylmethanol (7g). To a round-bottomed flask, charged with Mg turnings (149.2 mg, 6.14 mmol) was added a solution of bromobenzene (0.63 mL, 6.0 mmol), in ether (2 mL). The mixture was treated with ultrasonic waves for 10 min, and then stirred an additional 20 min. The solution was cooled to 0°C, and a solution of **9** (373 mg, 2.00 mmol) in ether (3 mL) was added, and the mixture stirred for 18 h, allowing it to warm to room temperature. The reaction was quenched with water, ether was added, and the layers were separated. The aqueous layer was extracted twice more with ether, and the combined organic extracts were washed with brine and dried over $MgSO_4$. Column chromatography (SiO_2, 2% ethyl acetate/98% hexane) afforded 251.5 mg of **7g** (0.948 mmol, 47%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.61 (2H, m), 7.49 (2H, m), 7.36–7.13 (6H, m), 5.98 (1H, dq, $J = 10.6$, 3.2 Hz), 5.51 (1H, dq, $J = 10.6$, 1.9 Hz), 3.44 (1H, m), 2.23 (1H, br s), 2.02 (2H, m), 1.79 (1H, m), 1.61–1.42 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 147.1, 145.7, 134.0, 128.5, 128.2, 126.8, 126.6, 126.4, 126.3, 125.7, 79.6, 43.9, 25.5, 24.0, 22.2; IR (neat): 3553 (m), 3024 (w), 2972 (m), 1493 (m), 1447 (m) cm^{-1}.

(1R*, 5R*, 8R*)-8-Iodo-6-oxabicyclo[3.2.1]octane (11a). To a solution of silver (I) *bis*-collidine perchlorate (262 mg, 0.464 mmol) in

CH_2Cl_2 (8 mL) was added solid iodine (136 mg, 0.536 mmol), and the solution was stirred for 60 min. To this mixture was added 2-cyclohexene-1-methanol **7a** (52.1 mg, 0.464 mmol), and the mixture was stirred for 18 h. The solid silver iodide was filtered out, and the solution was washed with sodium thiosulfate (10% aq.), dilute HCl (1 M), saturated aq. sodium bicarbonate, dried over $MgSO_4$, and the solvent removed in vacuo. Column chromatography (SiO_2, 5% ethyl acetate/95% hexane) afforded 43.9 mg of **11a** (0.184 mmol, 40%) as a slightly yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.20 (1H, m), 4.15 (1H, t, $J = 4.8$ Hz), 3.87 (1H, s), 3.86 (1H, s), 2.28 (1H, m), 2.10 (1H, ddd, $J = 15.5$, 13.8, 4.1 Hz), 1.97 (1H, m), 1.35–1.75 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 77.4, 69.9, 39.7, 30.0, 27.6, 26.9, 17.5; IR (neat): 2942 (s), 2873 (s), 1089 (m), 1066 (m), 980 (m), 750 (m) cm^{-1}.

(1R*,5S*,6S*)-5-Iodo-8,8-dimethyl-7-oxabicyclo[4.2.0]octane (10d) and (1R*,5R*,8R*)-8-iodo-7,7-dimethyl-6-oxabicyclo[3.2.1]octane (11d). To a solution of silver (I) *bis*-collidine perchlorate (640 mg, 1.42 mmol) in CH_2Cl_2 (5 mL) was added solid iodine (370 mg, 1.46 mmol), and the solution was stirred for 40 min. To this mixture was added a solution of **7d** (39.0 mg, 0.278 mmol) in CH_2Cl_2 (2 mL), and the mixture was stirred for 2d. The solid silver iodide was filtered out, and the solution was washed with sodium thiosulfate (10% aq.), dilute HCl (1 M), saturated aq. sodium bicarbonate, dried over $MgSO_4$, and the solvent removed in vacuo. Column chromatography (SiO_2, 5% ethyl acetate/95% hexane) afforded 13.6 mg of **10d** (0.051 mmol, 18%) and 13.2 mg of **11d** (0.050 mmol, 18%) as colorless oils.

10d: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.91 (1H, dd, $J = 8.3$, 6.1 Hz), 4.32 (1H, ddd, $J = 9.2$, 5.7, 4.4 Hz), 2.59 (1H, q, $J = 7.6$ Hz), 2.17 (1H, dtd, $J = 14.5$, 6.1, 4.4 Hz), 1.42–1.92 (5H, m), 1.40 (3H, s), 1.26 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 84.8, 80.3, 41.7, 32.4, 30.5, 30.3, 25.2, 20.8, 18.4; IR (neat): 2943 (s), 1458 (m), 1369 (m), 1143 (s), 1000 (m), 947 (m) cm^{-1}.

11d: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.77 (1H, dd, $J = 5.7$, 4.4 Hz), 4.26 (1H, dd, $J = 5.3$, 4.4 Hz), 2.21 (1H, m), 2.09 (1H, m), 1.89 (1H, q, $J = 3.4$ Hz), 1.69–1.83 (3H, m), 1.49 (3H, s), 1.45 (1H, m), 1.27 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 81.0, 78.5, 47.8, 32.5, 32.4, 28.9, 25.3, 25.1, 17.5; IR (neat): 2936 (s), 1446 (m), 1277 (m), 1238 (m), 1090 (m), 1056 (m), 949 (s) cm^{-1}.

(1R*,5S*,6S*)-8,8-Diethyl-5-iodo-7-oxabicyclo[4.2.0]octane (10e) and (1R*,5R*,8R*)-7,7-diethyl-8-iodo-6-oxabicyclo[3.2.1]octane (11e). To a solution of silver (I) *bis*-collidine perchlorate (812 mg, 1.81 mmol) in CH_2Cl_2 (7 mL) was added solid iodine (428 mg, 1.69 mmol), and

the solution was stirred for 30 min. To this mixture was added a solution of **7e** (59.4 mg, 0.353 mmol) in CH_2Cl_2 (3 mL), and the mixture was stirred for 22 h. The solid silver iodide was filtered out, and the solution was washed with sodium thiosulfate (10% aq.), dilute HCl (1 M), saturated aq. sodium bicarbonate, dried over $MgSO_4$, and the solvent removed in vacuo. Column chromatography (SiO_2, 3% ethyl acetate/97% hexane) afforded 9.9 mg of **10e** (0.034 mmol, 10%) and 30.4 mg of **11e** (0.103 mmol, 29%) as colorless oils.

10e: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.88 (1H, dd, $J = 8.2$, 6.6 Hz), 4.37 (1H, ddd, $J = 10.2$, 6.6, 4.9 Hz), 2.62 (1H, q, $J = 8.2$ Hz), 2.23 (1H, quin of d, $J = 7.1$, 4.9 Hz), 1.5–2.0 (9H, m), 0.88 (3H, t, $J = 7.4$ Hz), 0.79 (3H, t, $J = 7.4$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) d: 89.4, 80.6, 40.6, 32.6, 31.1, 30.2, 27.3, 21.0, 17.7, 7.6, 7.5; IR (neat): 2966 (s), 2941 (s), 2879 (m), 1460 (m), 1002 (m), 938 (m), 901 (m) cm^{-1}.

11e: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.80 (1H, t, $J = 5.1$ Hz), 4.24 (1H, t, $J = 4.9$ Hz), 2.23 (1H, m), 2.09 (1H, m), 1.94 (1H, q, $J = 3.3$ Hz), 1.4–1.9 (8H, m), 0.92 (3H, t, $J = 7.6$ Hz), 0.86 (3H, t, $J = 7.6$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) d: 85.2, 77.2, 44.3, 32.2, 30.5, 28.3, 24.6, 23.9, 16.7, 9.8, 8.9; IR (neat) 2961 (s), 2941 (s), 2876 (m), 1467 (m), 1060 (s), 962 (m), 933 (s) cm^{-1}.

(1R*,5S*,6S*,8R*)-5-Iodo-8-phenyl-7-oxabicyclo[4.2.0]octane (10f) and (1R*,5R*,7R*,8R*)-8-iodo-7-phenyl-6-oxabicyclo[3.2.1]octane (11f). To a solution of silver (I) *bis*-collidine perchlorate (1010 mg, 2.25 mmol) in CH_2Cl_2 (12 mL) was added solid iodine (480 mg, 1.89 mmol), and the solution was stirred for 30 min. To this was added a solution of **7f** (258 mg, 1.35 mmol) in CH_2Cl_2 (3 mL), and the solution was stirred for 18 h. The solid silver iodide was filtered out, and the solution was washed with sodium thiosulfate (10% aq.), dilute HCl (1 M), saturated aq. sodium bicarbonate, dried over $MgSO_4$, and the solvent removed in vacuo. Column chromatography (SiO_2, 1% ethyl acetate/99% hexane) afforded two fractions, one containing 58.4 mg of **11f**, and the other containing 187.2 mg of a 3:1 mixture of **10f** and **11f** (Yield of **10f** is 140.4 mg (0.447 mmol, 33%), yield of **11f** is 105.2 mg (0.335 mmol, 25%)).

10f: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.25–7.41 (5H, m), 5.85 (1H, d, $J = 6.7$ Hz); 5.25 (1H, dd, $J = 6.4$, 3.5 Hz); 4.60 (1H, q, $J = 4.6$ Hz); 3.25 (1H, tt, $J = 8.5$, 6.4 Hz), 2.04 (1H, m), 1.96 (1H, m), 1.52 (1H, m), 1.40 (3H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 139.5, 128.4, 127.4, 125.2, 81.4, 77.3*, 37.0, 31.4, 30.6, 20.0, 19.3; IR (neat): 3026 (m), 2940 (s), 2864 (m), 1494 (m), 1448 (s), 1077 (s), 1063 (s), 954 (s), 722 (s), 700 (s) cm^{-1}. HRMS (EI, m/z): 313.0098, Calcd. for $C_{13}H_{14}IO$ $(M-H)^+$ 313.0089.

11f: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.18–7.36 (5H, m), 5.19 (1H, d, $J = 3.8$ Hz), 4.54 (1H, t, $J = 4.8$ Hz), 4.41 (1H, t, $J = 5.0$ Hz), 2.56 (1H, t, $J = 3.4$ Hz), 2.18 (1H, ddd, $J = 14.1$, 11.7, 6.8 Hz), 1.83 (1H, td, $J = 13.8$, 6.8 Hz), 1.72 (1H, dt, $J = 13.7$, 5.9 Hz), 1.35 (1H, m), 1.25 (1H, m), 1.08 (1H, dt, $J = 13.7$, 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 139.5, 128.3, 126.9, 125.5, 80.0, 78.2, 43.4, 30.3, 27.6, 22.9, 16.4; IR (neat): 2937 (s), 2861 (m), 1448 (m), 1077 (s), 1065 (s), 954 (s), 764 (m), 721 (s), 700 (s) cm^{-1}. HRMS (EI, m/z): 313.0087, Calcd. for $C_{13}H_{14}IO$ $(M-H)^+$ 313.0089.

(1R*,5S*,6S*)-5-Iodo-8,8-diphenyl-7-oxabicyclo[4.2.0]octane (10g) and (1R*,5R*,8R*)-8-Iodo-7,7-diphenyl-6-oxabicyclo[3.2.1]octane (11g). To a solution of silver (I) *bis*-collidine perchlorate (0.31 g, 0.69 mmol) in CH_2Cl_2 (3 mL) was added solid iodine (173 mg, 0.68 mmol), and the solution was stirred for 40 min. To this was added a solution of **7 g** (36.1 mg, 0.136 mmol) in CH_2Cl_2 (2 mL) and the solution was stirred for 18 h. The solid silver iodide was filtered out, and the solution was washed with sodium thiosulfate (10% aq.), dilute HCl (1 M), saturated aq. sodium bicarbonate, dried over $MgSO_4$, and the solvent removed in vacuo. Column chromatography (SiO_2, 5% ethyl acetate/95% hexane) afforded two fractions, one containing 12.9 mg of **10 g**, and the other containing 13.2 mg of a 1:1 mixture of **10 g** and **11 g** (Yield of **10 g** is 19.5 mg (0.050 mmol, 37%), yield of **11 g** is 6.6 mg (0.017 mmol, 12%)).

10g: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.18–7.50 (10H, m), 5.06 (1H, dd, $J = 7.0$, 4.8 Hz), 4.56 (1H, dt, $J = 7.5$, 4.8 Hz), 3.56 (1H, q, $J = 7.8$ Hz), 1.3–2.1 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 146.9, 143.6, 128.5, 128.4, 127.3, 126.9, 125.4, 125.3, 89.4, 80.5, 43.2, 31.1, 30.8, 21.8, 20.0; IR (neat): 3059 (m), 3025 (m), 2939 (s), 2867 (m), 1447 (s), 748 (m), 704 (s) cm^{-1}.

11g: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.12–7.60 (10H, m), 4.56 (1H, m), 4.42 (1H, td, $J = 3.7$, 1.7 Hz), 3.13 (1H, q, $J = 3.4$ Hz), 2.25 (1H, ddd, $J = 14.1$, 11.8, 6.6 Hz), 1.3–2.1 (4H, m), 1.15 (1H, tt, $J = 14.1$, 5.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 148.5, 144.1, 128.6, 128.2, 126.8, 126.6, 125.7, 124.8, 87.3, 78.2, 47.0, 30.0, 27.9, 24.1, 16.6. IR (neat): 3060 (m), 3027 (m), 2940 (s), 2867 (m), 1491 (m), 1448 (s), 908 (s), 734 (s) cm^{-1}.

CONCLUSION

Various 3-cyclohexenemethanol derivatives **7** were transformed into mixtures of bicyclic ethers with I^+. The presence of alkyl groups along

the backbone between the double bond and the alcohol altered both the rate and the stereoselectivity of the reactions. When benzene rings were present, the major products were the oxetane-containing bicyclics **10f** and **10g**.

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