Trans Dialkoxylation of Cyclic Alkenes: A Prévost-Type Reaction

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Abstract: Reaction of anhydrous silver perchlorate, *sym*-collidine, and iodine (2:1:1 molar ratio) with cyclic alkenes and an excess of an alcohol in CH_2Cl_2 affords *trans*-1,2-dialkoxycycloalkanes in high yields and purity. The reaction occurs via initial formation of the *trans*-iodoethers, which undergo Ag-assisted iodide abstraction to give the *trans*-diethers.

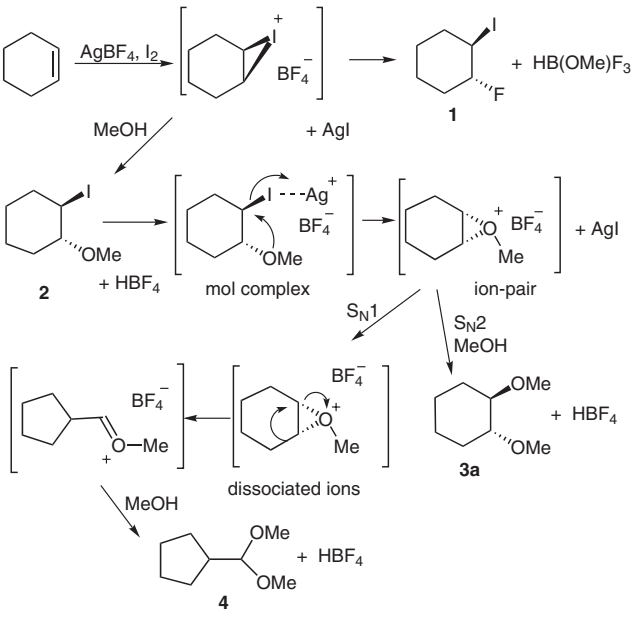
Keywords: alkenes, iodoalkoxylation, dialkoxylation, silver perchlorate, collidine

A variety of reactions have been described for the stereoselective iodoesterification and diesterification of alkenes. In contrast to the Prévost-type reactions for conversion of alkenes to *trans*-1,2-diesters via intermediate 1,2-iodoesters, analogous procedures for dietherification of alkenes via *vic*-iodoethers have apparently not been developed. Herein, we report the facile *trans*-dialkoxylation of cyclic alkenes using silver perchlorate, *sym*-collidine, iodine (2:1:1 molar ratio relative to the alkene), plus an excess of the appropriate alcohol in CH_2Cl_2 solution.

An initial attempt to develop a one-step dialkoxylation of alkenes in our lab involved reaction of cyclohexene with silver tetrafluoroborate and iodine (1:1:1 molar ratio), plus MeOH (20 mol equiv) in CH_2Cl_2, resulting in a mixture of *trans*-1-fluoro-2-iodocyclohexane (**1**), *trans*-1-iodo-2-methoxycyclohexane (**2**), *trans*-1,2-dimethoxycyclohexane (**3a**), and (dimethoxymethyl)cyclopentane (**4**), in relative yields of 24%, 13%, 21% and 42%.

Proposed pathways for formation of the major products are shown in Scheme 1. Initial formation of cyclohexene iodiranium ion followed by anti-mode nucleophilic attack by either tetrafluoroborate (with transfer of fluoride ion),[5] or by MeOH provides the iodofluoride **1** and intermediate iodoether **2**. The paths for methanolysis of iodoether **2** to the diether **3a** and acetal **4** are based on results of studies on Ag^+-assisted solvolyses of alkyl halides by Pocker and Kevill and coworkers,[6,7] Vona and Steigman,[8] and others.[7] Such reactions appear to occur via alkyl halide–silver salt complexes, followed by iodide abstraction by silver ion to give ion-paired species, which then undergo either nucleophilic displacement by S_N2Ag-type processes, or dissociate to free carbocations, followed by nucleophile trapping via S_N1Ag-type processes; the latter being favored by more electrophilic silver salts such as perchlorate or tetrafluoroborate, weak nucleophiles, and by strong acids and polar solvents. It was thus considered likely that the diether **3a** and ring-contracted acetal **4** were being formed via the iodoether **2** by concerted methoxyl- and Ag-assisted iodide abstraction to give the oxiranium-tetrafluoroborate ion pair. The ion-pair then undergoes rearside attack by MeOH to give the diether **3a**, or dissociates and rearranges to the oxocarbenium ion, which is trapped by methanol to give acetal **4**.

It should be noted (Scheme 1) that two molar equivalents of silver tetrafluoroborate per equivalent of alkene and iodine are required for complete conversion of cyclohexene to the diether **3a** and acetal **4**; the first equivalent reacting with iodine to form cyclohexene iodiranium tetrafluoroborate and AgI. The second equivalent of silver salt is required for Ag-assisted abstraction of iodide from the intermediate iodoether, leading to formation of **3a** and **4**. Since the amount of silver tetrafluoroborate employed in our initial study was only half of that required for complete conversion of cyclohexene to **3a** and **4**, their formation as major products indicated that iodide abstraction from the iodoether **2** occurred more rapidly than the initial iodoetherification step.



Overall reaction for formation of **3a, 4**:

Cyclohexene + 2 $AgBF_4$ + I_2 + 2 MeOH ⟶ **3a, 4** + 2 AgI + 2 HBF_4

Scheme 1

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In order to eliminate formation of the acetal **4**, it was necessary to develop reaction conditions under which tetrafluoroboric acid would be neutralized. Although dicollidine silver tetrafluoroborate (prepared in situ from collidine and silver tetrafluoroborate in a 2:1 molar ratio)[5] was essentially unreactive toward the iodoether **2**; by using one, rather than two equivalents of collidine, the diether **3a** was obtained in 90% relative yield, accompanied by acetal **4** (5%). This result is apparently due to the more electrophilic mono-collidine silver salt, expected to be formed under these conditions.[9]

The increased reactivity of silver tetrafluoroborate–collidine (1:1) in converting iodoether **2** to diether **3a** suggested its potential for carrying out one-step dietherification of alkenes. Thus, reaction of cyclohexene with silver tetrafluoroborate, collidine, iodine (1:2:2:1) and MeOH (20 mol equiv) in CH_2Cl_2 netted the diether **3a** in 73% yield, with only 2% of acetal **4**. However, the iodofluoride **1** was also obtained in 25% relative yield. To preclude forming the iodofluoride, it was desired to replace silver tetrafluoroborate with the perchlorate. However, since silver perchlorate–collidine (1:1) was too unreactive to convert the iodoether to the diether **3a**, it was necessary to utilize the uncomplexed silver salt for this step.

Thus, by using silver perchlorate–collidine–iodine in 2:1:1 molar ratio and MeOH (20 mol equiv), cyclohexene was converted to **3a** in 87% yield; no acetal **4** being detected by GC.

The composition resulting from combination of silver perchlorate, collidine, and iodine in 2:1:1 molar ratio is of importance here, since this mixture has proven effective for conversion of cyclic alkenes to *trans*-diethers. Such a mixture, prepared in $CDCl_3$, resulted in precipitation of AgI (1 equiv). A ^{1}H NMR study on the solution phase indicated formation a 1:1 mixture of silver and mono-iodonium perchlorates,[10,11] in which collidine is bonded principally to iodine (experimental section).

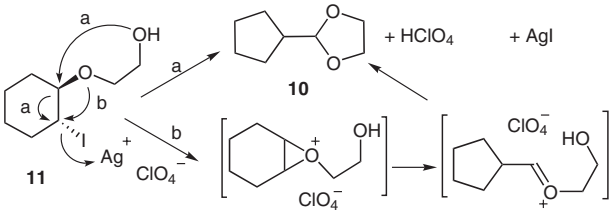
The decreased reactivity toward iodide abstraction resulting from substitution of silver perchlorate for tetrafluoroborate is consistent with other studies indicating that the ability of silver salts to form n-type complexes with amines or ethers decreases in the order: tetrafluoroborate > perchlorate > nitrate.[12] The same stability order has been observed for silver salt–alkene π-complexes.[13] Thus it may be expected that silver perchlorate would be a weaker Lewis acid (electrophile) than silver tetrafluoroborate. The same would be expected for the congeneric pairs of mono- and di-collidine silver salts.

The complete suppression of acetal formation observed by substitution of silver perchlorate for the tetrafluoroborate was surprising, since the amount of collidine employed was only half that required for neutralization of perchloric acid formed in the overall reaction. However, it is likely that the intermediate oxiranium–tetrafluoroborate ion pair proposed for conversion of iodoether **2** to diether **3a** (Scheme 1) would be more prone to dissociation and rearrangement than the corresponding oxiranium–perchlorate complex.

Results obtained for dietherification of cyclopentene and cyclohexene with silver perchlorate pentahydrate, collidine, iodine (2:1:1) and 20 molar equivalents of various saturated alcohols in CH_2Cl_2 at room temperature are shown in Table 1. Yields of diethers from cyclopentene were generally higher than those from cyclohexene. In several reactions, particularly for cyclohexene, the diethers were accompanied by small to moderate amounts of the undesired *trans*-1,2-hydroxyethers. The hydroxyether–diether ratios increased with steric bulk of the alcohols, consistent with increased hindrance for rear-side displacement on oxiranium ion intermediates by alcohols (Scheme 1) relative to water. As shown for the synthesis of *trans*-1,2-di-*tert*-butoxycyclopentane (**6d**), hydroxyether formation was eliminated by use of anhydrous silver perchlorate.

Dietherification of *trans*-bicyclo[4.4.0]dec-3-ene (**8**) with anhydrous silver perchlorate collidine, and iodine (2:1:1) and excess MeOH in CH_2Cl_2 gave only *trans*-(diaxial)-3,4-dimethoxy-*trans*-bicyclo[4.4.0]decane (**9**), consistent with axial mode nucleophilic displacement by MeOH on the oxiranium species derived from the expected intermediate *trans*-(diaxial)-3-iodo-4-methoxy[4.4.0]decane.

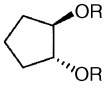
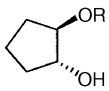
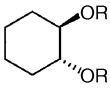
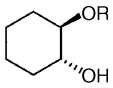
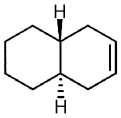
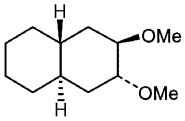
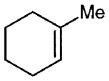
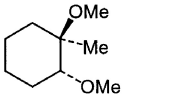
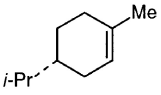
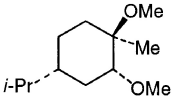
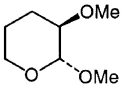
Attempted dialkoxylation of cyclohexene using anhydrous silver perchlorate, collidine iodine (2:1:1) and ethane-1,2-diol as solvent gave only 2-cyclopentyl-1,3-dioxolane (**10**) in 80% yield (Scheme 2). By analogy to the formation of acetal **4**, dioxolane **10** could form via 1-iodo-(2-hydroxyethoxy)cyclohexane (**11**) by Ag-assisted iodide abstraction with anchimeric assistance by vicinal ether oxygen to give the oxiranium–perchlorate ion pair, followed by dissociation and rearrangement to the oxocarbenium ion and ring closure (path b), which would be expected to be favored by increased solvent polarity due to ethanediol. Alternately, dioxolane **10** could form simply by Ag-assisted iodide abstraction with concerted intramolecular hydroxyl attack and rearrangement (path a).



Scheme 2

Reaction of 1-methylcyclohexene with silver perchlorate pentahydrate, collidine, iodine (2:2:1) and excess MeOH gave *trans*-1,2-dimethoxy-1-methylcyclohexane (**12**), methyl cyclopentyl ketone, and 2-methylcyclohexanone in 28%, 24%, and 27% relative yields (Table 1).[14] The former ketone apparently derives from Ag-assisted rearrangement of 2-iodocyclohexanol (resulting from competitive nucleophilic attack by water on the initial 1-

Table 1 Dietherification of Cyclic Alkenes with Silver Perchlorate,[a] Iodine, Collidine and Alcohols

Alkene	Alcohol	Products, yield (%)[b]	
			
		6	**7**
	a: MeOH	98 (99)	0
	b: *n*-BuOH	98 (99)	< 1
	c: *i*-BuOH	79 (80)	16
	d: *t*-BuOH	89 (96)[a]	0
			
		3	**5**
	a: MeOH	87 (92)	(0)
	b: *i*-PrOH	91 (99)	0
	c: *n*-BuOH	60 (81)	10 (8)
	d: *i*-BuOH	70 (71)	22 (25)
	e: *t*-BuOH	49 (60)	(26)
	MeOH		68
8		**9**	
	MeOH		28[c,d] 57 (66)[e]
		12	
	MeOH		47 (66)[e]
		13	
	MeOH		80 (51)
		18	

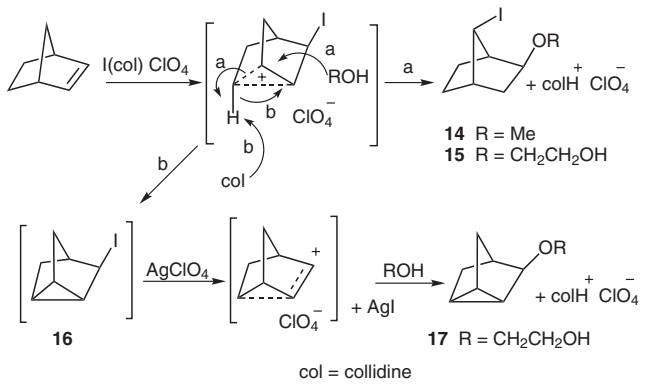
[a] Reactions of cyclopentene, cyclohexene, except for synthesis of **6d** were run using $AgClO_4 \cdot 5H_2O$; all others with anhyd. $AgClO_4$, except for synthesis of **12**.
[b] Yields of isolated products; relative yields by GC.
[c] Reaction run using $AgClO_4 \cdot 5H_2O$.
[d] Plus cyclopentyl methyl ketone (27%), 2-methylcyclohexanone (28%), and 12 minor products (1–5%) (GC–MS).
[e] Several side products (1–13%).

methylcyclohexene iodiranium ion); the latter, via Ag-assisted conversion of the iodohydrin to the epoxide, and rearrangement.[15] By using anhydrous silver perchlorate, the yield of **12** increased to ca 65%.

Dimethoxylation of 1-methyl-4*R*-isopropylcyclohexene under anhydrous conditions gave the diether **13** in similar yield. The ^{1}H NMR spectrum of **13** indicated the C-2 methoxyl to be equatorial. Presuming rear side attack by MeOH at C_1 (electronic control) on the oxiranium ion derived from the likely *trans*-diaxial iodoether intermediate, (1*S*, 2*S*, 4*R*)-2-iodo-4-isopropyl-1-methoxy-1-methylcyclohexane, the configuration of **13** is (1*R*, 2*R*, 4*R*)-1,2-dimethoxy-4-isopropyl-1-methylcyclohexane (diequatorial methoxyls).

Reaction of bicyclo[2.2.1]heptene with anhydrous silver perchlorate, collidine, iodine (2:2:1) and excess MeOH gave 7-*syn*-iodo-2-exo-methoxybicyclo[2.2.1]heptane (**14**)[16] in 76% yield (Scheme 3, path a). Failure of **14** to undergo further methoxylation apparently derives from its stereochemistry precluding methoxyl assistance to iodide abstraction by silver perchlorate. Likewise, reaction of norbornene using ethane-1,2-diol instead of MeOH gave

7-*syn*-iodo-2-exo-(2-hydroxyethoxy)bicyclo[2.2.1]heptane (**15**) in 61% yield and 3-*exo*-(2-hydroxyethoxy)tricyclo[2.2.1.$0^{2,6}$]heptane (**17**) in 8.5% (20% relative) yield; the latter likely formed via 3-*exo*-iodotricyclo[2.2.1.$0^{2,6}$]heptane (**16**) by iodide abstraction to give the relatively stable 3-nortricyclyl ion[17] which is trapped by ethylene glycol (path b).[18] 3-Iodonotricyclane **16** was previously obtained as the sole product from reaction of norbornene with dicollidine iodonium tetrafluoroborate.[5]



Scheme 3

Reaction of 3,4-dihydro-2*H*-pyran with anhydrous silver perchlorate, collidine, iodine (2:1:1) and excess MeOH in CH_2Cl_2 gave *trans*-(diaxial)-2,3-dimethoxytetrahydropyran (**18**) (Table 1) as the only isolable product in 80% yield. This result was consistent with the intermediacy of *trans*-(diaxial)-3-iodo-2-methoxytetrahydropyran, the latter having previously been obtained by reaction of dihydropyran with silver acetate and iodine in MeOH.[19] In light of the facile acid-catalyzed isomerization of 2-alkoxytetrahydropyrans,[20] the formation of solely the *trans* isomer of dimethoxytetrahydropyran under the reaction conditions employed was rather unexpected.

In summary, a one-step method for *trans*-1,2-dialkoxylation of cyclic alkenes has been developed based on a Prévost-type reaction using anhydrous silver perchlorate, *sym*- collidine, and iodine (2:1:1 molar ratio) and an excess of a monohydric alcohol in CH_2Cl_2. Cyclic alkenes with unsubstituted carbon-carbon double bonds give diethers in high yields and purity. Paralleling the Prévost reaction, alkenes with trisubstituted double bonds give lower yields of diethers, accompanied by side products.

Isolation of products was accomplished by flash liquid chromatography on Kieselgel 60 using CH_2Cl_2 or MeOH–CH_2Cl_2 as eluent. GC analyses were performed on a Hewlett-Packard 5890 instrument; 15 m, 530 μ macrocapillary silica column; 50% diphenylpolysiloxane–50% dimethylpolysiloxane; injector 200 °C, detector 140 °C, oven temperature ramped from 50–200 °C at 3°C/min; detection limit 0.1% rel. area. All NMR spectra were obtained on Varian Associates XL-200 spectrometer in $CDCl_3$, using TMS as internal standard. ^{13}C and ^1H shift assignments were assisted by empirical substituent effect additivity calculations,[21] using ChemDraw Ultra 7.01 (Cambridge Soft Corp., Cambridge, MA); ^{13}C multiplicities were determined by DEPT. *trans*-1-Fluoro-2-iodocyclohexane (**1**),[5] *cis*- and *trans*-1,2-dimethoxycyclohexane,[16] and *trans*-bicyclo[4.4.0]dec-3-ene,[22] were prepared by literature procedures.

Caution: Silver perchlorate *per se* is stable at temperatures below ca 485 °C. Its solubility in organic solvents is due to formation of complexes, which may be isolated as crystalline materials. Such perchlorate complexes are explosive, and may detonate, even upon handling when cold.[23,24]

Synthesis of *trans*-1-Iodo-2-methoxycyclohexane (2)

To a magnetically stirred solution of dicollidine silver tetrafluoroborate[5] (12.67 g, 29 mmol) in anhyd CH_2Cl_2 (85 mL) under an inert atmosphere, iodine (3.68 g, 29 mmol) was added in one portion, and the mixture stirred until all the iodine had reacted. AgI was removed by vacuum filtration to give a clear amber solution of dicollidine iodonium tetrafluoroborate,[5] to which were added, cyclohexene (2.30 g, 28 mmol) and MeOH (0.90 g, 28 mmol, in rapid succession. The mixture was stirred for 2 h at 25 °C, filtered, and the filtrate washed successively with 10% aq NaS_2O_3 (50 mL), 20% cold HCl (50 mL), and water (50 mL), dried (anhyd $MgSO_4$) and the solvent stripped under reduced pressure. Short-path distillation gave iodoether **2**; yield: 4.37 g (65%); bp 47 °C (0.5 Torr); stable at 0 °C.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.60–2.50 (m, 8 H, CH_2), 3.24 (ddd, 1 H, H_2), 3.40 (s, 3 H, OCH_3), 4.07 (ddd, $J_{1a,2a}$ = 10.7 Hz, $J_{1a,6a}$ = 8.74 Hz, $J_{1a,6e}$ = 4.28 Hz, 1 H, H_1).
The NMR data is consistent with literature[25] ^1H NMR data.

Anal. Calcd for $C_7H_{13}IO$: C, 35.02; H, 5.46; I, 52.86; O, 6.66. Found: C, 35.34; H, 4.88; I, 53.10; O, 6.90.

Synthesis of *trans*-1,2-Dimethoxycyclohexane (3a) from *trans*-1-Iodo-2-methoxycyclohexane

To a magnetically stirred solution of $AgClO_4 \cdot 5H_2O$ (2.97 g, ca 10 mmol) in CH_2Cl_2 (25 mL) in a 50 mL round-bottomed flask at r.t., were added successively, *trans*-1-iodo-2-methoxycyclohexane (2.40 g, 10 mmol) and MeOH (20 mmol). The mixture was stirred for 2 h at r.t., then filtered to remove AgI. AgI was extracted with CH_2Cl_2 (20 mL) and the combined filtrate washed successively with water (75 mL), cold HCl (1.4 M, 75 mL), and Na_2CO_3 (0.1%, 75 mL). After drying (anhyd. $MgSO_4$), the filtrate was evaporated under reduced pressure, then purified by flash chromatography to give **3a**; yield: 1.30 g (90%); GC and ^1H NMR data are consistent with those for a literature[16] preparation.

Composition of Reagent Mixture Used for Dialkoxylation

Sequential addition of $AgClO_4$, *sym*-collidine, and iodine in 1:2:1 mol ratio in $CDCl_3$–TMS solution at r.t. resulted in instantaneous quantitative precipitation of AgI. A ^1H NMR spectrum for the resulting solution of dicollidine iodonium perchlorate, $Icol_2ClO_4$,[26] revealed one set of collidine resonances, including a ring proton singlet at δ = 7.29 ppm (0.52 ppm downfield from neat collidine/$CDCl_3$). A similar solution prepared using 1 mol equiv of collidine showed a slight upfield shift of the ring proton singlet to δ = 7.19 ppm, consistent for formation of the mono-collidine iodonium salt. Further addition of 1 equiv of $AgClO_4$ to the latter solution had no additional effect on the collidine shifts, as expected for a 1:1 mixture of silver and mono-collidine iodonium perchlorates, with collidine bonded principally to iodine.

Synthesis of *trans*-1,2-Diethers 6d, 9, 12, 13, 18 (Table 1) Using Anhydrous Silver Perchlorate

Reactions of all alkenes except cyclopentene and cyclohexene were carried out using anhyd $AgClO_4$, prepared immediately prior to reaction by heating $AgClO_4 \cdot 5H_2O$ (2.97g, ca 10.0 mmol) to 150 °C at 50 torr for 4 h[24] in a 50 mL round-bottomed flask immersed in an oil bath. Upon cooling to 25 °C, anhyd CH_2Cl_2 (25 mL), *sym*-collidine (0.61 g, 5.0 mmol), alkene (5.0 mmol) and alcohol (80.0 mmol)

were added successively with magnetic stirring, care being taken to avoid unnecessary exposure to air. Stirring was continued for ca 5 min until the $AgClO_4$ dissolved completely, then iodine (1.27 g, 5.0 mmol) was added and the mixture stirred for 2 h longer at 25 °C, then filtered to remove AgI. The filtrate was washed successively with distilled water (75 mL), 10% $Na_2S_2O_3$ (75 mL), cold 1.4 M HCl (75 mL) and 0.1% Na_2CO_3 (75 mL), dried (anhyd $MgSO_4$) and evaporated under reduced pressure to yield the crude products which were assayed by GC and purified by flash liquid chromatography.

Reactions of cyclohexene and bicyclo[2.2.1]heptene with silver perchlorate, *sym*-collidine, iodine (2:1:1 mol ratio) and ethane-1,2-diol were carried out analogously, except that ethanediol (25 mL) was used as solvent; CH_2Cl_2 (2–3 mL) as co-solvent.

Dietherification of Cyclopentene, Cyclohexene, and 1-Methylcyclohexene Using Silver Perchlorate Pentahydrate (Table 1)

Reactions were carried out in the same manner as with anhyd silver perchlorate, except that the perchlorate was not dried.

Dimethoxylation of Cyclohexene Using Silver Tetrafluoroborate

The procedure used was similar to that for synthesis of *trans*-1,2-diethers using anhyd $AgClO_4$, except that $AgBF_4$ (1.95 g, 10.0 mmol) and *sym*-collidine (1.21 g, 10.0 mmol) were employed.

Spectral and Analytical Data for Representative *trans*-1,2-Diethers (3,6) and Alkoxyalcohols (5,7)

In most cases the ring methine (CHO) protons appeared as unresolved multiplets. Assignment of *trans* configurations to *vic*-diethers was supported by half-height peak widths, $\omega_{1/2}$. Only single configurational isomers were observed in all cases.

***trans*-1,2-Diisopropoxycyclohexane (3b)**

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.12 (d, *J* = 6.1 Hz, 6 H, 2 × CH_3), 1.19 (d, *J* = 6.1 Hz, 6 H, 2 × CH_3), 1.20–1.25 (m, 4 H), 1.55–1.70 (m, 2 H), 1.80–2.00 (m, 2 H), 3.05–3.15 (m, 2 H, 2 × CHOC), 3.82, [h, 2 H, $CH(CH_3)_2$; the diastereotopic CH_3 groups (δ = 1.12, 1.19) collapsed to doublets upon decoupling CH at 3.82].

^{1}H NMR shifts were consistent with literature[27] data.

^{13}C{^{1}H} NMR (50.3 MHz, $CDCl_3$): δ = 22.82 (q, CH_3), 23.99 (t, $C_{4,5}$), 32.10 (t, $C_{3,6}$), 70.91 [d, $CH(CH_3)_2$], 79.41 (s, $C_{1,2}$).

Anal. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08. Found: 71.94; H, 12.27.

***trans*-1,2-Di-*n*-butoxycyclohexane (3c)**

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.18 Hz, 6 H, 2 × CH_3), 1.15–1.70 (m, 14 H), 1.90–2.15 (m, 2 H), 3.06–3.20 (m, $\omega_{1/2}$ = 18 Hz, 2 H, $H_{1,2}$, dieq alkoxyls), 3.55 (dt, J_{vic} = 6.49 Hz, 4 H, 2 × OCH_2).

^{13}C{^{1}H} NMR (50.3 MHz, $CDCl_3$): δ = 13.82 (q, CH_3), 19.26 (t, CH_2CH_3), 25.53 (t, $C_{4,5}$), 30.19 (t, $C_{3,6}$), 32.36 (t, OCH_2CH_2), 69.69 (t, OCH_2), 81.23 (d, $C_{1,2}$).

***trans*-1,2-Diisobutoxycyclohexane (3d)**

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.67 Hz, 6 H, 2 × CH_3), 0.90 (d, *J* = 6.67 Hz, 6 H, 2 × CH_3), 1.81 [m, 2 H, 2 × $CH(CH_3)_2$], 1.32–2.04 (m, 8 H, H_{3-6}), 3.07–3.19 (m, $\omega_{1/2}$ = 20 Hz, 2 H, $H_{1,2}$; consistent for dieq alkoxyls), 3.55 (d, *J* = 6.49 Hz, 4 H, 2 × OCH_2); CH_3 groups are diasterotopic.

^{13}C{^{1}H} NMR (50.3 MHz, $CDCl_3$): δ = 19.47 (q, CH_3), 23.51 (t, $C_{4,5}$), 28.94 [d, $CH(CH_3)_2$], 30.01 (t, $C_{3,6}$), 76.97 (t, CH_2O), 81.26 ($C_{1,2}$).

Anal: Calcd for $C_{14}H_{28}O_2$: C, 72.85; H, 12.34. Found: C, 73.10; H, 12.23.

***trans*-1,2-Di-*tert*-butoxycyclohexane (3e)**

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.18 (s, 18 H, 6 × CH_3), 1.59 (m, 4 H, $H_{4,5}$), 1.83 (m, 4 H, $H_{3,6}$), 3.18 (m, 2 H, $H_{1,2}$).

^{13}C{^{1}H} NMR (50.3 MHz, $CDCl_3$): δ = 24.08 (t, $C_{4,5}$), 28.81 (q, CH_3), 34.01 (t, $C_{3,6}$), 73.22 (d, $C_{1,2}$), 73.27 [s, $OC(CH_3)_2$].

***trans*-2-*n*-Butoxycyclohexanol (5c)**

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.21 Hz, 3 H, CH_3), 1.10–2.18 (m, 12 H, 6 × CH_2), 2.27 (s, 1 H, OH), 2.90–3.10 (m, 1 H, H_2), 3.37, 3.60 (m, 2 H, OCH_aH_b, diastereotopic), 3.50–3.70 (m, 1 H, H_1).

^{13}C{^{1}H} NMR (50.3 MHz, $CDCl_3$): δ = 13.78 (q, CH_3), 19.26 (t, CH_2CH_3), 23.89 (t, C_5), 24.18 (t, C_4), 29.04 (t, C_3), 31.85 (t, C_6), 32.12 (t, $CH_2CH_2CH_3$), 68.39 (t, OCH_2), 73.75 (d, C_1), 83.56 (d, C_2).

***trans*-2-Isobutoxycyclohexanol (5d)**

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.91 (d, *J* = 6.67 Hz, 3 H, CH_3), 0.92 (d, *J* = 6.67 Hz, 3 H, CH_3), 1.84 [m, *J* = 6.67 Hz, 1 H, C*H*$(CH_3)_2$], 1.10–2.12 (m, 8 H, 4 × CH_2), 2.58 (s, 1 H, OH), 3.00 (ddd, $J_{1,2}$ = 10.41 Hz, $J_{2,3e}$ = 8.73 Hz, $J_{2,3a}$ = 4.21 Hz, 1 H, H_{2a}), 3.12 (dd, J_{vic} = 8.95 Hz, J_{gem} = 6.64 Hz, 1 H, OCH_a), 3.40 (dd, J_{vic} = 8.95 Hz, J_{gem} = 6.57 Hz, 1 H, OCH_b), 3.40 (ddd, 1 H, H_{1ax}); CH_3 groups and CH_aH_bO are diastereotopic; decoupling CH at δ = 1.84 collapsed CH_2O double doublets to doublets, permitting assignment of the overlapping H_1 at δ = 3.40.

^{13}C{^{1}H} NMR (50.3 MHz, $CDCl_3$): δ = 19.33 (q, CH_3), 23.89, 24.18 (t, $C_{4,5}$), 28.73 [d, $CH(CH_3)_2$], 28.98 (t, C_3), 31.82 (t, C_6), 73.83 (d, C_1), 75.50 (t, CH_2O), 83.69 (d, C_1).

***trans*-1,2-Dimethoxycyclopentane (6a)**

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.50–2.00 (m, 6 H, H_{3-5}), 3.35 (s, 6 H, 2 × OCH_3), 3.60–3.75 (m, 2 H, $H_{1,2}$).

^{13}C{^{1}H} NMR (50.3 MHz, $CDCl_3$): δ = 21.32 (t, C_4), 29.72 (t, $C_{3,5}$), 56.87 (q, OCH_3), 86.37 (d, $C_{1,2}$).

^{1}H and ^{13}C data for **6a** are consistent with published[28] data.

***trans*-1,2-Di-*n*-butoxycyclopentane (6b)**

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.2 Hz, 6 H, 2 × CH_3), 1.24–2.00 (m, 14 H, 7 × CH_2), 3.44 (t, J_{vic} = 6.4 Hz, 4 H, 2 × OCH_2), 3.71 (m, $\omega_{1/2}$ = 14 Hz, 2 H, $H_{1,2}$).

^{13}C{^{1}H} NMR (50.3 MHz, $CDCl_3$): δ = 13.73 (q, CH_3), 19.24, 21.30 (t, CH_2CH_3, C_4), 30.11, 31.95 (t, $C_{3,5}$, OCH_2CH_2), 68.80 (t, OCH_2), 84.89 (d, $C_{1,2}$).

***trans*-1,2-Diisobutoxycyclopentane (6c)**

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.899 (d, *J* = 6.67 Hz, 6 H, 2 × CH_3), 0.894 (d, *J* = 6.67 Hz, 6 H, 2 × CH_3), 1.50–1.95 (m, 8 H, H_{3-5}, 2 × $CHCH_3$), 3.19 (d, 2 H, 2 × OCH_a), 3.21 (d, *J* = 6.67 Hz, 2 H, 2 × OCH_b), 3.65–3.75 (m, 2 H, $H_{1,2}$); CH_3 groups and OCH_aH_b are diastereotopic.

^{13}C{^{1}H} NMR (50.3 MHz, $CDCl_3$): δ = 19.45 (q, CH_3), 21.42 [d, $CH(CH_3)_2$], 28.63 (t, C_4), 30.18 (t, $C_{3,5}$), 76.18 (t, OCH_2), 85.06 (d, $C_{1,2}$).

***trans*-1,2-Di-*tert*-butoxycyclopentane (6d)**

^{13}C{^{1}H} NMR (50.3 MHz, $CDCl_3$): δ = 20.55 (t, C_4), 28.60 (q, CH_3), 31.86 (t, $C_{3,5}$), 72.97 (s, $C(CH_3)_2$), 78.56 ($C_{1,2}$).

Anal: Calcd for $C_{13}H_{26}O_2$: C, 72.85; H, 12.24. Found: C, 72.59; H, 12.28.

***trans*-2-Isobutoxycyclopentanol (7c)**

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.67 Hz, 6 H, 2 × CH_3), 1.50–2.05 (m, 7 H, C*H*$(CH_3)_2$, H_{3-5}), 3.21 (d, *J* = 6.67 Hz, 2 H,

OCH_2), 3.52 (m, $\omega_{1/2}$ = 18 Hz, 1 H, H_2), 4.10 (m, $\omega_{1/2}$ = 22 Hz, 1 H, H_1).

$^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$): δ = 19.31 (q, CH_3), 20.33 (t, C_4), 29.17 (t, C_5), 31.96; (t, C_3), 76.32 (t, OCH_2), 77.30 (d, C_1), 86.82 (d, C_2).

***trans*-2,3-Dimethoxy-*trans*-bicyclo[4.4.0]decane (9)[29]**

^1H NMR (200 MHz, $CDCl_3$): δ = 1.5–2.5 (m, 14 H), 3.35 (s, 6 H, 2 × OCH_3), 3.42 (m, $\omega_{1/2}$ = 6.4 Hz, 2 H, $H_{2e,3e}$).

$^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$): δ = 26.49 ($C_{6,7}$), 32.04, 33.45 (t, $C_{1,4;5,8}$), 36.19 (d, $C_{9,10}$), 56.40 (OCH_3), 76.83 ($C_{2,3}$).

***trans*-1,2-Dimethoxy-1-methylcyclohexane (12)**

^1H NMR (200 MHz, $CDCl_3$): δ = 1.15 (s, 3 H, CH_3), 1.25–2.0 (m, 8 H, H_{3-6}), 3.11 (dd, $J_{2a,3a}$ = 7.0 Hz, $J_{2a,3e}$ = 3.5 Hz, 1 H, H_2), 3.22, 3.38 (s, 6 H, 2 × OCH_3).

$^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$): δ = 18.19, 21.51, 21.83 (CH_3, $C_{4,5}$), 25.58 (C_3), 32.26 (C_6), 48.43, 57.01 (2 × OCH_3), 76.48 (C_1), 82.63 (C_2).

1*R*,2*R*-Dimethoxy-1-methyl-4*R*-isopropylcyclohexane (13)

^1H NMR (200 MHz, $CDCl_3$): δ = 0.86 [d, 6 H, $(CH_3)_2C$], 1.15 (s, 3 H, CH_3), 1.20–2.11 [m, 8 H, H_{3-6}, $(CH_3)_2CH$], 3.17 (dd, $J_{2a,3a}$ = 11.2 Hz, $J_{2a,3e}$ = 4.6 Hz, 1 H, H_2), 3.2 (s, 3 H, OCH_3), 3.4 (s, 3 H, OCH_3).

$^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$): δ = 15.0, 19.7 (q, CH_3), 25.9, 32.2, 34.4 (3 × t, $C_{3,5,6}$), 48.9 (q, OCH_3), 57.2 (q, OCH_3), 77.80 (s, C_1), 84.3 (d, C_2).

***syn*-7-Iodo-2-*exo*-methoxybicyclo[2.2.1]heptane (14)[16]**

^1H NMR (200 MHz, $CDCl_3$): δ = 0.91–1.05 (m, 1 H, H_{5n}), 1.14–1.28 (m, 1 H, H_{6n}), 1.50–1.74 (m, 2 H, H_{5x}, H_{6x}), 1.76–1.90 (ddd, $J_{2n,3n}$ = 7.4 Hz, $J_{3n,4}$ = 1.3 Hz, $J_{3n,3x}$ = 13.2 Hz, 1 H, H_{3n}), 2.02–2.17 (ddd, $J_{3n,3x}$ = 13.2 Hz, $J_{2n,3x}$ = 3.7 Hz, $J_{3x,4}$ = 6.2 Hz, 1 H, H_{3x}), 2.37–2.50 (m, 1 H, H_4), 2.57–2.65 (m, 1 H, H_1), 3.30 (s, 3 H, OCH_3), 3.40–3.46 (ddd, $J_{2n,3n}$ = 7.4 Hz, $J_{1,2n}$ = 1.3 Hz, $J_{2n,3x}$ = 3.7 Hz, 1 H, H_{2n}), 3.69–3.75 (dd. J = 1.4 Hz, 1 H, H_7).

$^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$): δ = 25.41 (t, $C_{5,6}$), 27.64 (d, C_7), 38.67 (t, C_3), 43.46 (d, C_4), 45.39 (d, C_1), 56.05 (q, OCH_3), 84.45 (d, C-2).

7-*syn*-Iodo-2-*exo*-(2-hydroxyethoxy)bicyclo[2.2.1]heptane (15)

^1H NMR (200 MHz, $CDCl_3$): δ = 0.85–1.15 (m, 1 H, H_{5n}), 1.15–1.30 (m, 1 H, H_{6n}), 1.60–1.75 (m, 2 H, H_{5x}, H_{6n}), 1.87 (ddd, $J_{3n,3x}$ = 13.4 Hz, $J_{2n,3n}$ = 7.3 Hz, $J_{3n,4}$ = 1.5 Hz, 1 H, H_{3n}), 2.10 (ddd, $J_{3n,3x}$ = 13.3 Hz, $J_{3x,4}$ = 6.1 Hz, $J_{2n,3x}$ = 3.4 Hz, 1 H, H_{3x}), 2.40, 2.50 (2 × s, 2 H, H_1, H_4), 3.25, 3.35 (2 × m, 4 H, OCH_2CH_2O), 3.60 (m, $\omega_{1/2}$ = 20 Hz, 1 H, H_{2n}), 3.73 (m, $\omega_{1/2}$ = 10 Hz, 1 H, H_7).

$^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$): δ = 25.06, 25.36 (2 × t, $C_{5,6}$), 28.46 (d, C_7), 38.86 (t, C_3), 43.44 (d, C_4), 45.95 (d, C_1), 61.70 (t, CH_2OH), 69.19 (t, OCH_2), 82.63 (d, C_2).

3-*exo*-(2-Hydroxyethoxy)tricyclo[2.2.1.0^{2,6}]heptane (17)

^1H NMR (200 MHz, $CDCl_3$): δ = 1.1–1.8 (m, 7 H, $H_{1,2,5-7}$), 1.95 (m, 1 H, H_4), 2.17 (s, 1 H, OH), 3.51 (dd, 2 H, OCH_2), 3.58 (m, 1 H, H_3), 3.73 (dd, 2 H, CH_2OH).

$^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$): δ = 10.80, 12.75, 13.90 (3 × d, $C_{1,2,6}$), 29.44, 30.25 (2 × t, CH_2, $C_{5,7}$), 32.30 (d, C_4), 61.91 (t, CH_2OH), 69.78, (t, CH_2O), 84.48 (d, C_3).

***trans*-2,3-Dimethoxytetrahydropyran (18)[20,30]**

^1H NMR (200 MHz, $CDCl_3$): δ = 1.50–2.05 (m, 4 H, $H_{4,5}$), 3.42 (s, 3 H, OCH_3), 3.43 (s, 3 H, OCH_3), 3.72–3.90 (m, 2 H, H_6), 3.90–4.01 (m, 1 H, H_3), 4.54 (d, $J_{2,3}$ = 5.6 Hz, 1 H, H_2).

$^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$): δ = 25.63 (t, C_5), 27.00 (t, C_4), 53.84 (q, OCH_3), 54.89 (q, OCH_3), 69.50 (t, C_6), 78.18 (d, C_3), 105.82 (d, C_2).

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