Convenient Synthesis of *meso*-Cyclohexa-1,3-dienes by One-Pot Two-Step Deoxygenation of 7-Oxabicyclo[2.2.1]hept-2-enes

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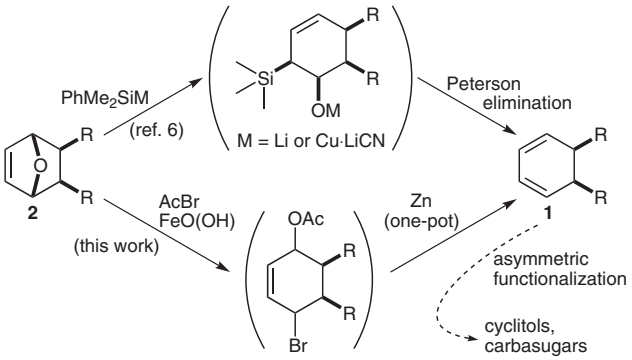
Abstract: Iron(III) hydroxide oxide was found to be an efficient catalyst for the ring-opening reaction of 5,6-*cis*-disubstituted 7-oxabicyclo[2.2.1]hept-2-enes with acetyl bromide in dichloromethane at room temperature to give cyclohexene derivatives with leaving groups (acetoxy or bromo groups) disposed on each allylic position. A successive one-pot treatment of the reaction mixture with zinc powder and tetrahydrofuran successfully induced reductive 1,4-elimination to afford synthetically useful 5,6-disubstituted *meso*-cyclohexa-1,3-dienes in good-to-high yields.

Key words: catalysis, ring opening, furans, reductions, eliminations, cyclohexadienes

Alka-1,3-dienes are versatile substrates in organic synthesis, as they are readily available and they undergo asymmetric functionalization reactions at the double bonds to produce useful chiral building blocks.[1] Dienes in the *meso*-form are more valuable because they undergo asymmetric desymmetrization to give optically active products with a simultaneous increase in the number of stereogenic centers.[2] In this respect, σ-symmetric 5,6-*cis*-disubstituted cyclohexa-1,3-dienes **1** are of particular interest as precursors of densely functionalized chiral cyclohexane derivatives, such as cyclitols or carbasugars (Scheme 1).[3] This is well illustrated by the synthesis of conduritol E from cyclohexa-3,5-diene-1,2-diol (**1**, R = OH).[4] Furthermore, Toste et al.[5] recently demonstrated a catalytic asymmetric Kornblum DeLaMare rearrangement of endoperoxides derived from the cyclohexa-1,3-diene **1** (R = CH_2OBn) and analogous dienes to give optically active 4-hydroxy enones, which should be useful as chiral building blocks. Accordingly, an efficient method is required for the synthesis of cyclohexa-1,3-dienes **1**.

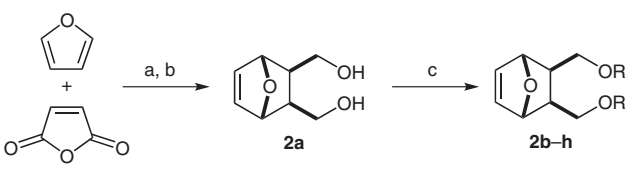
Lautens et al.[6] devised an elegant S_N2' displacement–Peterson elimination cascade for the direct conversion of 7-oxabicyclo[2.2.1]hept-2-enes **2** into cyclohexa-1,3-dienes **1** with dimethyl(phenyl)silyllithium or lithium dimethyl(phenyl)silylcuprate (Scheme 1). On the other hand, 7-oxabicyclo[2.2.1]hept-2-enes **2** undergo a neighboring group-induced diastereoselective nucleophilic C–O displacement with acetyl bromide or acetyl chloride in the presence of sulfuric acid as a catalyst to afford cyclohexene derivatives with acetoxy and bromo or chloro groups, respectively, disposed at each allylic carbon.[7] These transformations prompted us to seek further refinements, because the reaction products are considered to be masked cyclohexa-1,3-dienes that could be unmasked by reductive elimination of the allylic functional groups.[8]

Here we report a convenient one-pot synthesis of cyclohexa-1,3-dienes **1** from 7-oxabicyclo[2.2.1]hept-2-enes **2** actuated by iron(III) hydroxide oxide-catalyzed cleavage of the 2,5-dihydrofuran ring with acetyl bromide, followed by zinc-mediated reductive 1,4-elimination (Scheme 1).



Scheme 1 Strategies for the synthesis of σ-symmetric 5,6-*cis*-disubstituted cyclohexa-1,3-dienes **1**, useful as chiral building blocks for densely functionalized cyclohexane derivatives

The starting materials, the 5,6-*cis*-disubstituted 7-oxabicyclo[2.2.1]hept-2-enes **2**, are readily accessible from furan and maleic anhydride, which undergo an *exo*-selective Diels–Alder reaction followed by reduction with lithium aluminum hydride to give the diol **2a**[9]; its derivatives **2b**–**h** are obtained after appropriate protection of the hydroxy groups of **2a** (Scheme 2).



Scheme 2 Synthesis of 5,6-*cis*-disubstituted 7-oxabicyclo[2.2.1]hept-2-enes **2a**–**h**. *Reagents and conditions*: a) Et_2O, r.t., 48 h, 91%; b) LAH, THF, r.t., 24 h, 97%; c) for details, see the experimental section. The alphabetical suffixes for compounds **2** represent the various substituents: **b**, R = Bz; **c**, R = Ac; **d**, R = Ms; **e**, R = CO_2Me; **f**, R = $CONMe_2$; **g**, R = Me; **h**, R = Bn.

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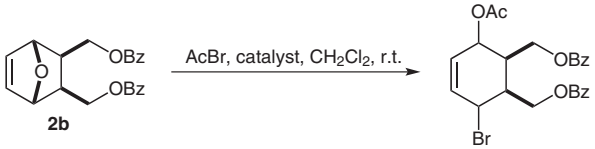
By using **2b** as a test substrate, we first optimized the conditions for cleavage of the 2,5-dihydrofuran ring. It has been reported that 2,5-dihydrofuran itself reacts with acetyl bromide at room temperature in the absence of a catalyst to give (2*Z*)-4-bromobut-2-en-1-yl acetate.[10] In fact, treatment of **2b** with acetyl bromide under the reported conditions occasionally afforded the desired 3-acetoxy-6-bromocyclohexene **3** (Table 1), but the reaction was not readily reproducible. When sulfuric acid was employed either catalytically, or even stoichiometrically according to the literature,[7] significant amounts of the starting material were recovered and some unidentified byproducts were obtained. In contrast, the analogous compound **2** (R = OAc) underwent a clean conversion into the corresponding ring-opened product. After many unsuccessful trials, we eventually observed that rust on the needle attached to the syringe accelerated the reaction. Careful experiments showed that **2b** on its own did not, in fact, react with acetyl bromide (Table 1, entry 1), whereas iron(III) hydroxide oxide [FeO(OH), 5 mol%], the main component of rust, produced a remarkable rate acceleration to give **3** as a diastereomeric mixture (entry 2).[11] Acetyl bromide probably transforms iron(III) hydroxide oxide into an iron(III) salt of sufficient Lewis acidity[12] to assist the C–O displacement reaction of **2b** with the bromide anion through a carbenium-ion intermediate[13] by coordination to the furan oxygen (Scheme 3, path a). Alternatively, the acetyl cation, as the actual Lewis acid, could be generated by the reaction between acetyl bromide and an iron(III) salt (Scheme 3 path b). In fact, iron(III) bromide was found to be similarly effective to the hydroxide oxide (Table 1, entry 3). The use of acetyl bromide is more critical, as neither acetyl chloride nor acetic anhydride caused the reaction under the same conditions. Because it is readily available and stable in air, iron(III) hydroxide oxide was used throughout the remainder of the study.

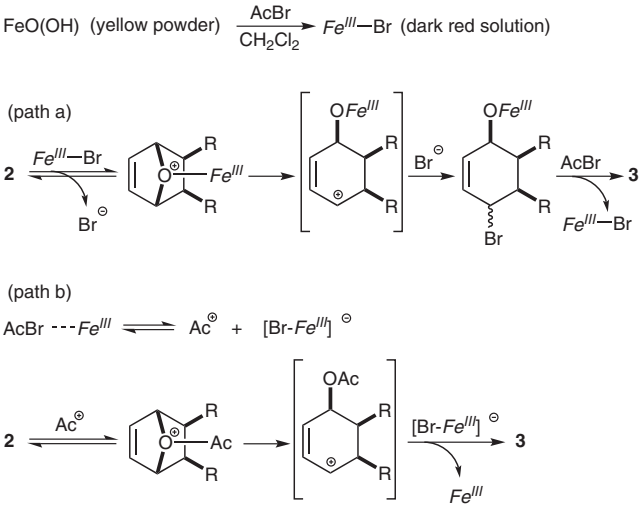
Table 1 Ring-Opening Reaction of 7-Oxabicyclo[2.2.1]hept-2-ene (**2b**) with Acetyl Bromide Catalyzed by Iron(III) Hydroxide Oxide



2b **3**

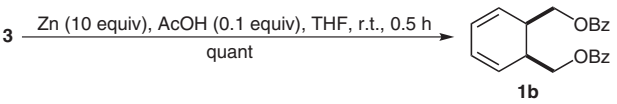
Entry	Catalyst[a]	AcBr (equiv)	Time (h)	Conversion (%)[b]
1	none	1	8	trace
2	FeO(OH) (5 mol%)[c]	1	0.5	>99
3	$FeBr_3$ (5 mol%)	1	0.5	92

[a] For the reaction conditions, see the experimental section.
[b] Determined by ^1H NMR analysis.
[c] The FeO(OH) was pretreated with AcBr for 30 min before addition of **2b**.



Scheme 3 Plausible mechanisms for the ring-opening reaction

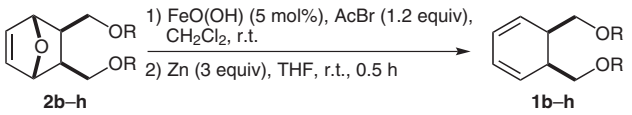
We next examined the 1,4-reductive elimination reaction with zinc and acetic acid in tetrahydrofuran, and found that the reaction gave the cyclohexa-1,3-diene **1b** quantitatively (Scheme 4).[8b]



Scheme 4 Reductive elimination reaction of **3** with Zn and AcOH in THF to give cyclohexa-1,3-diene **1b**

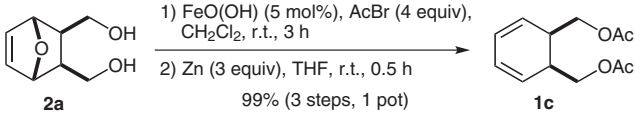
We then assumed that the iron(III) species would not interfere with the action of zinc, and that acetic acid could be supplied by hydrolysis of acetyl bromide used in a slight excess, so that a one-pot preparation of **1b** from **2b** without isolation of **3** should be possible. In fact, after we had confirmed by thin-layer chromatography that **2b** was completely converted into **3** by acetyl bromide (1.2 equiv) in the presence of iron hydroxide oxide (5 mol%), we added tetrahydrofuran and zinc dust successively to the mixture and obtained cyclohexa-1,3-diene **1b** quantitatively (Table 2, entry 1).[14] Other substrates **2c**–**h** bearing various hydroxy protecting groups were also examined to determine whether carboxylic acid ester (entries 1 and 2), sulfonic acid ester (entry 3), carbonate (entry 4), carbamate (entry 5), and methyl ether groups (entry 6) were compatible with the reaction conditions. The reaction of **2f** was slower, presumably because the carbamoyl group coordinated strongly to an iron(III) species, reducing the catalytic activity of the latter. The lower yields obtained with **2h** were attributed to partial detachment of the benzyl group (entry 7) during the iron(III)-catalyzed ring-opening step. Protecting groups that are more sensitive to acids, such as *tert*-butyl(dimethyl)silyl or methoxymethyl, were not suitable, as deprotection and acetylation by acetyl bromide occurred to give cyclohexa-3,5-diene-1,2-diyl-bis(methylene) diacetate (**1c**; data not shown). In fact, **1c** was obtained directly from **2a** by treatment with an excess of acetyl bromide (Scheme 5).

Table 2 One-Pot Diene Synthesis from Various 2,5-Dihydrofurans



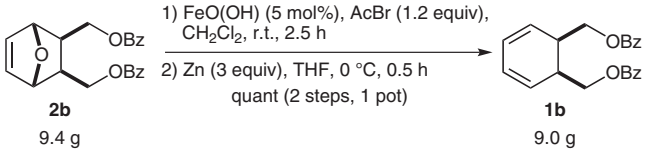
Entry	Substrate[a] (R)	Time (h)[b]	Yield (%)[c]
1	**2b** (Bz)	1	99
2	**2c** (Ac)	1	99
3	**2d** (Ms)	2.5	99
4	**2e** (CO_2Me)	2.5	99
5	**2f** ($CONMe_2$)	14	80
6	**2g** (Me)	1	92
7	**2h** (Bn)	1.5	52

[a] See the experimental section for typical reaction conditions.
[b] Reaction time for the iron-catalyzed ring-opening step.
[c] Isolated yields.



Scheme 5 Conversion of 7-oxabicyclo[2.2.1]hept-2-ene **2a** into cyclohexa-1,3-diene **1c** by one-pot acetylation, furan ring opening, and reductive elimination

Finally, we successfully performed the reaction with **2b** on a larger scale (26 mmol) to demonstrate the synthetic benefits of the present method (Scheme 6).[15]



Scheme 6 Large-scale synthesis of 7-oxabicyclo[2.2.1]hept-2-ene **2b**

In summary, we have developed a convenient synthesis of 5,6-*cis*-disubstituted cyclohexa-1,3-dienes, which are useful as starting materials for the synthesis of densely functionalized cyclohexane derivatives such as cyclitols or carbasugars, by means of a one-pot, two-step deoxygenation of 7-oxabicyclo[2.2.1]hept-2-enes. The method is readily scalable without any experimental difficulties.

All melting points were measured on a Yanaco Micro Melting Point Apparatus MP-J3 and are uncorrected. ^{1}H NMR spectra were recorded at 300 MHz or 400 MHz on a JEOL JNM-AL-300 or a JEOL JNM-AL-400 instrument, respectively. ^{13}C NMR spectra were recorded at 75 MHz on a JEOL JNM-AL-300 instrument. IR spectra were recorded on a SHIMADZU FTIR-8400 instrument. High-resolution mass (HR-FABMS) spectra were recorded on a JEOL JMS-HX-110 mass spectrometer with 3-nitrobenzyl alcohol as the matrix. Column chromatography was conducted on silica gel 60N (spherical, neutral), 63–210 μm, obtained from Kanto Chemical Co., Inc. TLC was performed on Merck silica gel plate (60 F-254). FeO(OH) and AcBr were purchased from Kanto Chemical Co., Inc. and from Nacalai Tesque, Inc., respectively, and were used as received. Zn powder was purchased from Tokyo Chemical Industry Co., Ltd. and was activated before use by washing with 1 M aq HCl. CH_2Cl_2 was purchased from Wako Pure Chemical Industries, Ltd. and freshly distilled over CaH_2 before use. THF was used as received from Wako Pure Chemical Industries, Ltd. Compound **2a** was prepared as previously reported.[9]

1,3-Dienes (1b–h); General Procedure

A Schlenk flask was charged with diene **2** (0.5 mmol), FeO(OH) (2.2 mg, 25 μmol), and CH_2Cl_2 (2 mL) under argon. AcBr (44 μL, 0.6 mmol) was added to the resulting suspension, and the mixture was stirred at r.t. for the time shown in Table 2 until the starting material was completely consumed (TLC). Zn powder (0.10 g, 1.5 mmol) was added and the mixture was stirred for 5 min, and then THF (1 mL) was added and the mixture was stirred for a further 30 min. The mixture was treated with sat. aq. $NaHCO_3$ then filtered through a pad of Celite to remove unreacted Zn powder. The filtrate was extracted with CH_2Cl_2 (2 × 20 mL), and the organic layer was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography (silica gel).

(1*R**,2*S**)-Cyclohexa-3,5-diene-1,2-diylbis(methylene) Dibenzoate (1b)

Column chromatography: hexane–EtOAc, 5:1; yield: 99%; R_f = 0.6 (hexane–EtOAc, 5:1).

IR (KBr): 1717, 1273, 1111, 710 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 7.3 Hz, 4 H), 7.52 (t, *J* = 7.3 Hz, 2 H), 7.37 (t, *J* = 7.7 Hz, 4 H), 6.10–6.06 (m, 2 H), 5.84–5.81 (m, 2 H), 4.47 (d, *J* = 6.6 Hz, 4 H), 3.12–3.04 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5, 132.9, 130.0, 129.5, 128.3, 126.3, 125.6, 63.5, 35.2.

HRMS-FAB: *m/z* [M + H]$^+$ calcd for $C_{20}H_{20}O_4$: 349.1440; found: 349.1451.

The synthesis of **1b** was also carried out in a 26 mmol scale under almost the same conditions as described in the general procedure, except for a prolonged reaction time at the Fe-catalyzed ring-opening reaction step and a lower reaction temperature at the Zn-mediated reductive elimination step (Scheme 6). **Safety note**: When scaled up, the second step of the one-pot protocol should be performed at 0 °C because it is significantly exothermic.

(1*R**,2*S**)-Cyclohexa-3,5-diene-1,2-diylbis(methylene) Diacetate (1c)

Column chromatography: hexane–EtOAc, 4:1; yield: 99%; R_f = 0.4 (hexane–EtOAc, 3:1).

IR (KBr): 1744, 1242, 1231 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.02–5.99 (m, 2 H), 5.72–5.67 (m, 2 H), 4.19–4.06 (m, 4 H,), 2.87–2.77 (m, 2 H), 2.05 (s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.0, 126.3, 125.4, 63.0, 34.9, 20.9.

HRMS-FAB: *m/z* [M + H]$^+$ calcd for $C_{12}H_{16}O_4$: 225.1127; found: 225.1131.

1c was also synthesized from **2a** by following the general procedure, except for the use of an excess (4 equiv) of AcBr and a prolonged reaction time (3 h) before the reductive elimination step (Scheme 5).

(1*R,2*S**)-Cyclohexa-3,5-diene-1,2-diylbis(methylene) Dimethanesulfonate (1d)**
Column chromatography: hexane–EtOAc, 1:2; yield: 99%; R_f = 0.5 (hexane–EtOAc, 1:3).

Because **1d** gradually decomposed upon standing at r.t., only the ^{1}H and ^{13}C NMR spectra are presented here.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.10–6.07 (m, 2 H), 5.74–5.70 (m, 2 H), 4.34 (dd, *J* = 7.8 and 9.8 Hz, 2 H), 4.23 (dd, *J* = 5.9 and 9.8 Hz, 2 H), 3.04 (s, 6 H), 3.01–2.95 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 126.3, 124.7, 67.4, 37.5, 35.3.

(1*R,2*S**)-Cyclohexa-3,5-diene-1,2-diylbis(methylene) Dimethyl Biscarbonate (1e)**
Column chromatography: hexane–EtOAc, 3:1; yield: 99%; mp 58–59 °C; R_f = 0.4 (hexane–EtOAc, 3:1).

IR (KBr): 1755, 1454, 1443, 1275, 961, 937 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.04–6.00 (m, 2 H), 5.73–5.68 (m, 2 H), 4.28–4.12 (m, 4 H,), 3.77 (s, 6 H), 2.90–2.83 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.6, 125.8, 125.6, 66.3, 54.7, 34.8.

HRMS-FAB: *m/z* $[M + H]^+$ calcd for $C_{12}H_{16}O_6$: 257.1025; found: 257.1017.

(1*R,2*S**)-Cyclohexa-3,5-diene-1,2-diylbis(methylene) Bis(dimethylcarbamate) (1f)**
Column chromatography: hexane–EtOAc, 1:3; yield: 80%; R_f = 0.5 (hexane–EtOAc, 1:4).

IR (KBr): 1705, 1497, 1456, 1402, 1360, 1194, 1057, 770 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.00–5.97 (m, 2 H), 5.74–5.69 (m, 2 H), 4.20–4.09 (m, 4 H,), 2.90 (s, 12 H), 2.90–2.80 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.3, 126.4, 125.0, 63.8, 36.2, 35.7, 35.3.

HRMS-FAB: *m/z* $[M + H]^+$ calcd for $C_{14}H_{22}N_2O_4$: 283.1658; found: 283.1659.

(5*R,6*S**)-5,6-Bis(methoxymethyl)cyclohexa-1,3-diene (1g)**
Column chromatography: CH_2Cl_2; yield: 92%.

The ^{1}H and ^{13}C NMR spectra were consistent with those reported in the literature.[6]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.96–5.92 (m, 2 H), 5.74–5.70 (m, 2 H), 3.51–3.46 (m, 2 H), 3.38–3.32 (m, 2 H), 3.32 (s, 6 H), 2.78–2.68 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 127.9, 124.5, 71.8, 58.6, 35.8.

(5*R,6*S**)-5,6-Bis(benzyloxymethyl)cyclohexa-1,3-diene (1h)**
Column chromatography: hexane–CH_2Cl_2, 1:1; yield: 52%.

The ^{1}H and ^{13}C NMR spectra were consistent with those reported in the literature.[6]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37–7.24 (m, 10 H), 5.96–5.92 (m, 2 H), 5.78–5.73 (m, 2 H), 4.46 (s, 4 H), 3.61–3.56 (m, 2 H,), 3.48–3.43 (m, 2 H), 2.86–2.76 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.5, 128.3, 128.1, 127.6, 127.5, 124.5, 73.0, 69.5, 36.0.

(1*R,2*S**,3*R**,4*S**)-7-Oxabicyclo[2.2.1]hept-5-ene-2,3-diylbis(methylene) Dibenzoate (2b)**
BzCl (6.3 mL, 55 mmol) was added dropwise to a soln of **2a** (3.8 g, 25 mmol), DMAP (0.3 g, 2.5 mmol), and Et_3N (7.6 mL, 55 mmol) in CH_2Cl_2 (100 mL) at 0 °C under argon, and the mixture was allowed to warm to r.t. with stirring overnight. The mixture was then treated with sat. aq. $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude product was recrystallized [CH_2Cl_2–hexane (2:1; 30 mL)] to give **2b** as crystals; yield: 7.3 g (81%); mp 165–166 °C; R_f = 0.4 (hexane–EtOAc, 5:1).

IR (KBr): 1717, 1279, 1269, 1119, 712 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 7.2 Hz, 4 H), 7.59 (t, *J* = 7.2 Hz, 2 H), 7.47 (t, *J* = 7.2 Hz, 4 H), 6.44 (s, 2 H), 4.98 (s, 2 H,), 4.65 (dd, *J* = 5.7 and 10.8 Hz, 2 H), 4.39 (dd, *J* = 9.2 and 10.8 Hz, 2 H), 2.28–2.22 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.3, 135.7, 133.1, 130.0, 129.6, 128.5, 80.6, 64.4, 39.5.

HRMS-FAB: *m/z* $[M + H]^+$ calcd for $C_{22}H_{20}O_5$: 365.1389; found: 365.1419.

(1*R,2*S**,3*R**,4*S**)-7-Oxabicyclo[2.2.1]hept-5-ene-2,3-diylbis(methylene) Diacetate (2c)**
This compound was prepared by a slight modification of the literature procedure.[16]

The ^{1}H and ^{13}C NMR spectra are consistent with those reported.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.40 (s, 2 H), 4.82 (s, 2 H), 4.28 (dd, *J* = 5.1 and 11.0 Hz, 2 H), 4.07–3.97 (m, 2 H), 2.09 (s, 6 H), 2.07–1.88 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.9, 135.6, 80.4, 63.8, 39.2, 21.0.

(1*R,2*S**,3*R**,4*S**)-7-Oxabicyclo[2.2.1]hept-5-ene-2,3-diylbis(methylene) Dimethanesulfonate (2d)**
The compound was prepared by a slight modification of the literature procedure.[17]

The ^{1}H and ^{13}C NMR spectra were consistent with those reported.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.43 (t, *J* = 0.9 Hz, 2 H), 4.89 (t, *J* = 0.9 Hz, 2 H), 4.37 (dd, *J* = 5.7 and 9.7 Hz, 2 H), 4.25–4.19 (m, 2 H,), 3.07 (s, 6 H), 2.24–2.16 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.6, 80.2, 68.8, 40.2, 37.6.

(1*R,2*S**,3*R**,4*S**)-7-Oxabicyclo[2.2.1]hept-5-ene-2,3-diylbis(methylene) Dimethyl Biscarbonate (2e)**
MeO_2CCl (0.4 mL, 6.5 mmol) was added to a soln of **2a** (0.17 g, 1.1 mmol), DMAP (6 mg, 50 μmol), and pyridine (0.4 mL, 5 mmol) in CH_2Cl_2 (4 mL) at 0 °C under argon, and the mixture was allowed to warm to r.t. with stirring for 3 h. The mixture was treated with sat. aq $NaHCO_3$ (2 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine (5 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography [silica gel, hexane–EtOAc (2:1)] to give **2e** as an oil; yield: 0.25 g (88%); mp 57–58 °C; R_f = 0.5 (hexane–EtOAc, 1:1).

IR (KBr): 1744, 1445, 1323, 1263, 949, 901, 840, 795 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.38 (s, 2 H), 4.86 (s, 2 H), 4.32 (dd, *J* = 7.9 and 10.3 Hz, 2 H), 4.16–4.05 (m, 2 H), 3.81 (s, 6 H), 2.12–2.03 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.4, 135.5, 80.3, 67.3, 54.9, 39.3.

HRMS-FAB: *m/z* $[M + H]^+$ calcd for $C_{12}H_{16}O_7$: 273.0974; found: 273.0989.

(1*R,2*S**,3*R**,4*S**)-7-Oxabicyclo[2.2.1]hept-5-ene-2,3-diylbis(methylene) Bis(dimethylcarbamate) (2f)**
A soln of **2a** (0.78 g, 5.0 mmol) in THF (20 mL) was cooled to 0 °C, NaH (60% in mineral oil, 0.39 g, 11 mmol) was slowly added, and the mixture was stirred for 30 min. Me_2NCOCl (1.0 mL, 11 mmol) was added dropwise and the mixture was allowed to warm to r.t. with stirring overnight. After treatment with H_2O (10 mL), the mix-

ture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography [silica gel, hexane–EtOAc (1:3)] to give **2f** as crystals; yield: 0.85 g (57%); mp 85–86 °C; R_f = 0.3 (hexane–EtOAc, 1:4).

IR (KBr): 1697, 1501, 1445, 1400, 1366, 1182, 1059, 768, 679 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.38 (s, 2 H), 4.83 (s, 2 H), 4.35 (dd, *J* = 12.2 and 15.8 Hz, 2 H), 4.12–4.01 (m, 2 H), 2.93 (s, 12 H), 2.07–1.98 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.3, 135.6, 80.4, 64.7, 39.6, 36.4, 35.9.

HRMS-FAB: *m/z* $[M + H]^+$ calcd for $C_{14}H_{22}N_2O_5$: 299.1607; found: 299.1565.

(1*R,2*S**,3*R**,4*S**)-2,3-Bis(methoxymethyl)-7-oxabicyclo[2.2.1]hept-5-ene (2g)**

The compound was prepared by a slight modification of the literature procedure.[18]

The ^1H and ^{13}C NMR spectra were consistent with those reported.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.35 (t, *J* = 0.9 Hz, 2 H), 4.83 (t, *J* = 0.9 Hz, 2 H), 3.48 (dd, *J* = 5.1 and 8.8 Hz, 2 H), 3.36 (s, 6 H), 3.34–3.28 (m, 2 H), 1.95–1.86 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.5, 80.5, 72.0, 58.8, 39.8.

(1*R,2*S**,3*R**,4*S**)-2,3-Bis(benzyloxymethyl)-7-oxabicyclo[2.2.1]hept-5-ene (2h)**

NaH (60% in mineral oil, 0.50 g, 13 mmol) was slowly added to a soln of **2a** (0.71 g, 4.7 mmol) in THF (20 mL) at 0 °C, and the mixture was stirred for 30 min. BnBr (1.5 mL, 13 mmol) was added dropwise, and the mixture was allowed to warm to r.t. with stirring overnight. After treatment with H_2O (10 mL), the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography [silica gel, hexane–EtOAc (8:1)] to give **2h** as an oil; yield: 0.97 g (62%); R_f = 0.3 (hexane–EtOAc, 8:1).

IR (KBr): 1497, 1454, 1366, 1310, 1028, 907, 737, 696 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.25 (m, 10 H), 6.35 (s, 2 H), 4.87 (s, 2 H), 4.51 and 4.49 (ABq, *J* = 12.1 Hz, 4 H), 3.59 (dd, *J* = 5.1 and 8.8 Hz, 2 H), 3.42–3.36 (m, 2 H), 2.01–1.92 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.2, 135.5, 128.4, 127.7, 127.7, 80.7, 73.3, 69.8, 40.0.

HRMS-FAB: *m/z* $[M + H]^+$ calcd for $C_{22}H_{24}O_3$: 337.1804; found: 337.1805.

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