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Intermolecular Diels−Alder Reactions of Brominated Masked *o*-Benzoquinones with Electron-Deficient Dienophiles. A Detour Method to Synthesize Bicyclo[2.2.2]octenones from 2-Methoxyphenols

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Intermolecular Diels−Alder reactions of masked *o*-benzoquinones, i.e., 6,6-dimethoxy-2,4-cyclohexadienones **5**−**7** and **21**−**24** generated from 2-methoxyphenols **1**−**3** and **17**−**20**, respectively, with electron-deficient dienophiles leading to highly functionalized bicyclo[2.2.2]octenones are described. The masked *o*-benzoquinones (MOBs) **5**−**7** underwent Diels−Alder cycloadditions with methyl acrylate, methyl methacrylate, and methyl vinyl ketone to provide bicyclo[2.2.2]octenones **13a**−**c** to **15a**−**c** (direct method) in low to moderate yields with the concomitant formation of considerable amounts of dimers **9**−**11**. To retard dimerization and to improve the yields of the requisite bicyclo[2.2.2]octenones, a detour method comprised of sequential bromination of 2-methoxyphenols **1**−**4**, oxidation and Diels−Alder reaction, and debromination has been developed. The oxidation of bromophenols **17**−**20** produced MOBs **21**−**24** which are stable enough to be isolated. The MOBs **21**−**24** underwent cycloaddition with electron-deficient dienophiles in a very efficient manner to afford the corresponding cycloadducts **25a**−**c** to **28a**−**c** in good to high yields without self-dimerization. When the cycloadducts **25a**−**c** to **28a**−**c** were treated with either Bu_3SnH/AIBN or tributylammonium formate−palladium reagent, the corresponding debrominated products **13a**−**c** to **16a**−**c** were obtained in high to excellent yields. In general, the cycloadducts **13a**−**c** to **15a**−**c** were obtained in 20−40% higher yields via the detour method than those via the direct method. In both routes, the Diels−Alder reactions proceeded in a highly regio- and stereoselective manner to furnish a single cycloadduct in each case.

Introduction

The Diels−Alder reactions are the most versatile and synthetically useful reactions in which four new contiguous stereogenic centers can be generated in a single laboratory operation.[1−3] The methodology allows the introduction of a plethora of functionality in an expeditious manner with regio- and stereoselectivity.[4] A wide variety of ring structures have been constructed by using various dienes and dienophiles bearing an array of functionalities in the Diels−Alder reactions.[5] Bicyclo[2.2.2]octenones[6,7] obtained via the Diels−Alder reactions are useful synthons for polysubstituted cyclohexanes,[8] bicyclo[3.2.1]octenones,[9] bicyclo[4.2.0]octenones,[10,11] tricyclo[3.3.0.$0^{2,8}$]octanones,[10] variously fused triquinanes,[12] *cis*-decalins,[13] and bicyclo[4.2.2]decenones.[13a] Bicyclo[2.2.2]-octenones can undergo interesting and useful photochemical reactions, viz., oxa-di-π-methane rearrangement and 1,3-acyl migration.[10,14] Further, they have a wide range of applications in the synthesis of natural products.[15]

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We have found that oxidation of simple and readily available 2-methoxyphenols in methanol with diacetoxyiodobenzene (DAIB) or [bis(trifluoroacetoxy)]iodobenzene (BTIB) produces unstable *o*-benzoquinone monodimethylacetals which are generically called masked *o*-benzoquinones (MOBs).[16] We have previously reported a methodology based on intermolecular Diels−Alder reactions of MOBs[17,18] wherein we encountered some MOBs that were not stable enough to be isolated and were found to dimerize under reaction conditions. In most of these MOBs, the competition between self-dimerization and the Diels−Alder reaction with external dienophiles was often observed, though to a varying degree. To avoid dimerization, a large excess of the dienophiles is used and the concentration of the MOB in the reaction mixture is kept low throughout the course of the reaction by employing a high dilution technique. In some cases (vide infra), even high dilution could not overcome the high propensity of MOBs toward dimerization, which still was the main constraint for their use in organic synthesis.[19] To prevent dimerization and to improve the yields of requisite bicyclo[2.2.2]octenones, a detour method comprised of sequential bromination of 2-methoxyphenols **1**−**4**, oxidation, Diels−Alder reaction, and debromination has been developed.[20] We present herein a detailed account of our investigations on the intermolecular Diels−Alder reactions of unstable MOBs **5**−**7**, their stable brominated equivalents **21**−**23** and brominated MOB **24** with electron-deficient dienophiles, methyl acrylate (MA), methyl methacrylate (MMA), and methyl vinyl ketone (MVK) to synthesize bicyclo[2.2.2]octenones.

Results and Discussion

The oxidation of the parent 2-methoxyphenol, i.e., guaiacol (**1**), in methanol was first carried out with DAIB at room temperature. In the absence of an external dienophile, the reaction produced exclusively dimer **9**, which indicates the high unstable nature of MOB **5**. Therefore, high dilution technique and a large ratio of the dienophile to MOB was maintained throughout the course of the reaction to minimize dimerization and to increase the yield of the Diels−Alder adduct. Thus, to a mixture of DAIB and MA (25 equiv) in methanol was added guaiacol (**1**) slowly at room temperature, using a syringe pump, over a period of 10 h. The reaction was continued for another hour at the same temperature. Usual workup and chromatography still furnished mainly the dimer **9** in 70% yield along with the Diels−Alder adduct **13a** in only 29% yield (Scheme 1, Table 1). However, the yield of the cycloadduct **13a** was marginally improved to 40% and the yield of dimer was dropped to 60% when **1** was added to a mixture of DAIB and MA (25 equiv) under reflux (Method A). When the MOB **5** was allowed to react with MMA, the yield of the cycloadduct **13b** was substantially dropped (9% at room temperature and 28% under reflux), presumably due to the steric hindrance caused by the additional methyl group in the dienophile. We then utilized another electron-deficient dienophile MVK in the Diels−Alder reaction with MOB **5**, which afforded the cycloadduct **13c** (54% yield when addition time of **1** to the reaction mixture was 5 h and 62% when the addition time was 10 h) at room temperature.

Taking the electron-deficient nature of the diene moiety in MOB **5** into account, we then considered the MOBs **6** and **7** bearing an electron-releasing methyl group at positions 2 and 3, respectively. Gratifyingly, the formation of dimer **10** was supressed drastically and the requisite bicyclic derivative **14a** was obtained in good yield. When these conditions (Table 1) were extended to MMA and MVK, the cycloadducts **14b** and **14c** were obtained in lower yields due to the formation of dimer **10** in considerable amounts. Similarly, the reactions of MOB **7** generated from phenol **3** with MA, MMA, and MVK produced substantial amounts of dimer **11** with poor yields of the Diels−Alder adducts **15a**−**c**. Though the chemical yields are not encouraging, each of these reactions provided a single isomer indicating the excellent regio- and stereoselectivities.

SCHEME 1

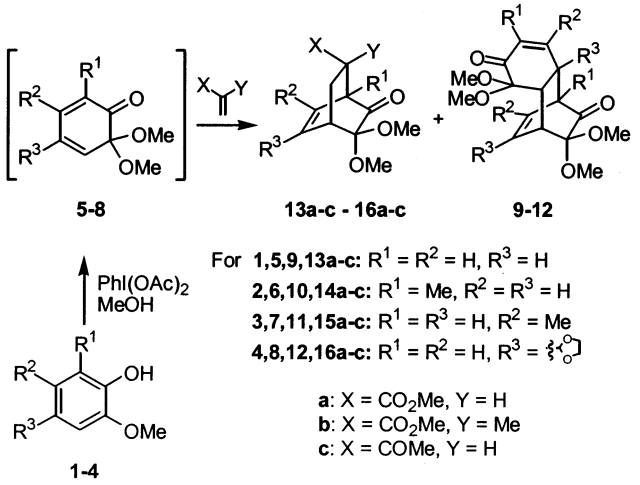

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TABLE 1. Intermolecular Diels–Alder Reactions of Masked *o*-Benzoquinones 5–8 with MA, MMA, and MVK (direct method)[a]

				reaction conditions			
entry	phenol	MOB	dienophile[b]	addition time[c]/temp	after addition[d]	adduct/Y (%)	dimer/Y (%)
1	**1**	**5**	MA	10 h/rt	rt/1 h	**13a**/29	**9**/70
2			MA	10 h/reflux	reflux/1 h	**13a**/40	**9**/60
3			MMA	10 h/rt	rt/1 h	**13b**/9	**9**/90
4			MMA	48 h/reflux	reflux/1 h	**13b**/28	**9**/65
5			MVK	5 h/rt	rt/1 h	**13c**/54	**9**/24
6			MVK	10 h/rt	reflux/1 h	**13c**/62	**9**/10
7	**2**	**6**	MA	8 h/reflux	reflux/1 h	**14a**/86	**10**/13
8			MMA	8 h/reflux	reflux/1 h	**14b**/43	**10**/38
9			MVK	8 h/reflux	reflux/1 h	**14c**/22	**10**/42
10	**3**	**7**	MA	8 h/reflux	reflux/1 h	**15a**/35	**11**/34
11			MMA	8 h/reflux	reflux/1 h	**15b**/19	**11**/45
12			MVK	8 h/reflux	reflux/1 h	**15c**/25	**11**/48
13[e]	**4**	**8**	MA	rt[f]	rt/60 h	**16a**/86	**12**/0
14[e]			MMA	rt[f]	rt/72 h	**16b**/84	**12**/0
15[e]			MVK	rt[f]	rt/20 h	**16c**/88	**12**/0

[a] Reactions in entries 1–12 were carried out following Method A. [b] About 25 equiv of dienophiles was used in Method A. [c] Time during which 2-methoxyphenol (**1**–**3**) was added to the reaction mixture. [d] Temperature of the reaction and the time for which the reaction mixture was stirred after the complete addition of 2-methoxyphenol (**1**–**4**). [e] Data taken from ref 15 for comparing the results. [f] 2-Methoxyphenol (**4**) was added in one portion.

From the above results, it appears that the lower yields of the desired Diels–Alder adducts obtained in one step (direct method) are mainly due to the rapid dimerization of these MOBs under reaction conditions. On the basis of our earlier observations on MOB chemistry, it is apparent that the presence of a bulky group on MOB retards dimerization significantly. We have shown previously that a dioxolane in the 4-position also gives higher yields of Diels–Alder product and no dimer.[18] Thus, we envisioned that a bromine atom introduced as an additional removable substituent at the 4-position of MOBs **21**–**23** would retard the dimerization, consequently increasing the yields of the Diels–Alder adducts.[20]

The required 4-bromophenols **17**–**19** were prepared from phenols **1**–**3**, respectively, by bromination with NBS/AcOH, using a modified literature procedure.[21] The oxidation of 4-bromophenol **17** in methanol carried out with DAIB at room temperature reached completion within 10 min to afford MOB **21** in 94% yield with no traces of the dimer of MOB **21** (Scheme 2). The oxidation of **18** in a similar manner furnished a minor product **29** (5%) in addition to MOB **22** in 82% yield. The aromatized product **29** was presumably derived from dimer **30** via dehydrobromination, reduction, and loss of methanol. Upon oxidation of **19** with DAIB in methanol, MOB **23** and its dimer **31** were obtained in 77% and 5% yields, respectively (Chart 1). Obviously, the introduction of a bromine atom at the 4-position increased the stability of the corresponding brominated MOBs, thereby facilitating their isolation in the pure form and in good yields. We thus anticipated the increased yields of the Diels–Alder adducts with these brominated MOBs **21**–**23**.

As indicated in Scheme 2 and Table 2, we have examined the Diels–Alder reactions of MOBs **21**–**23** obtained from bromophenols **17**–**19**, respectively, with MA, MMA, and MVK. The crude MOB **21** obtained from **17** was taken in CH_2Cl_2, MA was added, and the mixture was stirred for 10 h at room temperature. The usual workup followed by column chromatography furnished

SCHEME 2

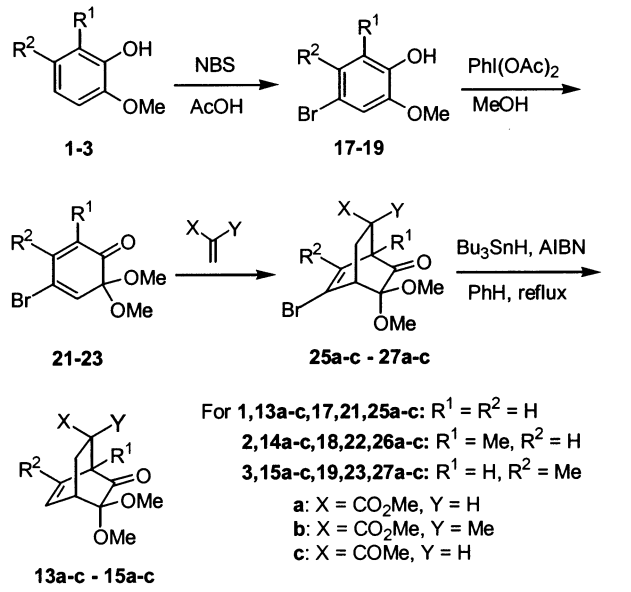
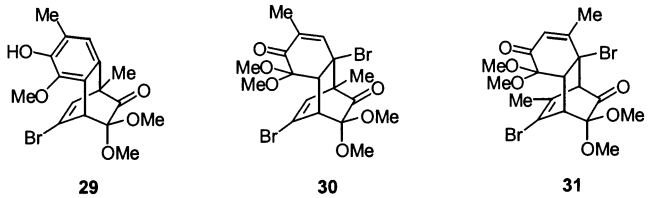


CHART 1



the cycloadduct **25a** in 72% yield. When the MOB **21** was generated in situ and subjected to cycloaddition with MA (10 h) (Method B), the adduct **25a** was obtained in 70% yield. Since the bicyclic derivative **25a** was produced in almost the same yields in these two conditions, it was planned to generate MOB in situ for latter cycloadditions. The dienophiles MMA and MVK reacted efficiently with MOB **21** to provide the Diels–Alder adducts **25b** and **25c**, respectively. The reactions of MOB **22** (Method C) with MA, MMA, and MVK produced the adducts **26a**–**c** in good to excellent yields. We then carried out the reaction

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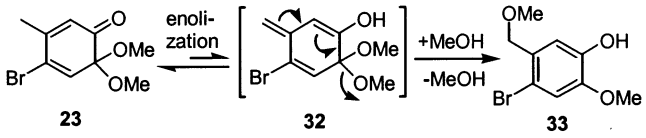
TABLE 2. Intermolecular Diels–Alder Reactions of Masked 4-Bromo-*o*-benzoquinones 21–24 with MA, MMA, and MVK (detour method)

	Diels–Alder reaction					debrominated	overall yields of **13–16a–c**	
entry	phenol	MOB	dienophile[a]	method/time[b]	adduct/Y (%)	product[c]/Y (%)	direct	detour
1	**17**	**21**	MA	B/10 h	**25a**/70	**13a**/95	40	65
2			MMA	B/48 h	**25b**/65	**13b**/94	28	59
3			MVK	B/5 h	**25c**/85	**13c**/90	62	76
4	**18**	**22**	MA	C/17 h	**26a**/75	**14a**/96	86	66
5			MMA	C/22 h	**26b**/72	**14b**/93	43	61
6			MVK	C/17 h	**26c**/83	**14c**/81	22	61
7	**19**	**23**	MA	C/36 h	**27a**/72	**15a**/85	35	60
8			MMA	C/60h	**27b**/62	**15b**/87	19	53
9			MVK	C/10 h	**27c**/90	**15c**/77	25	68
10	**20**	**24**	MA	D/4 h	**28a**/94	**16a**/86	86	81
11			MMA	D/10 h	**28b**/95	**16b**/88	84	84
12			MVK	D/3 h	**28c**/96	**16c**/84	88	83

[a] 1.1 equiv of dienophiles in Method B, 1.5 equiv in Method C, and 2 equiv in Method D were used. [b] Time for which the reaction mixtures were allowed to stir. [c] Debrominated products (**13a–c** to **15a–c** (entries 1–9) were obtained from Method E and **16a–c** (entries 10–12) were obtained from Method F.

SCHEME 3



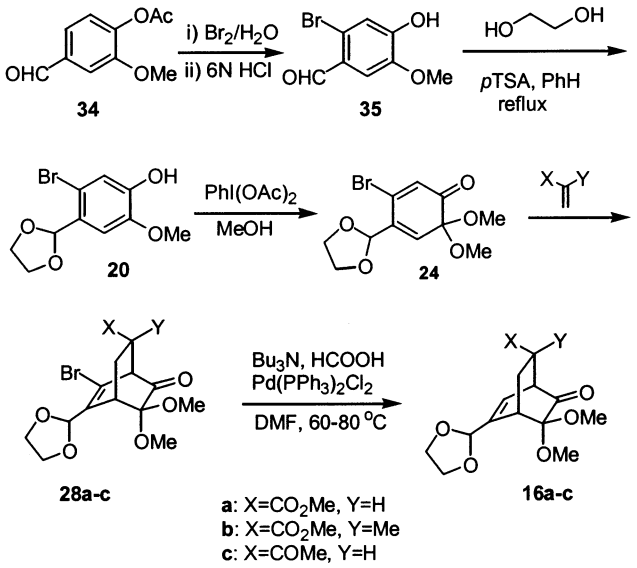
of MOB **23** with MA, MMA, and MVK (Method C). The MOB **23** generated in situ from **19** underwent the Diels–Alder cycloaddition smoothly with MA, MMA, and MVK to provide bromo-adducts **27a–c** in good to high yields. The ^{1}H NMR (400 MHz) spectra of the crude reaction mixtures did not show the peaks corresponding to the minor isomer(s), indicating that the cycloaddition proceeded in a highly regio- and stereoselective manner.

In the DAIB-mediated oxidation of **19** in the presence of MA and MMA (but not in the case of MVK) we have also isolated the compound **33** in 6 and 13% yields, respectively. The formation of **33** might be explained through the tandem, one-step addition–elimination of methanol to **32** as shown in Scheme 3.

In an effort to ascertain whether the bromo-substitution at the 3-position of MOB **24** has influenced the cycloaddition, we have synthesized MOB **24** and studied its Diels–Alder reactivity. The bromination of vanillin acetate (**34**) with bromine/water followed by hydrolysis[22] and *p*-TSA-catalyzed ketalization of the resulting aldehyde **35** provided the requisite bromophenol **20** in near quantitative yield (Scheme 4). The oxidation of phenol **20** with DAIB at 0 °C in methanol in the presence of $KHCO_3$ proceeded efficiently to produce MOB **24** in 92% yield. The yield of **28a**, the adduct of MOB **24** with MA, was better when **24** was used after isolation and purification than that when **24** was generated in situ. The reactions of MOB **24** with MMA and MVK were also quite efficient to give the corresponding adducts **28b**,**c** in excellent yields (Table 2).

Then the cycloadducts **25a–c** to **28a–c** were subjected to debromination by using either Bu_3SnH/AIBN[23] or tributylammonium formate–palladium reagent [Bu_3N, HCO_2H/$Pd(PPh_3)_2Cl_2$][24] to afford the corresponding products **13a–c** to **16a–c** in high to excellent yields. Thus, we have achieved the desired cycloadducts via the detour method in overall yields, in general, 20–40% higher than those obtained via the direct method in one step (see Table 2 for comparison of yields). In addition, only 1 molar equiv or a slight excess of dienophile is enough for the brominated MOBs **21–24** to undergo the Diels–Alder reactions, whereas a large excess of dienophiles is necessary for MOBs **5–8**.

SCHEME 4



The structures of all the new compounds were established by IR, ^{1}H and ^{13}C NMR, DEPT, and low- and high-resolution mass spectral analyses. For the majority of the cycloadducts, satisfactory elemental analyses were obtained. For most of the adducts in both low-resolution and high-resolution mass spectra recorded in electron impact mode (70 eV), the peaks corresponding to the molecular ion could not be seen; instead, the peaks corresponding to $M^+ - 28$ were observed, indicating the facile extrusion of CO from the molecular ions. The IR specta of all the cycloadducts showed a strong absorption at 1733–1741 cm^{-1}, characteristic of the carbonyl group

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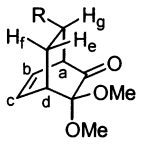
CHART 2



adjacent to the α,α-dimethoxyl groups in the functionalized bicyclo[2.2.2]octenone skeletons.[18,25]

The regio- and stereochemistries of the adducts **13a**−**c** to **16a**−**c** which are in line with the literature precedents[6e,18,25,26] were thoroughly determined by ^{1}H−^{1}H decoupling experiments. The coupling patterns of H_a−H_g (J = 1.4−2.0 Hz) and H_d−H_e or H_d−H_f (J = 2.4−3.6 Hz) are in agreement with the assigned regiochemistry (see Chart 2). The chemical shifts of the bridgehead protons H_a and H_d were observed between δ 3.21−3.75 and δ 3.01−3.44, respectively. The methylenic protons H_e and H_f were observed at δ 2.14−2.92 and δ 1.50−1.94, respectively. The observed long-range W-type coupling between H_b and H_g and/or H_c and H_e supports the endo stereochemistry. The coupling constants between H_e−H_g (J = 9.6−10.3 Hz) and H_f−H_g (J = 5.7−6.8 Hz) clearly show the cis relationship of protons H_e and H_g, which further confirm the assigned stereochemistry.

The structural assignments of **25a**−**c** to **28a**−**c** were based on the spectroscopic methods and the chemical transformation into the corresponding debrominated products **13a**−**c** to **16a**−**c**. The chemical shifts and the coupling patterns in the ^{1}H NMR spectra of **25a**−**c** to **28a**−**c** are analogous to those observed in case of **13a**−**c** to **16a**−**c** respectively. The ortho regiochemistry and endo stereochemistry of the cycloadduct **26b** were further confirmed from the single-crystal X-ray diffraction method.[27]

Conclusion

In summary, we have developed a new and useful strategy to synthesize the hitherto unknown derivatives of bicyclo[2.2.2]octenones. The MOBs **5**−**7** and **21**−**24** generated from 2-methoxyphenols **1**−**3** and **17**−**20**, respectively, underwent highly regio- and stereoselective intermolecular Diels−Alder reactions with electron-deficient dienophiles to furnish exclusively ortho,endo adducts **13a**−**c** to **15a**−**c** and **25a**−**c** to **28a**−**c**. The introduction of a bromine atom at the 4-position of the 2-methoxyphenols allowed us to isolate and characterize the resultant MOBs. Furthermore, the reduced propensity of these bromo-substituted MOBs to dimerize made it possible to use stoichiometric amounts or a slight excess of dienophiles. These vinly bromides **25a**−**c** to **28a**−**c** may be considered to act as valuable handles for the olefin synthesis by organometallic coupling reactions. Standard debromination of cycloadducts **25a**−**c** to **27a**−**c** afforded bicyclo[2.2.2]octenones **13a**−**c** to **15a**−**c** in overall 20−40% higher yields via the detour method than those obtained via the direct method. The present protocol has already been utilized as a key step in the total synthesis of a *cis*-clerodane diterpenic acid.[28]

Experimental Section

General Methods. For general experimental details and instrumentation, see our earlier publication.[18]

General Procedures for Diels−Alder Reactions of MOBs: Method A. To a suspension of DAIB (1.8 mM, 1.2 equiv) and a dienophile (25 equiv) in methanol (2 mL) was added a solution of phenol (**1**−**3**, 1.5 mM, 1 equiv) in methanol (6 mL) over a period of time at either room temperature (only for the reaction of **1** with MVK) or under reflux in nitrogen atmosphere. Stirring was continued for an additional hour under reflux (see Table 1). After the reaction was complete, the reaction mixture was cooled to room temperature and concentrated under reduced pressure, and the residue was purified by silica gel column chromatography with EtOAc/hexanes as eluent to furnish the pure cycloadduct (**13a**−**c** to **15a**−**c**).

Method B. To a suspension of DAIB (1.1 mM, 1.1 equiv) and a dienophile (2 equiv) in methanol (5 mL) was added in one portion a solution of phenol **17** (1 mM, 1 equiv) in methanol (5 mL) at room temperature under nitrogen atmosphere. Stirring was continued for a further period of time (see Table 2). Then the reaction mixture was worked up and the residue was purified as described in Method A to afford the adduct (**25a**−**c**).

Method C. To a suspension of DAIB (1 mM, 1.1 equiv) and $KHCO_3$ (2.5 mM, 2.5 equiv) in methanol (5 mL) was added in one portion a solution of phenol (**18** or **19**, 1 mM, 1 equiv) in methanol (5 mL) at 0 °C under nitrogen atmosphere. After the mixture was stirred for 5 min, dienophile (1.5 mM, 1.5 equiv) was added in one portion and the reaction mixture was allowed to warm to room temperature. After the solution was stirred for a period of time (Table 2), the volatiles were removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 mL), washed with water followed by brine, and dried over anhydrous $MgSO_4$. Removal of the solvent followed by silica gel column chromatography yielded the pure cycloadduct (**26a**−**c** and **27a**−**c**).

Method D. To MOB **24** (1 mM, 1 equiv) in CH_2Cl_2 (1 mL) was added a dienophile (1.1 mM, 1.1 equiv) in one portion at room temperature under nitrogen atmosphere. After the mixture was stirred for a period of time (see Table 2), the volatiles were removed under reduced pressure and the residue was recrystallized to give the pure product (**28a**−**c**).

General Procedure for the Debromination of Cycloadducts: Method E.[23] A mixture of bromo compound (**25a**−**c** to **27a**−**c**, 0.5 mM), AIBN (0.02 mM), and Bu_3SnH (0.74 mM) in dry benzene (5 mL) was heated under reflux for 3 h under nitrogen atmosphere. Then additional amounts of AIBN (0.014 mM) and Bu_3SnH (0.37 mM) were added and the heating was continued for another 3 h at the same temperature. The reaction contents were cooled to room temperature, silica gel (1 g, 70−230 mesh) was added, and stirring was continued for an additional 2 h at the same temperature. The reaction mixture was then filtered and the filtrate was concentrated under reduced pressure. The residue was subjected to silica gel column chromatography (EtOAc/hexanes) to furnish the pure product (**13a**−**c** to **15a**−**c**).

Method F.[24] To the bromo compound (**28a**−**c**, 0.65 mM) were added successively Bu_3N (1.95 mM), HCO_2H (1.3 mM), and $Pd(PPh_3)_2Cl_2$ (0.02 mM) in dry DMF (0.6 mL) under nitrogen atmosphere and the contents were heated at 60−80 °C for 8 h. The reaction mixture was cooled to room temperature and diluted with EtOAc and worked up as usual. The residue was subjected to silica gel column chromatography (EtOAc/hexanes) to afford pure product (**16a**−**c**).

2-Methoxy-6-methylphenol (2).[29] A mixture of 2-hydroxy-3-methoxybenzaldehyde (*o*-vanillin, 22.88 g, 150.42 mM) and 10% Pd/C (2 g) in EtOAc (225 mL) was taken in a 500-mL

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flask and subjected to hydrogenation at 40 psi at room temperature. After 5 h, the reaction mixture was filtered through Celite and the filtrate was evaporated. The residue was distilled under vacuum (50 °C, 0.05 mm) to give **2** (19.72 g, 95% yield) as a light yellow solid. Mp 41−42 °C (from hexanes, lit.[29] mp 40−41 °C); IR (film) 3426, 2949, 1271 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H), 3.88 (s, 3H), 5.68 (br s, 1H), 6.70−6.78 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 55.9, 108.2, 119.1, 123.12, 123.9, 143.7, 146.2; MS (EI, 70 eV) *m*/*z* (rel intensity) 138 (M^+, 78), 123 (100), 95 (29), 77 (61), 67 (51), 65 (47), 63 (14), 55 (41), 53 (30), 51 (61); HRMS (EI) calcd for $C_8H_{10}O_2$ (M^+) 138.0680, found 138.0689. Anal. Calcd for $C_8H_{10}O_2$: C, 69.55; H, 7.30. Found: C, 69.54; H, 7.32.

2-Methoxy-5-methylphenol (3).[30] Following the above procedure with 3-hydroxy-4-methoxybenzaldehyde (isovanillin, 20.42 g, 134.22 mM), the crude product was recrystallized to provide **3** (16.67 g, 90% yield) as a colorless solid. Mp 33−34 °C (from hexanes); IR (film) 3507, 2937, 1275 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H), 3.86 (s, 3H), 5.55 (br, 1H), 6.63−6.75 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 56.0, 110.6, 115.4, 120.2, 131.1, 144.5, 145.4; MS (EI, 70 eV) *m*/*z* (rel intensity) 138 (M^+, 85), 123 (100), 95 (27), 77 (16), 55 (15); HRMS (EI) calcd for $C_8H_{10}O_2$ (M^+) 138.0680, found 138.0689. Anal. Calcd for $C_8H_{10}O_2$: C, 69.55; H, 7.30. Found: C, 69.45; H, 7.32.

(1*R,2*R**,7*R**,8*S**)-3,3,10,10-Tetramethoxytricyclo-[6.2.2.0^{2,7}]dodeca-5,11-diene-4,9-dione (9).**[31] Following the general procedure (Method A), MOB **5** was generated in situ from phenol **1** to react with MA, MMA, or MVK and the residue was purified by column chromatography (EtOAc/hexanes) to furnish dimer **9** as a colorless solid (see Table 1 for yields). Mp 187−190 °C (from EtOAc−hexanes); IR (film) 1735, 1690, 1621 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.06 (s, 3H), 3.12 (ddd, *J* = 6.6, 1.6, 1.6 Hz, 1H), 3.21 (m, 1H), 3.22 (s, 3H), 3.29 (dd, *J* = 8.0, 1.6 Hz, 1H), 3.37 (m, 1H), 3.39 (s, 3H), 3.43 (s, 3H), 5.90 (ddd, *J* = 8.0, 6.6, 1.6 Hz, 1H), 6.03 (dd, *J* = 10.1, 1.8 Hz, 1H), 6.25 (ddd, *J* = 8.0, 6.6, 1.4 Hz, 1H), 6.41 (dd, *J* = 10.1, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 38.8, 39.1, 40.1, 48.7, 49.6, 49.9, 50.4, 52.5, 94.7, 98.4, 128.5, 128.8, 132.1, 146.3, 193.6, 202.0; MS (EI, 70 eV) *m*/*z* (rel intensity) 280 (M^+ − CO, 100), 205 (71), 189 (54), 173 (38), 115 (40), 111 (46), 77 (51), 75 (33), 59 (70); HRMS (EI) calcd for $C_{16}H_{20}O_6$ (M^+) 308.1260, found 308.1265.

(1*R,2*R**,7*R**,8*S**)-5,8-Dimethyl-3,3,10,10-tetramethoxytricyclo[6.2.2.0^{2,7}]dodeca-5,11-diene-4,9-dione (10).**[31] Following the general procedure (Method A), MOB **6** generated in situ from phenol **2** was reacted with MA, MMA, or MVK. The residue was purified by column chromatography (EtOAc/hexanes) and dimer **10** was isolated as a colorless solid. Mp 155−156 °C (from EtOAc−hexanes, lit.[31] mp 152−155 °C); IR (film) 1733, 1694, 1626 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 3H), 1.85 (s, 3H), 2.91 (ddd, *J* = 8, 4.2, 1.6 Hz, 1H), 3.04 (s, 3H), 3.09 (ddd, *J* = 6.8, 1.6, 1.2 Hz, 1H,), 3.22 (s, 3H), 3.27 (dd, *J* = 8.0, 1.3 Hz, 1H), 3.39 (s, 3H), 3.46 (s, 3H), 5.54 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.20 (dd, *J* = 8, 6.8 Hz, 1H), 6.27 (dd, *J* = 4.2, 1.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 16.1, 39.4, 39.9, 43.1, 48.8, 49.5, 50.3, 50.4, 52.2, 94.7, 98.7, 131.4, 133.9, 137.12, 139.0, 195.1, 204.1; MS (EI, 70 eV) *m*/*z* (rel intensity) 308 (M^+ − CO, 100), 293 (11), 261 (24), 233 (22), 201 (19), 171 (25), 159 (20), 105 (73), 91 (16), 59 (12); HRMS (EI) calcd for $C_{17}H_{24}O_5$ (M^+ − CO) 308.1624, found 308.1626. Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.29; H, 7.28.

(1*S,2*R**,7*S**,8*R**)-6,12-Dimethyl-3,3,10,10-tetramethoxytricyclo[6.2.2.0^{2,7}]dodeca-5,11-diene-4,9-dione (11).** Following the general procedure (Method A), MOB **7** generated in situ from phenol **3** was reacted with MA, MMA, or MVK and the residue was purified by column chromatography (EtOAc/hexanes) to afford dimer **11** as a colorless solid (see Table 1 for yields). Mp 211−214 °C (from EtOAc−hexanes); IR (neat) 1735, 1695, 1637 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.65 (d, *J* = 1.6 Hz, 3H), 1.97 (d, *J* = 1.6 Hz, 3H), 3.01 (dd, *J* = 6.8, 1.6 Hz, 1H), 3.05 (s, 3H), 3.15−3.23 (m, 3H), 3.24 (s, 3H), 3.39 (s, 3H), 3.44 (s, 3H), 5.83 (ddq, *J* = 6.8, 1.6, 1.6 Hz, 1H), 5.92 (dq, *J* = 1.6, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 22.1, 38.6, 39.7, 43.2, 48.8, 49.4, 50.0, 50.6, 57.7, 94.8, 98.6, 124.7, 126.4, 137.4, 155.9, 193.0, 202.3; MS (EI, 70 eV) *m*/*z* (rel intensity) 308 (M^+ − CO, 93), 261 (20), 248 (39), 201 (82), 159 (53), 115 (41), 105 (100), 91 (60), 75 (49), 59 (71); HRMS (EI) calcd for $C_{17}H_{24}O_5$ (M^+ − CO) 308.1624, found 308.1620. Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.14; H, 7.23.

Methyl (1*S,2*S**,4*S**)-8,8-Dimethoxy-7-oxobicyclo[2.2.2]-oct-5-ene-2-carboxylate (13a).** Following the general procedure (Method A), MOB **5** generated in situ from phenol **1** was reacted with MA and the crude residue was subjected to column chromatography (EtOAc/hexanes 1:3) to give **13a** (40% yield) as a colorless liquid. IR (film) 1739, 1635, 1200 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.75 (ddd, *J* = 13.2, 5.7, 3.2 Hz, 1H), 2.24 (ddd, *J* = 13.2, 10.2, 2.8 Hz, 1H), 3.01 (ddd, *J* = 10.2, 5.7, 1.8 Hz, 1H), 3.11−3.15 (m, 1H), 3.30 (s, 3H), 3.31 (s, 3H), 3.49 (ddd, *J* = 6.5, 1.8, 1.6 Hz, 1H), 3.65 (s, 3H), 6.10 (ddd, *J* = 7.9, 6.5, 1.0 Hz, 1H), 6.44 (ddd, *J* = 7.9, 6.8, 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.3, 38.4, 38.7, 49.8, 49.9, 50.2, 52.2, 93.8, 125.7, 135.3, 173.3, 200.9; MS (EI, 70 eV) *m*/*z* (rel intensity) 212 (100, M^+ − CO), 181 (74), 165 (41), 153 (62), 151 (23), 105 (19), 79 (37), 77 (49); HRMS (EI) calcd for $C_{12}H_{16}O_5$ (M^+) 240.0998, found 240.0963.

Methyl (1*S,2*S**,4*S**)-2-Methyl-8,8-dimethoxy-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (13b).** Following the general procedure (Method A), MOB **5** generated in situ from phenol **1** was reacted with MMA and the residue was purified by column chromatography (EtOAc/hexanes 1:2) to provide **13b** (28% yield) as a colorless solid. Mp 112.5−113.2 °C (from EtOAc−hexanes); IR (film) 1737, 1637 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.25 (s, 3H), 1.77 (dd, *J* = 14.0, 2.4 Hz, 1H), 2.24 (dd, *J* = 14.0, 3.6 Hz, 1H), 3.01−3.05 (m, 1H), 3.25 (s, 3H), 3.29 (s, 3H), 3.28−3.31 (m, 1H), 3.61 (s, 3H), 6.10 (ddd, *J* = 7.9, 6.4, 1.6 Hz, 1H), 6.33 (ddd, *J* = 7.9, 6.6, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.5, 31.7, 38.5, 46.4, 49.5, 50.2, 52.4, 56.4, 94.1, 127.9, 134.6, 176.2, 202.3; MS (EI, 70 eV) *m*/*z* (rel intensity) 226 (M^+ − CO, 100), 195 (15), 179 (31), 167 (51), 151 (38), 135 (49), 107 (20), 93 (45), 77 (43); HRMS (EI) calcd for $C_{13}H_{18}O_5$ (M^+) 254.1154, found 254.1148. Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.41; H, 7.14. Found: C, 61.52; H, 7.51.

(1*S,4*S**,7*S**)-7-Acetyl-3,3-dimethoxybicyclo[2.2.2]oct-5-ene-2-one (13c).** Following the general procedure (Method A), MOB **5** generated in situ from phenol **1** was reacted with MVK and the residue was subjected to column chromatography (EtOAc/hexanes 1:10) to furnish **13c** (62% yield) as a colorless liquid. IR (film) 1741, 1711, 1616 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.68 (ddd, *J* = 12.8, 6.4, 2.8 Hz, 1H), 2.14 (s, 3H), 2.17 (m, 1H), 3.05 (ddd, *J* = 9.6, 6.4, 1.4 Hz, 1H), 3.13−3.16 (m, 1H), 3.30 (s, 3H), 3.32 (s, 3H), 3.44 (ddd, *J* = 6.4, 1.4, 1.2 Hz, 1H), 6.07 (ddd, *J* = 7.3, 6.4, 0.8 Hz, 1H), 6.38 (ddd, *J* = 7.4, 7.3, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.2, 28.2, 38.4, 46.6, 49.4, 49.7, 50.2, 93.9, 125.5, 134.7, 201.1, 205.7; MS (EI, 70 eV) *m*/*z* (rel intensity) 196 (M^+ − CO, 94), 165 (24), 153 (88), 151 (20), 121 (60), 79 (54), 77 (68), 75 (49), 43 (100); HRMS (EI) calcd for $C_{12}H_{16}O_4$ (M^+) 224.1049, found 224.1050.

Methyl (1*S,2*S**,4*S**)-8,8-Dimethoxy-1-methyl-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (14a).** Following the general procedure (Method A), MOB **6** generated in situ from phenol **2** was reacted with MA and the residue was purified by column chromatography (EtOAc/hexanes 2:7) to afford **14a** (86% yield) as a colorless liquid. IR (film) 1738, 1715 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.24 (s, 3H), 1.67 (ddd, *J* = 12.8, 6.4, 2.8 Hz, 1H), 2.33 (ddd, *J* = 12.8, 9.8, 3.0 Hz, 1H), 2.76 (ddd, *J* = 9.4, 6.4, 1.1 Hz, 1H), 3.14−3.18 (m, 1H), 3.33 (s, 3H),

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3.34 (s, 3H), 3.67 (s, 3H), 5.80 (ddd, J = 8.0, 1.2, 1.1 Hz, 1H), 6.48 (dd, J = 8.0, 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 28.0, 38.3, 43.6, 49.9, 50.1, 50.7, 51.7, 93.7, 130.8, 134.1, 173.9, 201.1; MS (EI, 70 eV) *m*/*z* (rel intensity) 226 (M^+ − CO, 100), 211 (25), 195 (26), 179 (26), 167 (35), 151 (25), 135 (35), 91 (39), 77 (19), 59 (27); HRMS (EI) calcd for $C_{12}H_{18}O_4$ (M^+ − CO) 226.1205, found 226.1199.

Methyl (1*S,2*S**,4*S**)-8,8-Dimethoxy-1,2-dimethyl-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (14b).** Following the general procedure (Method A), MOB **6** generated in situ from phenol **2** was reacted with MMA and the residue was purified by column chromatography (EtOAc/hexanes 2:7) to give **14b** (43% yield) as a colorless liquid. IR (film) 1738, 1721 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.91 (s, 6H), 1.93 (dd, J = 13.4, 2.7 Hz, 1H), 2.18 (dd, J = 13.4, 3.3 Hz, 1H), 3.10 (apparent m, dddd, J = 6.8, 3.3, 2.7, 1.7 Hz, 1H), 3.32 (s, 3H), 3.36 (s, 3H), 3.66 (s, 3H), 5.83 (dd, J = 8.1, 1.7 Hz, 1H), 6.48 (dd, J = 8.1, 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4, 21.7, 36.0, 38.4, 48.0, 49.6, 49.9, 51.9, 55.5, 94.0, 133.0, 133.5, 175.6, 202.4; MS (EI, 70 eV) *m*/*z* (rel intensity) 240 (M^+ − CO, 100), 225 (22), 193 (26), 181 (58), 165 (37), 149 (39), 107 (16), 91 (20), 75 (14), 59 (8); HRMS (EI) calcd for $C_{13}H_{20}O_4$ (M^+ − CO) 240.1362, found 240.1367.

(1*S,4*S**,7*S**)-7-Acetyl-3,3-dimethoxy-1-methylbicyclo[2.2.2]oct-5-ene-2-one (14c).** Following the general procedure (Method A), MOB **6** generated in situ from phenol **2** was reacted with MVK and the residue was subjected to column chromatography (EtOAc/hexanes 1:3) to provide **14c** (22% yield) as a colorless solid. Mp 99−100 °C (from EtOAc−hexanes); IR (film) 1738, 1713 cm^{-1} ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (s, 3H), 1.50 (ddd, J = 12.8, 6.9, 2.8 Hz, 1H), 2.14 (s, 3H), 2.34 (ddd, J = 12.8, 9.8, 3.0 Hz, 1H), 2.90 (dd, J = 9.8, 6.9 Hz, 1H), 3.10 (apparent m, dddd, J = 6.8, 3.0, 2.8, 1.3 Hz, 1H), 3.33 (s, 3H), 3.35 (s, 3H), 5.86 (dd, J = 8.0, 1.3 Hz, 1H), 6.43 (dd, J = 8.0, 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 27.7, 38.4, 49.9, 50.1, 50.5, 50.7, 93.8, 131.3, 133.3, 201.3, 207.7; MS (EI, 70 eV) *m*/*z* (rel intensity) 210 (M^+ − CO, 47), 167 (100), 135 (24), 121 (11), 91 (37), 75 (66), 65 (12), 43 (90); HRMS (EI) calcd for $C_{12}H_{18}O_3$ (M^+ − CO) 210.1256, found 210.1260. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.51; H, 7.62. Found: C, 65.48; H, 7.60.

Methyl (1*R,2*S**,4*S**)-8,8-Dimethoxy-6-methyl-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (15a).** Following the general procedure (Method A), MOB **7** generated in situ from phenol **3** was reacted with MA and the residue was purified by column chromatography (EtOAc/hexanes 1:4) to afford **15a** (35% yield) as a colorless liquid. IR (film) 1738, 1716 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.72 (ddd, J = 13.0, 5.9, 2.9 Hz, 1H), 1.85 (d, J = 1.6 Hz, 3H), 2.28 (ddd, J = 13.0, 10.1, 2.9 Hz, 1H), 3.02−3.06 (m, 2H), 3.32−3.33 (m, 7H), 3.69 (s, 3H), 6.07 (ddq, J = 6.7, 1.7, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 25.3, 37.9, 38.4, 49.86, 50.0, 52.0, 55.1, 94.0, 127.5, 135.4, 173.5, 200.6; MS (EI, 70 eV) *m*/*z* (rel intensity) 226 (M^+ − CO, 100), 195 (16), 179 (90), 151 (18), 135 (23), 107 (14), 91 (31), 77 (15), 59 (14); HRMS (EI) calcd for $C_{12}H_{18}O_4$ (M^+ − CO) 226.1205, found 226.1197.

Methyl (1*S,2*S**,4*S**)-8,8-Dimethoxy-2,6-dimethyl-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (15b).** Following the general procedure (Method A), MOB **7** generated in situ from phenol **3** was reacted with MMA and the residue was purified by column chromatography (EtOAc/hexanes 1:3) to furnish **15b** (19% yield) as a colorless liquid. IR (film) 1733, 1722 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.80 (d, J = 1.6 Hz, 3H), 1.85 (dd, J = 13.7, 2.5 Hz, 1H), 2.92 (dd, J = 13.7, 3.6 Hz, 1H), 2.99 (ddd, J = 6.6, 3.6. 2.5 Hz, 1H), 3.21 (d, J = 1.6 Hz, 1H), 3.15 (s, 3H), 3.34 (s, 3H), 3.68 (s, 3H), 6.00 (ddq, J = 6.6, 1.6, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 25.5, 32.4, 38.3, 46.0, 49.6, 49.9, 52.2, 61.9, 94.3, 127.3, 137.2, 176.3, 201.9; MS (EI, 70 eV) *m*/*z* (rel intensity) 240 (M^+ − CO, 79), 193 (100), 165 (41), 149 (37), 133 (24), 121 (28), 105 (43), 91 (56), 59 (39), 43 (39); HRMS (EI) calcd for $C_{13}H_{20}O_4$ (M^+ − CO) 240.1362, found 240.1368.

(1*R,4*S**,7*S**)-7-Acetyl-3,3-dimethoxy-6-methylbicyclo[2.2.2]oct-5-ene-2-one (15c).** Following the general procedure (Method A), MOB **7** generated in situ from phenol **3** was reacted with MVK and the residue was subjected to column chromatography (EtOAc/hexanes 1:3) to give **15c** (25% yield) as a colorless liquid. IR (film) 1736, 1715 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.61 (ddd, J = 12.7, 10.3, 3.0 Hz, 1H), 1.86 (d, J = 1.6 Hz, 3H), 2.17 (s, 3H), 2.25 (ddd, J = 12.7, 10.3, 3.0 Hz, 1H), 3.05 (ddd, J = 6.7, 3.0, 3.0 Hz, 1H), 3.09 (ddd, J = 10.3, 6.7, 1.7 Hz, 1H), 3.11 (d, J = 1.6 Hz, 1H), 3.33 (s, 3H), 3.34 (s, 3H), 6.01 (ddq, J = 6.7, 1.7, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 24.5, 28.2, 38.0, 46.4, 50.0, 50.0, 54.6, 94.2, 127.1, 135.4, 100.9, 206.1; MS (EI, 70 eV) *m*/*z* (rel intensity) 210 (M^+ − CO, 52), 163 (72), 135 (75), 119 (25), 91 (65), 75 (82), 43 (100); HRMS (EI) calcd for $C_{12}H_{18}O_3$ (M^+ − CO) 210.1256, found 210.1248.

4-Bromo-2-methoxy-6-methylphenol (18).[32] To 2-methoxy-6-methylphenol (2.77 g, 20.0 mM) in acetic acid (40 mL) was added *N*-bromosuccinamide (3.56 g, 20.0 mM) in acetic acid (93 mL) slowly and the reaction mixture was stirred at room temperature for 4 h. Solvent was removed under vacuum and the residue was treated with water (140 mL) and $NaHCO_3$ (140 g) and extracted with CH_2Cl_2 (3 × 150 mL). The combined organic layer was dried over $MgSO_4$ and concentrated. The residue was chromatographed (EtOAc/hexanes 1:3) to provide **18** (3.94 g, 91% yield) as a colorless liquid. IR (film) 3496, 1275, 1089 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.20 (s, 3H), 3.85 (s, 3H), 5.58 (br, 1H), 6.81 (d, J = 1.8 Hz, 1H), 6.87 (d, J = 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 56.2, 110.7, 111.6, 125.5, 125.7, 142.8, 146.7; MS (70 eV) *m*/*z* (rel intensity) 218 (M^+ + 2, 99), 216 (M^+, 100), 203 (35), 201 (36), 94 (39), 77 (11), 66 (27); HRMS (EI) calcd for $C_8H_9O_2Br$ 215.9785, found 215.9785.

4-Bromo-2-methoxy-5-methylphenol (19).[33] Following the above procedure (for **18**), 2-methoxy-5-methylphenol (2.283 g, 20.0 mM) was reacted with NBS (3.56 g, 20.0 mM) and the crude product was purified by column chromatography (EtOAc/hexanes 1:3) to afford **19** (4.35 g, 98% yield) as colorless needles. Mp 70−71 °C (from hexanes, lit.[33] mp 70 °C); IR (film) 3394, 1253, 1029 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27 (s, 3H), 3.83 (s, 3H), 5.49 (br, 1H), 6.79 (s, 1H), 6.97 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.1, 56.1, 113.4, 114.6, 116.5, 130.4, 144.7, 145.1; MS (70 eV) *m*/*z* (rel intensity) 218 (M^+ + 2, 44), 216 (M^+, 43), 203 (12), 201 (11), 137 (8), 94 (29), 89 (100), 61 (28); HRMS (EI) calcd for $C_8H_9O_2{}^{79}Br$ (M^+) 215.9785, found 215.9794. Calcd for $C_8H_9O_2{}^{81}Br$ 217.9766, found 217.9766.

5-Bromo-4-(1,3-dioxolan-2-yl)-2-methoxyphenol (20). To bromo compound **36** (1.52 g, 10 mM) and *p*-toluenesulfonic acid (19 mg, 0.1 mM) in benzene (15 mL) was added ethylene glycol (1.24 g, 20 mM) and the reaction mixture was heated under reflux for 10 h in a Dean−Stark apparatus. The contents were cooled to room temperature and concentrated and the residue was chromatographed (EtOAc/hexanes 1:2) to furnish **20** (1.91 g, 97% yield) as a colorless solid. Mp 97−98 °C (EtOAc−hexanes); IR (film) 3345, 1662, 1510, 1085 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.91 (s, 3H), 4.05−4.20 (m, 4H), 5.71 (s, 1H), 5.98 (s, 1H), 7.11 (s, 1H), 7.12 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.0, 65.2, 102.6, 109.7, 113.8, 118.6, 127.5, 146.0, 147.0; MS (70 eV) *m*/*z* (rel intensity) 276 (M^+ + 2, 50), 274 (M^+, 50), 231 (80), 229 (75), 215 (25), 202 (25), 189 (20), 135 (30), 73 (100); HRMS (EI) calcd for $C_{10}H_{11}O_4{}^{79}Br$ (M^+) 273.9840, found 273.9857; HRMS (EI) calcd for $C_{10}H_{11}O_4{}^{81}Br$ 275.9834, found 275.9820.

4-Bromo-6,6-dimethoxy-2,4-cyclohexadien-1-one (21). To a solution of DAIB (384.9 mg, 1.10 mM) in methanol (5 mL) was added a solution of phenol **17** (206.2 mg, 1.02 mmol) in methanol (5 mL) at room temperature under nitrogen

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(33) Chan, H. T. J.; Elix, J. A. *Aust. J. Chem*. **1973**, *26*, 1069.

atmosphere and the reaction mixture was stirred for 10 min. The solvent was then removed and the residue was purified (EtOAc/hexanes 1:5) to give MOB **21** (223.3 mg, 94% yield) as a greenish yellow oil. IR (film) 1690, 1628, 1257 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.35 (s, 6H), 5.94 (dd, J = 10.2, 0.8 Hz, 1H), 6.65 (dd, J = 2.4, 0.8 Hz, 1H), 6.85 (dd, J = 10.2, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.2, 92.9, 119.4, 126.6, 135.3, 143.1, 192.8; MS (EI, 70 eV) m/z (rel intensity) 234 (M^+ + 2, 22), 232 (M^+, 36), 162 (67), 160 (62), 153 (28), 120 (60), 119 (73), 118 (100), 117 (91), 116 (69), 115 (61), 114 (55); HRMS (EI) calcd for $C_8H_9O_3{}^{79}Br$ (M^+) 231.9735, found 231.9728; HRMS (EI) calcd for $C_8H_9O_3{}^{81}Br$ 233.9715, found 233.9727.

4-Bromo-6,6-dimethoxy-2-methyl-2,4-cyclohexadien-1-one (22). To a suspension of DAIB (709.2 mg, 2.2 mM) and $KHCO_3$ (512.5 mg, 5.12 mM) in methanol (10 mL) was added slowly a solution of phenol **18** (436.5 mg, 2.0 mM) in methanol (5 mL) in one portion at 0 °C under nitrogen atmosphere. After 5 min stirring, the reaction mixture was quenched with brine (10 mL). Then water (10 mL) was added and extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by column chromatography (EtOAc/hexanes 1:4) to furnish MOB **22** (405.5 mg, 82% yield) as a yellow oil. IR (film) 1685, 1634, 1244 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.89 (d, J = 1.6 Hz, 3H), 3.34 (s, 6H), 6.54 (d, J = 1.6 Hz, 1H), 6.66 (td, J = 1.6, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 50.3, 93.2, 119.9, 132.8, 134.9, 139.1, 193.4; MS (70 eV) m/z (rel intensity) 248 (M^+ + 2, 6), 246 (M^+, 6), 218 (69), 216 (70), 203 (53), 201 (49), 94 (53), 89 (97), 65 (44), 61 (100); HRMS (EI) calcd for $C_9H_{11}O_3{}^{79}Br$ (M^+) 245.9891, found 245.9885; HRMS (EI) calcd for $C_9H_{11}O_3{}^{81}Br$ 247.9871, found 247.9861.

4-Bromo-6,6-dimethoxy-3-methyl-2,4-cyclohexadien-1-one (23). To a suspension of DAIB (354.5 mg, 1.1 mM) and $KHCO_3$ (245.6 mg, 2.45 mM) in methanol (5 mL) was added slowly a solution of phenol **19** (216.0 mg, 1.0 mM) in methanol (5 mL) in one portion at 0 °C under nitrogen atmosphere. After 5 min of stirring, the reaction mixture was quenched with brine (10 mL). Then water (10 mL) was added and extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by column chromatography (EtOAc/hexanes 1:3) to furnish MOB **23** (189.5 mg, 77% yield) as a greenish yellow oil. IR (film) 1681, 1631, 1037 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.15 (d, J = 1.6 Hz, 3H), 3.35 (s, 6H), 5.96 (q, J = 1.6 Hz, 1H), 6.73 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.0, 50.2, 92.6, 124.2, 124.5, 135.7, 150.5, 192.9; MS (70 eV) m/z (rel intensity) 248 (M^+ + 2, 21), 246 (M^+, 22), 217 (98), 215 (100), 167 (40), 139 (100), 108 (24), 93 (32), 65 (12); HRMS (EI) calcd for $C_9H_{11}O_3{}^{79}Br$ (M^+) 245.9891, found 245.9899; HRMS (EI) calcd for $C_9H_{11}O_3{}^{81}Br$ 247.9871, found 247.9885.

3-Bromo-6,6-dimethoxy-4-(1,3-dioxolan-2-yl)-2,4-cyclohexadien-1-one (24). To a suspension of DAIB (1.75 g, 5.44 mM) and $KHCO_3$ (1.3 g, 12.98 mM) in methanol (10 mL) was added slowly a solution of phenol **20** (1.42 g, 5.18 mM) in methanol (10 mL) in one portion at 0 °C under nitrogen atmosphere. After 5 min of stirring, the reaction mixture was quenched with brine (10 mL) and extracted with ethyl acetate. The organic layer was dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by column chromatography (EtOAc/hexanes 1:3 with 1% Et_3N) to furnish MOB **24** (1.45 g, 92% yield) as a yellow oil. IR (film) 1680, 1640, 1450, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.34 (s, 6H), 3.98−4.05 (m, 4H), 5.73 (s, 1H), 6.52 (s, 1H), 6.58 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.2, 65.2, 91.5, 101.0, 129.5, 132.4, 133.6, 139.2, 191.4; MS (70 eV) m/z (rel intensity) 306 (M^+ + 2, 20), 304 (M^+, 20), 292 (80), 290 (80), 276 (50), 274 (50), 264 (20), 262 (20), 246 (25), 244 (25), 196 (30), 168 (40), 105 (100), 75 (60).

Methyl (1*S,2*S**,4*R**)-5-Bromo-8,8-dimethoxy-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (25a).** Following the general procedure (Method B), MOB **21** generated in situ from phenol **17** was reacted with MA and the crude product was purified by column chromatography (EtOAc/hexanes 1:10) to give **25a** (70% yield) as a colorless solid. Mp 83.3−83.6 °C (from CH_2Cl_2−hexanes); IR (film) 1763, 1710, 1610, 1222, 1056 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.93 (ddd, J = 13.4, 6.0, 2.8 Hz, 1H), 2.26 (ddd, J = 13.1, 10.1, 3.1 Hz, 1H), 2.96 (ddd, J = 10.1, 6.0, 2.0 Hz, 1H), 3.25−3.28 (m, 1H), 3.27 (s, 3H), 3.32 (s, 3H), 3.47 (dd, J = 6.8, 2.0 Hz, 1H), 3.63 (s, 3H), 6.22 (dd, J = 6.8, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9, 38.7, 49.0, 50.0, 50.7, 51.9, 52.3, 93.6, 124.8, 125.0, 172.5, 198.7; MS (EI, 70 eV) m/z (rel intensity) 292 (63), 290 (M^+ − CO, 64), 233 (25), 231 (28), 211 (38), 151 (19), 77 (32), 59 (100); HRMS (EI) calcd for $C_{11}H_{15}O_4{}^{79}Br$ (M^+ − CO) 290.0154, found 290.0141. Anal. Calcd for $C_{12}H_{15}O_5Br$: C, 45.16; H, 4.74. Found: C, 45.07; H, 4.74.

Methyl (1*S,2*S**,4*R**)-5-Bromo-8,8-dimethoxy-2-methyl-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (25b).** Following the general procedure (Method B), MOB **21** generated in situ from phenol **17** was reacted with MMA and the crude product was purified by column chromatography (EtOAc/hexanes 1:10) to give **25b** (65% yield) as a colorless liquid. IR (film) 1737, 1706, 1606, 1290, 1051 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.24 (s, 3H), 1.84 (dd, J = 14.0, 2.4 Hz, 1H), 2.45 (dd, J = 14.0, 3.6 Hz, 1H), 3.20 (ddd, J = 3.6, 2.8, 2.4 Hz, 1H), 3.30 (s, 3H), 3.32 (d, J = 6.8 Hz, 1H), 3.33 (s, 3H), 3.64 (s, 3H), 6.25 (dd, J = 6.8, 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.1, 32.0, 46.4, 49.2, 49.7, 50.7, 52.6, 58.3, 93.8, 124.9, 126.9, 175.6, 200.0; MS (EI, 70 eV) m/z (rel intensity) 306 (85), 304 (M^+ − CO, 87), 275 (11), 273 (11), 247 (40), 245 (43), 225 (43), 91 (70), 59 (100); HRMS (EI) calcd for $C_{12}H_{17}O_4{}^{79}Br$ (M^+ − CO) 304.0310, found 304.0297.

(1*S,4*R**,7*S**)-7-Acetyl-5-bromo-3,3-dimethoxybicyclo[2.2.2]oct-5-ene-2-one (25c).** Following the general procedure (Method B), MOB **21** generated in situ from phenol **17** was reacted with MVK and the crude product was purified by column chromatography (EtOAc/hexanes 1:4) to provide **25c** (85% yield) as a colorless liquid. IR (neat) 1752, 1708, 1610, 1061 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.85 (ddd, J = 13.1, 6.6, 2.8 Hz, 1H), 2.13 (s, 3H), 2.25 (ddd, J = 13.1, 10.0, 2.8 Hz, 1H), 3.01 (ddd, J = 10.0, 6.6, 1.6 Hz, 1H), 3.29 (dt, J = 2.8, 2.5 Hz, 1H), 3.31 (s, 3H), 3.34 (s, 3H), 3.43 (dd, J = 1.6, 6.7, 1.6 Hz, 1H), 6.21 (dd, J = 6.7, 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.0, 28.2, 46.8, 49.1, 50.1, 50.8, 51.4, 93.9, 124.0, 125.1, 199.1, 204.9; MS (EI, 70 eV) m/z (rel intensity) 276 (63), 274 (M^+ − CO, 63), 233 (78), 231 (79), 78 (28), 77 (40), 75 (25), 43 (100); HRMS (EI) calcd for $C_{11}H_{15}O_3{}^{79}Br$ (M^+ − CO) 274.0205, found 274.0208; HRMS (EI) calcd for $C_{11}H_{15}O_3{}^{81}Br$ 276.0185, found 276.0180.

Methyl (1*S,2*S**,4*R**)-5-Bromo-8,8-dimethoxy-1-methyl-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (26a).** Following the general procedure (Method C), MOB **22** generated in situ from phenol **18** was reacted with MA and the crude product was purified by column chromatography (EtOAc/hexanes 2:7) to furnish **26a** (75% yield) as a colorless solid. Mp 70−71 °C (from hexanes); IR (film) 1739, 1714, 1613, 1264, 1051 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 3H), 1.87 (ddd, J = 13.1, 6.5, 3.0 Hz, 1H), 2.35 (ddd, J = 13.1, 9.6, 3.6 Hz, 1H), 2.71 (dd, J = 9.6, 6.5 Hz, 1H), 3.32 (m, 4H), 3.37 (s, 3H), 3.67 (s, 3H), 5.95 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.3, 28.3, 43.9, 48.8, 50.2, 50.7, 52.0, 53.5, 93.8, 123.3, 129.9, 173.2, 199.2; MS (70 eV) m/z (rel intensity) 306 (27), 304 (M^+ − CO, 29), 259 (22), 257 (21), 247 (18), 245 (21), 225 (100), 91 (35); HRMS (EI) calcd for $C_{12}H_{17}O_4{}^{79}Br$ (M^+ − CO) 304.0310, found 304.0305; HRMS (EI) calcd for $C_{12}H_{17}O_4{}^{81}Br$ 306.0290, found 306.0309. Anal. Calcd for $C_{13}H_{17}O_5Br$: C, 46.86; H, 5.14. Found: C, 46.81; H, 5.14.

Methyl (1*S,2*S**,4*R**)-5-Bromo-8,8-dimethoxy-1,2-dimethyl-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (26b).** Following the general procedure (Method C), MOB **22** generated in situ from phenol **18** was reacted with MMA and the crude product was purified by column chromatography (EtOAc/hexanes 2:11) to afford **26b** (72% yield) as a colorless solid. Mp 82−82.5 °C (from hexanes); IR (film) 1734, 1713, 1619,

1231, 1048 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.18 (s, 3H), 1.19 (s, 3H), 1.94 (dd, J = 13.5, 2.8 Hz, 1H), 2.36 (dd, J = 13.5, 3.2 Hz, 1H), 3.25 (ddd, J = 3.2, 2.8, 2.8 Hz, 1H), 3.34 (s, 3H), 3.38 (s, 3H), 3.66 (s, 3H), 5.96 (d, J = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4, 21.2, 36.0, 48.2, 48.8, 49.7, 50.5, 52.1, 58.0, 93.8, 122.6, 132.2, 174.9, 200.2; MS (70 eV) *m*/*z* (rel intensity) 320 (98), 318 (M^+ − CO, 100), 303 (7), 289 (19), 287 (21), 261 (52), 259 (60), 239 (59), 105 (43), 75 (42); HRMS (EI) calcd for $C_{13}H_{19}O_4{}^{79}Br$ (M^+ − CO) 318.0467, found 318.0431; HRMS (EI) calcd for $C_{13}H_{19}O_4{}^{81}Br$ 320.0447, found 320.0446. Anal. Calcd for $C_{14}H_{19}O_5Br$: C, 48.43; H, 5.52. Found: C, 48.42; H, 5.47.

(1*S,4*R**,7*S**)-7-Acetyl-5-bromo-3,3-dimethoxy-1-methylbicyclo[2.2.2]oct-5-ene-2-one (26c).** Following the general procedure (Method C), MOB **22** generated in situ from phenol **18** was reacted with MVK and the crude product was purified by column chromatography (EtOAc/hexanes 4:7) to give **26c** (83% yield) as a colorless solid. Mp 104−104.5 °C (from hexanes); IR (film) 1725, 1712, 1613, 1223, 1053 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.23 (s, 3H), 1.69 (ddd, J = 12.8, 6.8, 2.7 Hz, 1H), 2.13 (s, 3H), 2.37 (ddd, J = 12.8, 9.7, 3.4 Hz, 1H), 2.85 (dd, J = 9.7, 6.8 Hz, 1H), 3.33 (m, 4H), 3.37 (s, 3H), 6.01 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 27.8, 30.8, 48.8, 50.1, 50.6, 50.7, 53.4, 93.8, 122.2, 130.5, 199.4, 206.7; MS (EI, 70 eV) *m*/*z* (rel intensity) 290 (33), 288 (M^+ − CO, 35), 259 (13), 257 (13), 247 (100), 245 (82), 209 (13), 165 (16), 91 (36), 75 (33), 65 (15); HRMS (EI) calcd for $C_{13}H_{17}O_4{}^{79}Br$ (M^+) 316.0310, found 316.0334; HRMS (EI) calcd for $C_{13}H_{17}O_4{}^{81}Br$ 318.0290, found 318.0293. Anal. Calcd for $C_{13}H_{17}O_4Br$: C, 49.23; H, 5.40. Found: C, 49.05; H, 5.43.

Methyl (1*R,2*S**,4*R**)-5-Bromo-8,8-dimethoxy-6-methyl-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (27a).** Following the general procedure (Method C), MOB **23** generated in situ from phenol **19** was reacted with MA and the residue was subjected to column chromatography (EtOAc/hexanes 1:3) to give **27a** (72% yield) as a colorless liquid. IR (film) 1740, 1713, 1646, 1266, 1059 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.87 (s, 3H), 1.92 (ddd, J = 13.2, 6.0, 3.0 Hz, 1H), 2.32 (ddd, J = 13.2, 10.0, 3.0 Hz, 1H), 3.11 (ddd, J = 10.0, 6.0, 1.6 Hz, 1H), 3.27 (dd, J = 3.0, 3.0 Hz, 1H), 3.30 (s, 3H), 3.36 (s, 3H), 3.45 (d, J = 1.6 Hz, 1H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 25.8, 38.7, 48.9, 50.1, 50.4, 52.2, 56.7, 94.0, 118.7, 132.5, 172.8, 198.4; MS (70 eV) *m*/*z* (rel intensity) 306 (87), 304 (M^+ − CO, 100), 275 (21), 273 (25), 259 (20), 257 (22), 75 (41); HRMS (EI) calcd for $C_{13}H_{17}O_5{}^{79}Br$ (M^+) 332.0259, found 332.0367; HRMS (EI) calcd for $C_{13}H_{17}O_5{}^{81}Br$ 334.0239, found 334.0248.

Methyl (1*R,2*S**,4*R**)-5-Bromo-8,8-dimethoxy-2,6-dimethyl-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (27b).** Following the general procedure (Method C), MOB **23** generated in situ from phenol **19** was reacted with MA and the residue was purified by column chromatography (EtOAc/hexanes 1:4) to furnish **27b** (62% yield) as a colorless liquid. IR (film) 1737, 1715, 1648, 1290, 1117 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.27 (s, 3H), 1.82 (s, 3H), 1.87 (dd, J = 13.8, 3.0 Hz, 1H), 2.47 (dd, J = 13.8, 3.0 Hz, 1H), 3.21 (dd, J = 3.0, 3.0 Hz, 1H), 3.32 (s, 1H), 3.33 (s, 3H), 3.36 (s, 3H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7, 25.2, 32.7, 46.3, 49.2, 49.9, 50.5, 52.4, 63.5, 94.1, 119.3, 134.0, 175.7, 199.7; MS (70 eV) *m*/z (rel intensity) 320 (94), 318 (M^+ − CO, 100), 289 (15), 287 (16), 273 (22), 271 (22), 261 (19), 259 (19), 239 (26), 229 (18), 227 (18), 105 (29), 75 (59); HRMS (EI) calcd for $C_{14}H_{19}O_5{}^{79}Br$ (M^+) 346.0416, found 346.0407; HRMS (EI) calcd for $C_{14}H_{19}O_5{}^{81}Br$ 348.0396, found 348.0373.

(1*R,4R*,7*S**)-7-Acetyl-5-bromo-3,3-dimethoxy-6-methylbicyclo[2.2.2]oct-5-en-2-one (27c).** Following the general procedure (Method C), MOB **23** generated in situ from phenol **19** was reacted with **3** with MVK and the residue was subjected to column chromatography (EtOAc/hexanes 2:7) to afford **27c** (90% yield) as a colorless solid. Mp 126−127 °C (from hexanes); IR (film) 1739, 1714, 1261, 1057 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.78 (ddd, J = 12.8, 6.8, 3.2 Hz, 1H), 1.89 (s, 3H), 2.14 (s, 3H), 2.33 (ddd, J = 12.8, 10.2, 3.2 Hz, 1H), 3.04 (ddd, J = 10.2, 6.8, 1.6 Hz, 1H), 3.28 (dd, J = 3.2, 3.2 Hz, 1H), 3.30 (s, 3H), 3.36 (s, 3H), 3.38 (d, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 25.2, 28.1, 46.7, 48.9, 50.2, 50.5, 56.1, 94.2, 118.0, 132.8, 198.8, 205.4; MS (70 eV) *m*/*z* (rel intensity) 290 (63), 288 (M^+ − CO, 68), 287 (15), 285 (12), 259 (18), 257 (19), 247 (53), 245 (56), 177 (33), 91 (15), 75 (100); HRMS (EI) calcd for $C_{13}H_{17}O_4{}^{79}Br$ 316.0310, found 316.0305; HRMS (EI) calcd for $C_{13}H_{17}O_4{}^{81}Br$ 318.0290, found 318.0438. Anal. Calcd for $C_{13}H_{17}O_4Br$: C, 49.23; H, 5.40; Found: C, 49.12; H, 5.41.

Methyl (1*R,2*S**,4*S**)-6-Bromo-8,8-dimethoxy-5-(1,3-dioxolan-2-yl)-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (28a).** Following the general procedure (Method D), MOB **24** generated in situ from phenol **20** was reacted with MA and the crude product was crystallized from EtOAc−hexanes to give pure **28a** (94% yield) as a colorless solid. Mp 106−108 °C (from EtOAc−hexanes); IR (film) 1735, 1714, 1642, 1450, 1202, 1060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.83 (ddd, J = 13.2, 6.1, 2.9 Hz, 1H), 2.33 (ddd, J = 13.2, 9.9, 2.0 Hz, 1H), 3.11 (ddd, J = 2.0, 6.1, 9.9 Hz, 1H), 3.33 (s, 3H), 3.34 (s, 3H), 3.44 (dd, J = 2.9, 2.9 Hz, 1H), 3.72 (s, 3H), 3.75 (d, J = 2.0 Hz, 1H), 3.90−4.20 (m, 4H), 5.60 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.6, 39.4, 39.8, 49.8, 50.1, 52.3, 60.0, 65.1, 65.3, 93.2, 100.7, 116.1, 140.9, 172.1, 197.6; MS (70 eV) *m*/*z* (rel intensity) 392 (M^+ + 2, 2), 390 (M^+, 2), 364 (10), 362 (10), 332 (30), 299 (8), 287 (10), 251 (52), 229 (12), 199 (10), 179 (8), 149 (8), 103 (100), 73 (32), 59 (10); HRMS (EI) calcd for $C_{15}H_{19}O_7{}^{79}Br$ (M^+) 390.0314, found 390.0318; HRMS (EI) calcd for $C_{15}H_{19}O_7{}^{81}Br$ 392.0294, found 392.0294. Anal. Calcd for $C_{15}H_{19}O_7Br$: C, 46.05; H, 4.90. Found: C, 45.95; H, 4.90.

Methyl (1*R,2*S**,4*S**)-6-Bromo-8,8-dimethoxy-5-(1,3-dioxolan-2-yl)-2-methyl-7-oxobicyclo[2.2.2]oct-5-ene-2-carboxylate (28b).** Following the general procedure (Method D), MOB **24** generated in situ from phenol **20** was reacted with MMA and the crude product was crystallized from EtOAc−hexanes to furnish pure **28b** (95% yield) as a colorless solid. Mp 140−142 °C (from EtOAc−hexanes); IR (film) 1741, 1730, 1648, 1461, 1282, 1055 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.87 (dd, J = 13.7, 2.4 Hz, 1H), 2.40 (dd, J = 13.7, 3.5 Hz, 1H), 3.34 (s, 3H), 3.36 (s, 3H), 3.59 (s, 1H), 3.72 (s, 3H), 3.91 (dd, J = 3.5, 2.4 Hz, 1H), 3.90−4.15 (m, 4H), 5.6 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.7, 32.4, 39.9, 47.5, 49.8, 49.9, 52.5, 65.2, 65.4, 66.4, 93.4, 100.8, 117.5, 140.8, 174.9, 198.8; MS (70 eV) *m*/*z* (rel intensity) 378 (10), 376 (M^+ − CO, 10), 347 (10), 345 (10), 303 (8), 301 (8), 66 (40), 103 (100), 75 (10); HRMS (EI) calcd for $C_{16}H_{21}O_7{}^{79}Br$ 404.0470, found 404.0478. Anal. Calcd for $C_{16}H_{21}O_7Br$: C, 47.42; H, 5.22. Found: C, 47.24; H, 5.18.

(1*R,4*S**,7*S**)-7-Acetyl-6-bromo-3,3-dimethoxy-5-(1,3-dioxolan-2-yl)bicyclo[2.2.2]oct-5-ene-2-one (28c).** Following the general procedure (Method D), MOB **24** generated in situ from phenol **20** was reacted with MVK and the crude product was crystallized from EtOAc−hexanes to give **28c** (96% yield) as a colorless solid. Mp 116−117 °C (from EtOAc−hexanes); IR (film) 1740, 1708, 1640, 1205, 1050 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.76 (ddd, J = 12.4, 6.4, 3.2 Hz, 1H), 2.22 (s, 3H), 2.28 (ddd, J = 12.4, 9.0, 3.2 Hz, 1H), 3.14 (ddd, J = 9.0, 6.4, 2.0 Hz, 1H), 3.38 (s, 3H), 3.35 (s, 3H), 3.47 (dd, J = 3.2, 3.2 Hz, 1H), 3.72 (d, J = 2.0 Hz, 1H), 3.90−4.10 (m, 4H), 5.57 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7, 28.1, 39.4, 47.9, 49.8, 50.1, 59.4, 65.1, 65.3, 93.3, 100.7, 116.2, 140.5, 198.0, 204.4; MS (70 eV) *m*/*z* (rel intensity) 348, 346 (M^+ − CO, 12), 314 (15), 303 (10), 271 (15), 223 (80), 199 (13), 192 (10), 151 (16), 119 (8), 103 (50), 89 (40), 73 (100), 59 (16); HRMS (EI) calcd for $C_{15}H_{19}O_6{}^{79}Br$ (M^+) 374.0365, found 374.0360; HRMS (EI) calcd for $C_{15}H_{19}O_6{}^{81}Br$ 376.0345, found 376.0345. Anal. Calcd for $C_{15}H_{19}O_6Br$: C, 48.02; H, 5.10. Found: C, 47.95; H, 5.06.

(1*R,8*S**)-11-Bromo-4,8-dimethyl-5-hydroxy-6,10,10-trimethoxytricyclo[6.2.2.0^{2,7}]dodeca-2,4,6,11-tetraen-9-one (29).** A byproduct formed in the preparation of MOB **22**

from phenol **18** in 5% yield as a colorless solid. Mp 178−179 °C (from EtOAc−hexanes); IR (film) 1736, 1602, 1206, 1060 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.61 (s, 3H), 2.23 (s, 3H), 3.24 (s, 3H), 3.48 (s, 3H), 3.91 (s, 3H), 4.59 (d, J = 2.4 Hz, 1H), 5.61 (s, 1H), 6.31 (d, J = 2.4 Hz, 1H), 6.75 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.0, 15.9, 50.4, 51.1, 51.4, 57.4, 63.1, 92.2, 120.3, 123.9, 124.9, 128.0, 129.4, 135.2, 142.9, 146.3, 195.9; MS (70 eV) *m*/*z* (rel intensity) 384 (M^+ + 2, 2), 382 (M^+, 2), 356 (15), 354 (16), 325 (21), 323 (20), 303 (23), 282 (100), 280 (100), 275 (49), 267 (94), 265 (95), 75 (92); HRMS (EI) calcd for $C_{17}H_{19}O_5{}^{79}Br$ (M^+) 382.0415, found 382.0414; HRMS (EI) calcd for $C_{17}H_{19}O_5{}^{81}Br$ 384.0396, found 384.0381. Anal. Calcd for $C_{17}H_{19}O_5Br$: C, 53.28; H, 5.00. Found: C, 53.27; H, 5.02.

(1*R,2*S**,7*S**,8*S**)-7,12-Dibromo-6,11-dimethyl-3,3,9,9-tetramethoxytricyclo[6.2.2.0^{2,7}]dodeca-5,11-diene-4,10-dione (31).** A byproduct formed in the preparation of MOB **23** from phenol **19** in 5% yield as a colorless solid. Mp 164−166 °C (from hexanes); IR (film) 1742, 1705, 1646, 1622, 1216, 1063 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.67 (s, 3H), 2.12 (d, J = 1.4 Hz, 3H), 3.15 (s, 3H), 3.32 (d, J = 2.2 Hz, 1H), 3.35 (s, 3H), 3.39 (s, 3H), 3.48 (s, 3H), 3.59 (s, 1H), 4.02 (d, J = 2.2 Hz, 1H), 6.01 (q, J = 2.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 21.7, 49.0, 50.0, 50.2, 50.4, 51.1, 51.4, 61.2, 67.7, 94.1, 97.3, 118.7, 126.5, 135.5, 153.7, 190.7, 196.4; MS (70 eV) *m*/*z* (rel intensity) 468 (3), 466 (6), 464 (M^+ − CO, 3), 387 (99), 385 (100), 355 (28), 353 (29), 281 (39), 279 (40), 253 (25), 251 (28), 129 (26), 128 (22), 115 (21), 59 (39); HRMS (EI) calcd for $C_{18}H_{22}O_6{}^{79}Br{}^{79}Br$ (M^+) 491.9783, found 491.9770; HRMS (EI) calcd for $C_{18}H_{22}O_6{}^{79}Br{}^{81}Br$ 493.9763, found 493.9744; HRMS (EI) calcd for $C_{18}H_{22}O_6{}^{81}Br{}^{81}Br$ 495.9743, found 495.9740. Anal. Calcd for $C_{18}H_{22}O_6Br_2$: C, 43.75; H, 4.49. Found: C, 43.54; H, 4.47.

4-Bromo-2-methoxy-5-(methoxy)methylphenol (33). A byproduct formed in the Diels−Alder reactions of MOB **23** (derived from phenol **19**) with MA and MMA in 6 and 13% yields, respectively, as a colorless solid. Mp 85−86 °C (from hexanes); IR (film) 3396, 2932, 1614, 1278, 1029 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.39 (s, 3H), 3.86 (s, 3H), 4.41 (s, 2H), 5.51 (s, 1H), 6.99 (s, 1H), 7.00 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.2, 58.3, 73.5, 112.0, 114.8, 115.4, 130.3, 145.0, 146.5; MS (70 eV) *m*/*z* (rel intensity) 248 (74), 246 (M^+ − CO, 100), 217 (52), 215 (52), 167 (38), 165 (5), 137 (5), 65 (3); HRMS (EI) calcd for $C_9H_{11}O_3{}^{79}Br$ (M^+ − CO) 245.9891, found 245.9898; HRMS (EI) calcd for $C_9H_{11}O_3{}^{81}Br$ 247.9871, found 247.9880. Anal. Calcd for $C_9H_{11}O_3Br$: C, 43.75; H, 4.49. Found: C, 43.5; H, 4.46.

5-Bromo-4-formyl-2-methoxyphenol (35).[34] To the suspension of aldehyde **35** (3.23 g, 16.7 mM) in KBr (6.67 g) and distilled water (80 mL) was added bromine (2.94 g, 18.4 mmol) dropwise. The reaction mixture was stirred for 10 h at room temperature and then subjected to filtration. The precipitate was suspended in 6 N HCl (80 mL) at 90 °C for 10 h. The reation mixture was then cooled and filtered and the resulting solid was dissolved in EtOAc and washed with saturated $NaHCO_3$ solution. The organic layer was dried over $MgSO_4$ and concentrated. The residue was recrystallized from EtOAc−hexanes to give **35** (3.58 g, 93% yield) as a colorless solid. Mp 174−75 °C (from hexanes, lit.[34] mp 174−175 °C); IR (film) 3210, 2910, 1680, 1201, 1040 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.95 (s, 3H), 6.18 (s, 1H), 7.18 (s, 1H), 7.43 (s, 1H), 10.18 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.4, 110.4, 119.2, 120.8, 126.4, 146.5, 151.9, 190.8; MS (70 eV) *m*/*z* (rel intensity) 232 (M^+ + 2, 99), 230 (M^+, 100), 215 (10), 203 (16), 187 (13), 173 (12), 159 (30), 142 (11), 133 (10), 122 (10), 107 (9); HRMS (EI) calcd for $C_8H_7O_3{}^{79}Br$ 229.9578, found 229.9564; HRMS (EI) calcd for $C_8H_7O_3{}^{81}Br$ 231.955, found 231.954.

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Supporting Information Available: ^1H and ^{13}C NMR and DEPT spectra for compounds **13a**−**c** to **15a**−**c** and **25a**−**c** to **28a**−**c**, tables of selected ^1H NMR chemical shifts and coupling constants for compounds **13a**−**c** to **15a**−**c** and **25a**−**c** to **28a**−**c**, and an ORTEP plot of the crystal structure of Diels−Alder adduct **26b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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