Intramolecular 1,3-Dipolar Cycloadditions of Norbornadiene-Tethered Nitrones†

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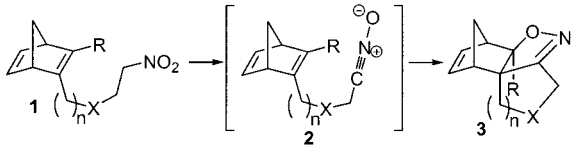
Efficient routes to the synthesis of norbornadiene-tethered nitrones have been developed, and their intramolecular 1,3-dipolar cycloadditions were studied. The cycloadditions occurred in moderate to good yields for a variety of substrates and were found to be highly regio- and stereoselective, giving single regio- and stereoisomers in most cases.

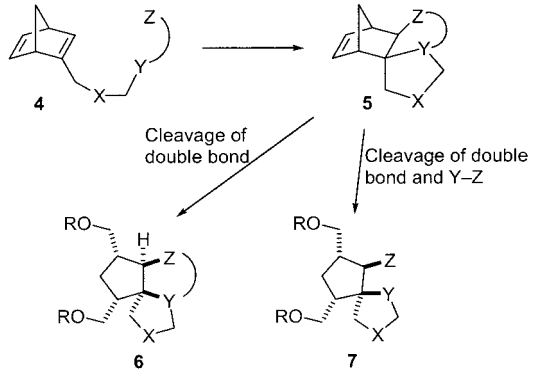
Introduction

Intramolecular cycloadditions with high regio- and stereocontrol are important tools for the efficient assembly of complex molecular structures. We have recently initiated a program on the study of various types of intramolecular cycloadditions of substituted norbornadienes.[1,2] For example, norbornadiene-tethered nitrile oxides **2** undergo highly regio- and stereoselective intramolecular cycloadditions to provide single regio- and stereoisomers **3** in good yields (Scheme 1).[1] Our long-term goal is to develop an efficient route for the construction of angular fused tricyclic frameworks and spirocyclic frameworks with high regio- and stereocontrol (Scheme 2). Unlike nitrile oxides that belong to the linear propargyl-type 1,3-dipole, nitrones belong to the bent allyl-type 1,3-dipole. The 1,3-dipolar cycloaddition of a nitrone is usually more complicated than that of a nitrile oxide as an additional stereocenter is generated in the nitrone cycloaddition. 1,3-Dipolar cycloadditions of nitrones are well-documented and provide efficient entries to the synthesis of isoxazolidines, which are valuable intermediates in organic synthesis.[3,4] In this paper, we report our results on the intramolecular 1,3-dipolar cycloadditions of norbornadiene-tethered nitrones (Scheme 3).[2]

Scheme 1. Intramolecular 1,3-Dipolar Cycloadditions of Norbornadiene-Tethered Nitrile Oxides



Scheme 2. General Outline for Construction of Tricyclic and Spirocyclic Frameworks via Intramolecular Cycloadditions of Norbornadienes and Subsequent Cleavage of the Cycloadducts



Four different types of regioisomers could be formed from the intramolecular 1,3-dipolar cycloaddition of the norbornadiene-tethered nitrone **13** (Scheme 4). Cycloaddition on the C_2-C_3 double bond could occur with the oxygen of the nitrone attached to C_3 and the sp^2 carbon of the nitrone attached to C_2 to give cycloadducts **14**−**17**. Cycloaddition on the C_2-C_3 double bond could also occur with the oxygen of the nitrone attached to C_2 and the sp^2 carbon of the nitrone attached to C_3 to give cycloadduct **18**. Cycloaddition on C_5-C_6 double bond would give **19** or **20**, and a [3 + 2 + 2] cycloaddition with both of the double bonds would give cycloadduct **21**. Other than regiochemistry problems, different stereoisomers are also possible. For example, cycloaddition on the C_2-C_3 double bond from the *exo* face with the oxygen of the nitrone attached to C_3 and the sp^2 carbon of the nitrone

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† Dedicated to Professor Gord Lange on the occasion of his retirement.

(1) (a) Yip, C.; Handerson, S.; Jordon, R.; Tam, W. *Org. Lett.* **1999**, *1*, 791. (b) Yip, C.; Handerson, S.; Tranmer, G. K.; Tam, W. *J. Org. Chem.* **2001**, *66*, 276.

(2) Preliminary results of this work have been published as a communication: Tranmer, G. K.; Keech, P.; Tam, W. *Chem. Commun.* **2000**, 863.

(3) (a) *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; John Wiley & Sons: New York, 1984; Vols. 1 and 2. (b) Gothelf, K. V.; Jorgensen, K. A. *Chem. Rev.* **1998**, *98*, 863 and references therein. (c) Padwa, A.; Schoffstall, A. M. Intramolecular 1,3-Dipolar Cycloaddition Chemistry. In *Advances in Cycloaddition*; Curran, D. P., Ed.; JAI Press: Greenwich, 1990; pp 1−89. (d) Grigg, R. *Chem. Soc. Rev.* **1987**, *16*, 89.

(4) (a) *Nitrile Oxides, Nitrones, and Nitronates in Organic Synthesis*; Torssell, K. B. G., Ed.; VCH: New York, 1988. (b) DeShong, P.; Lander, S. W., Jr.; Leginus, J. M.; Dicken, C. M. In *Advances in Cycloaddition*; Curran, D. P., Ed.; JAI Press: Greenwich, 1988; Vol. 1, pp 87−128. (c) Wade, P. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming I., Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol. 4, pp 1113−1124. (d) Frederickson M. *Tetrahedron* **1997**, *53*, 403. (e) Westling, M.; Smith, R.; Livinghouse, T. *J. Org. Chem.* **1986**, *51*, 1159. (f) Grigg, R.; Jordan, M.; Tangthongkum, A.; Einstein, F. W. B.; Jones, T. *J. Chem. Soc., Perkin Trans. 1* **1984**, 47. (g) Tsuge, O.; Ueno, K.; Kanemasa, S. *Chem. Lett.* **1984**, 285.

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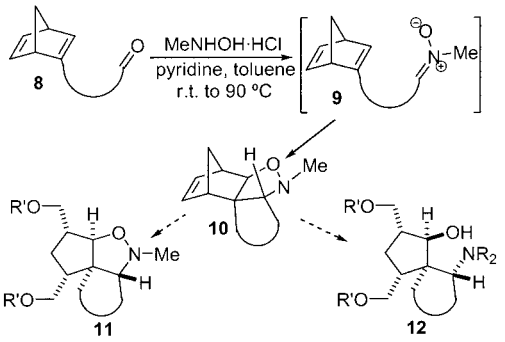
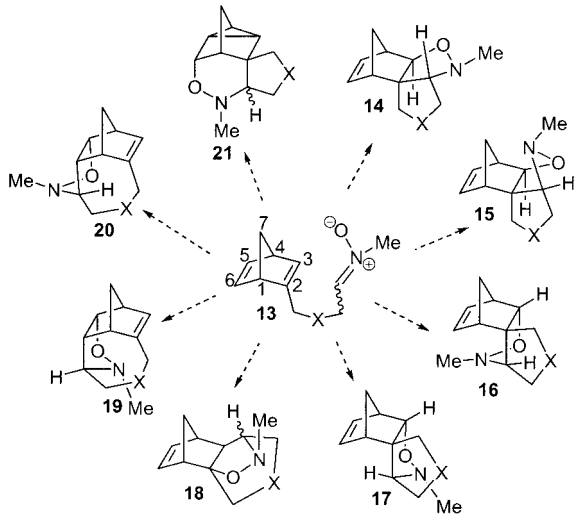
Scheme 3. Intramolecular 1,3-Dipolar Cycloadditions of Norbornadiene-Tethered Nitrones



Scheme 4. Possible Cycloadducts

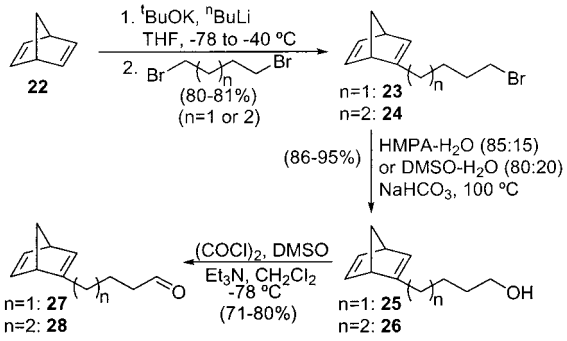


attached to C_2 would lead to the formation of two different *exo* cycloadducts **14** or **15** while cycloaddition from the *endo* face would give another two different *endo* cycloadducts **16** or **17**. Thus, many possible cycloadducts could be formed in the cycloaddition of norbornadiene-tethered nitrone **13**.

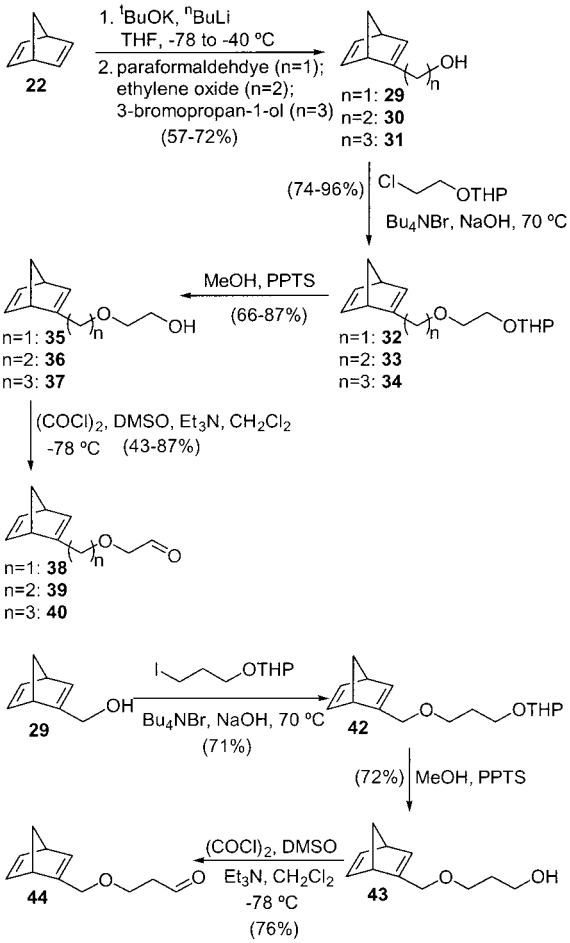
Results and Discussion

Efficient routes to the synthesis of norbornadiene-tethered aldehydes **27**, **28**, **38**−**40**, **44**, and **48** were developed (Schemes 5−7), and these aldehydes served as precursors of the required nitrones for the cycloadditions. Deprotonation of norbornadiene **22** with Schlosser's base (^{t}BuOK/^{n}BuLi)[5] in THF at −78 °C followed by addition of the resulting norbornadienyl anion to an excess of 1,4-dibromobutane or 1,5-dibromopentane provided the norbornadiene-tethered bromide **23** and **24** (Scheme 5).[1] Conversion of these bromides to the corresponding alcohols **25** and **26** followed by Swern oxidation provided the required aldehydes **27** and **28** with all-carbon tethers. Norbornadiene-tethered aldehydes with an oxygen atom within the tether were prepared using a similar protocol (Scheme 6). Trapping the norbornadienyl anion with paraformaldehyde, ethylene oxide, and 3-bromopropanol

Scheme 5. Synthesis of Norbornadiene-Tethered Aldehydes with All-Carbon Tether (27 and 28)



Scheme 6. Synthesis of Norbornadiene-Tethered Aldehydes with an Oxygen Atom within the Tether (38−40 and 44)

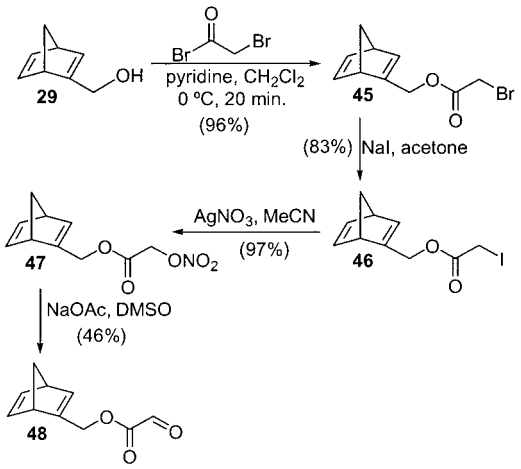


provided norbornadiene-tethered alcohols **29**−**31**. A two-carbon homologation to the alcohols **35**−**37** was achieved by a two-step sequence,[6] and Swern oxidation provided the required aldehydes **38**−**40**. Similarly, a three-carbon homologation of alcohol **29** to alcohol **43** was achieved in two steps, and Swern oxidation provided aldehyde **44**. An ester functionality within the tether was prepared from alcohol **29** (Scheme 7). Reaction of **29** with bromoacetyl bromide gave the α-bromo ester **45**, which was converted to the nitrate ester **47** in two steps.[7,8] Treatment of the nitrate ester **47** with sodium acetate in DMSO provided the required aldehyde **48**.[7,8]

(5) For deprotonation of bicyclic alkenes, see: (a) Stable, M.; Lehmann, R.; Kramar, J.; Schlosser, M. *Chimia* **1985**, *39*, 229. (b) Brandsma, L.; Verkuruijsse, H. D. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 66. (c) Tranmer, G. K.; Yip, C.; Handerson, S.; Jordan, R. W.; Tam, W. *Can. J. Chem.* **2000**, *78*, 527.

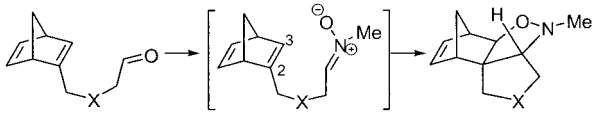
(6) Heinze, I.; Knoll, K.; Moller, R.; Eberbach, W. *Chem. Ber.* **1989**, *122*, 2147.

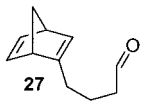
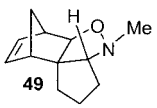
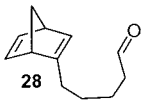
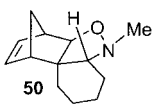
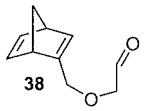
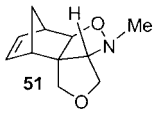
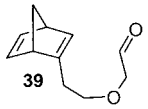
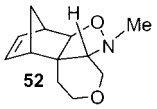
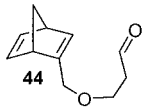
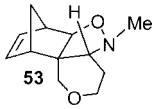
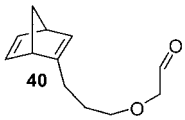
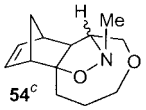
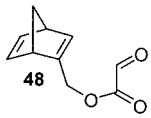
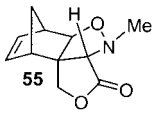
Scheme 7. Synthesis of Norbornadiene-Tethered Aldehydes with an Ester Functionality within the Tether (48)



The results of the intramolecular 1,3-dipolar cycloadditions of norbornadiene-tethered nitrones generated from the aldehydes **27**, **28**, **38**−**40**, **44**, and **48** are shown in Table 1. Addition of *N*-methylhydroxylamine to a solution containing aldehyde **27**, pyridine, and 4 Å molecular sieves in toluene at room temperature led to the formation of the corresponding norbornadiene-tethered nitrone, which underwent spontaneous intramolecular 1,3-dipolar cycloaddition at 80 °C to provide a single cycloadduct **49** in 51% isolated yield (Table 1, entry 1). Very little reaction was observed at a lower temperature, and prolonged heating led to decomposition of the cycloadduct. Although many possible cycloadducts could be formed in the reaction (Scheme 4), only cycloadduct **49** was isolated. With one more carbon in the tether (Table 1, entry 2), the only cycloadduct isolated was **50** but the yield was only 19%. For aldehydes with an oxygen atom within the tether (Table 1, entries 3−5), the yields of the cycloadditions were generally much better than the all-carbon tethered substrates. Aldehyde **38** provided the five-membered-ring cycloadduct **51** in 71% yield, while aldehydes **39** and **44** gave the corresponding six-membered-ring cycloadducts **52** and **53** in 60% and 47% yield. In all these reactions, cycloadducts **51**−**53** were the only cycloadducts isolated. Cycloaddition of the nitrone generated from aldehyde **40** led to the formation of an inseparable mixture of three isomers in 52% overall yield (Table 1, entry 6). Unlike all other cases in which the cycloadditions occur in such a way that the oxygen of the nitrone attached to C_3 and the sp^2 carbon of the nitrone attached to C_2, in this case with the nitrone generated from aldehyde **40**, the two major isomers formed were found to have the opposite regiochemistry, that is, with the oxygen of the nitrone attached to C_2 and the sp^2 carbon of the nitrone attached to C_3, *vide infra*. The switch of regiochemistry with increasing of the tether length is not uncommon, and it has been observed in some other intramolecular nitrone cycloadditions.[9] Cycloaddition of the substrate with an ester functionality (**48**) within the tether (Table 1, entry 7) gave a single cycloadduct **55** in 43% yield. As we noticed that most of the cycloadducts were thermally unstable and they decomposed on prolonged heating, we attempted the reactions at a lower temperature with the use of Lewis acid catalysts (e.g., $TiCl_4$, $ZrCl_4$, BF_3). Unfortunately, the isolated yields were even lower than the thermal reactions. We have also attempted to generate a six-membered ring cycloadduct containing an ester functionality; unfortunately, only decomposition was observed.

Table 1. Intramolecular 1,3-Dipolar Cycloadditions of Norbornadiene-Tethered Nitrones



entry	aldehyde	cycloadduct[a,b]	yield[d] (%)
1			51
2			19
3			71
4			60
5			47
6			52
7			43

[a] Reaction conditions: MeNHOH·HCl (1.2−2 equiv), pyridine (3−5 equiv), 4 Å molecular sieves, toluene, rt, 12−24 h then 60−90 °C 12−48 h. [b] Except in entry 6, the cycloadducts shown were the only regio- and stereoisomers isolated in the cycloadditions. [c] An inseparable mixture of three isomers was obtained. [d] Isolated yields after column chromatography.

The regio- and stereochemistry of the cycloadducts were proven by NMR techniques. The presence of two olefinic protons in the ^1H NMR spectrum eliminated the possibilities of cycloadducts **19** to **21** (Scheme 4). ^{13}C (APT-attached proton test) NMR spectra were useful to distinguish the regioisomers with the oxygen of the nitrone attached to C_3 and the sp^2 carbon of the nitrone attached to C_2 or the oxygen of the nitrone attached to C_2 and the sp^2 carbon of the nitrone attached to C_3. Except for cycloadduct **54** in which the oxygen of the nitrone attached to C_2 and the sp^2 carbon of the nitrone attached to C_3, all other cycloadducts were formed with

(7) Melnick, M. J.; Weinreb, S. M. *J. Org. Chem.* **1988**, *53*, 850.
(8) Annunziata, R.; Cinquini, M.; Cozzi F.; Raimondi, L. *J. Org. Chem.* **1990**, *55*, 1901.
(9) Oppolzer, W.; Siles, S.; Snowden, R. L.; Bakker, B. H.; Petrzilka, M. *Tetrahedron* **1985**, *41*, 3497.

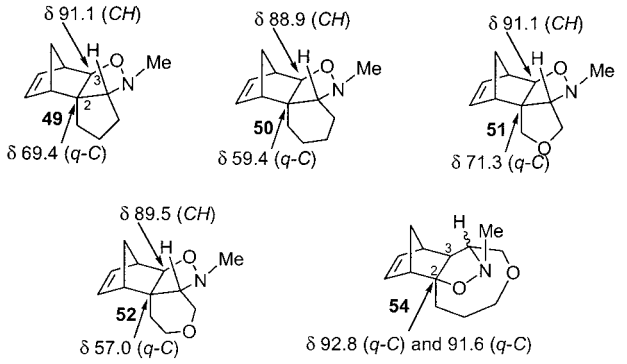


Figure 1. Determination of regiochemistry. Note: Chemical shift (δ) in ppm. *CH* = methine carbon and *q-C* = quaternary carbon: determined by ^{13}C (APT) NMR.

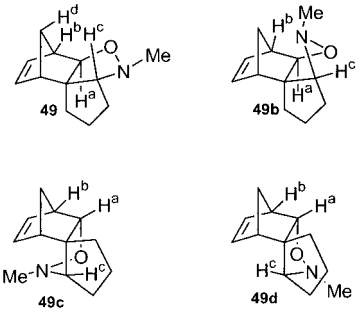
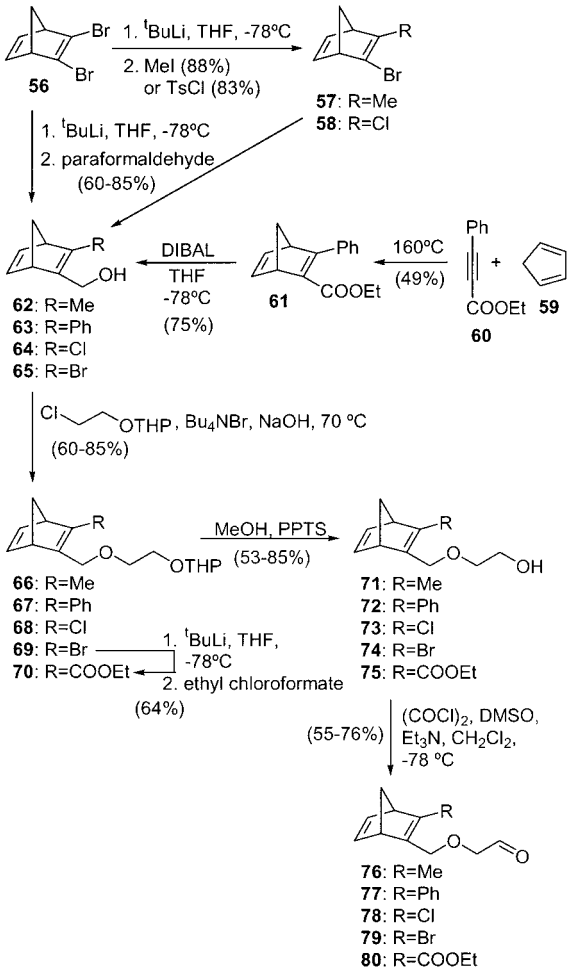


Figure 2. Determination of stereochemistry.

the oxygen of the nitrone attached to C_3 and the sp^2 carbon of the nitrone attached to C_2 (Figure 1). If the oxygen of the nitrone is attached to C_3, a methine (*CH*) carbon peak should be observed with chemical shift (δ) between 80 and 95 ppm. On the other hand, if the oxygen of the nitrone is attached to C_2, a quaternary carbon (*q-C*) signal should be observed with chemical shift (δ) between 80 and 95 ppm. Except for cycloadduct **54**, in all other cycloadducts the carbons attached to the oxygen with chemical shift ~88−95 ppm are methine (*CH*) carbons. For cycloadduct **54**, a mixture of three isomers was obtained. The two major isomers were found to have signals at δ 91.6 and 92.8 ppm (carbons attached to the oxygen), and these are quaternary carbons (*q-C*).

The *exo* and *endo* stereochemistry of the cycloadduct can easily be distinguished by the coupling constant of H^a and H^b (Figure 2) in the ^1H NMR.[10] As the dihedral angles between H^a and H^b in the *exo* cycloadducts **49** and **49b** are close to 90°, the coupling constant between H^a and H^b would be very small ($J \approx 0-2$ Hz). In the *endo* cycloadducts **49c** and **49d**, the dihedral angle between H^a and H^b is approximately 42° and would give a doublet with $J \approx 5$ Hz.[11] In all cases, H^a of all the cycloadducts (except cycloadduct **54**) are singlets in the ^1H NMR spectra, and therefore, all the cycloadducts must have *exo* stereochemistry (**49** or **49b**). To distinguish the two *exo* cycloadducts, NOESY NMR experiments were used.

Scheme 8. Synthesis of Norbornadiene-Tethered Aldehydes with a C_3 Substituent on the Norbornadiene (76−80)



As H^c of the cycloadducts showed +ve NOE effect with H^d, the structure of **49** was confirmed. These assignments were also supported by X-ray crystallography.[12]

To investigate the effect of a C_3 substituent on the norbornadiene in the cycloaddition, aldehydes **76**−**80** were prepared (Scheme 8). Monolithium−halide exchange of 2,3-dibromonorbornadiene **56**[5c] with ^{t}BuLi, followed by trapping the resulting organolithiums with methyl iodide or TsCl, provided bromides **57**−**58** in good yields.[5c] Lithium−halide exchange of bromides **56**−**58** followed by trapping with paraformaldehyde afforded norbornadiene-tethered alcohols **62** (R = Me), **64** (R = Cl), and **65** (R = Br). Alcohol **63** (R = Ph) was synthesized by a two-step sequence. Diels−Alder reaction of cyclopentadiene **59** with acetylene **60**[13] at 160 °C in a sealed tube provided norbornadiene **61**. DIBAL reduction of **61** afforded the required alcohol **63**. A two-carbon homologation to the alcohols **62**−**65** was achieved by a two-step sequence[6] to provide norbornadiene-tethered alcohols **71**−**74**. Norbornadiene-tethered alcohols with an ester on C_3 (**75**, R = COOEt) was synthesized from bromide **69** in two steps. Lithium−halide exchange of bromide **69** followed by trapping with ethyl chloroformate provided

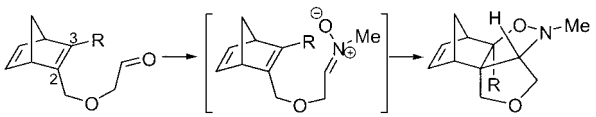
(10) A similar method has been used for the assignment of *exo* and *endo* stereochemistry of bicyclic alkanes; see: (a) Flautt, T. J.; Erman, W. F. *J. Am. Chem. Soc.* **1963**, *85*, 3212. (b) Mazzocchi, P. H.; Stahly, B.; Dodd, J.; Rondan, N. G.; Domelsmith, L. N.; Rozeboom, M. D.; Caramella, P.; Houk, K. N. *J. Am. Chem. Soc.* **1980**, *102*, 6482.

(11) The *exo* and *endo* cycloadducts **49** and **49d** were modeled for energy minimization at PM3 level (CS Chem 3D Pro Version 3.5.1) using MOPAC for the assessment of the dihedral angles between H^a and H^b. These dihedral angles were then compared to the Karplus curve for the determination of the theoretical coupling constants.

(12) Recrystallization of cycloadduct **55** in 20% EtOAc/hexanes provided suitable crystals for X-ray analysis. For details of the X-ray analysis, see: Tam, W.; Tranmer, G. K.; Lough, A. J. *Acta Crystallogr.* **2001**, *E57*, o269.

(13) Jordan, R. W.; Tam, W. *Org. Lett.* **2000**, *2*, 3031.

Table 2. Intramolecular 1,3-Dipolar Cycloadditions of C_3-Substituted Norbornadiene-Tethered Nitrones



entry	R	aldehyde	cycloadduct[a,b]	yield[d] (%)
1	H	**38**	**51**	71
2	Me	**76**	**81**	53
3	Ph	**77**	**82**	41
4	Cl	**78**	**83**	46
5	Br	**79**	**84**[c]	15
6	COOEt	**80**	**85**	57

[a] Reaction conditions: MeNHOH·HCl (1.2−2 equiv), pyridine (3−5 equiv), 4 Å molecular sieves, toluene, rt, 12−24 h, then 90 °C, 12−48 h. [b] Except in entry 5, the cycloadducts shown were the only regio- and stereoisomers isolated in the cycloadditions. [c] An inseparable mixture of two isomers (60:40) was obtained. [d] Isolated yields after column chromatography.

ester **70**. Removal of the THP group by PPTS in EtOH afforded norbornadiene-tethered alcohol **75**. Swern oxidation of these alcohols **71**−**75** provided aldehydes **76**−**80**, and these aldehydes served as precursors of the required nitrones for the cycloadditions.

The results of the intramolecular 1,3-dipolar cycloadditions of norbornadiene-tethered nitrones with a C_3 substituent are shown in Table 2. In all cases, the yields of the cycloadditions with norbornadiene-tethered nitrones with a C_3 substituent are lower than the unsubstituted case (Table 2, entry 1, R = H). This may due to the fact that the C_3 substituents retard the cycloadditions because of steric hindrance. Except with R = Br (Table 2, entry 5), in all other cases, single regio- and stereoisomers were obtained. With an alkyl group (R = Me) or aryl group (R = Ph) at C_3 (Table 2, entries 2 and 3), cycloadducts **81** and **82** were generated in moderate yields (53% and 41%). With halides at C_3 (Table 2, entries 4 and 5), R = Cl gave a single regio- and stereoisomer **83** in 46% yield, and R = Br gave cycloadduct **84** as a 60:40 mixture of two stereoisomers in only 15% yield. Cycloadducts **83** and **84** were rather unstable and decomposed gradually upon standing even at room temperature. With an ester functionality (R = COOEt) at C_3, a single regio- and stereoisomer **85** was obtained in 57% yield. The regio- and stereochemistry of these cycloadducts were confirmed by using NMR techniques (HCOSY, HSQC, HMBC, and NOESY or GOESY experiments).[14,15]

Several factors could control the regio- and stereoselectivity of the cycloadditions. Those factors include the following: the *E*/*Z* ratio of the nitrones generated from the corresponding aldehydes, the distance and the flexibility of the tether to reach the double bonds, the *exo*/*endo* selectivity of the double bond (C_2−C_3) in the norbornadiene in the cycloadditions, and the strain and the stability of the cycloadducts formed. We are not sure of the reasons for the formation of single cycloadducts in the cycloadditions. Either the *E*/*Z* selectivity of the formation of nitrones was very high and the cycloadditions were highly regio- and stereoselective or other cycloadducts were formed but were too unstable and decomposed under the reaction conditions. The cycloadditions can also be reversible, thus giving rise to the most stable cycloadducts.[16] But nevertheless, although up to eight possible cycloadducts could be formed in the cycloadditions, we were able to generate and to isolate single regio- and stereoisomers in the cycloadditions in most cases.

Conclusion

We have demonstrated the first examples of the intramolecular 1,3-dipolar cycloadditions of norbornadiene-tethered nitrones. Although eight possible cycloadducts could be formed in the cycloadditions, in most cases, single regio- and stereoisomers were formed. Thus, these cycloadditions were found to be highly regio- and stereoselective, giving the *exo* cycloadducts in moderate to good yields. Further investigations on subsequent cleavage reactions of the cycloadducts (Scheme 3) for the construction of angular-fused tricyclic and spirocyclic frameworks are ongoing in our laboratory.

Experimental Section

General Information. All reactions were carried out in an atmosphere of dry nitrogen at ambient temperature unless otherwise stated. Standard column chromatography was performed on 230−400 mesh silica gel (obtained from Silicycle) by use of flash column chromatography techniques.[17] Analytical thin-layer chromatography (TLC) was conducted on Merck precoated silica gel 60 F_{254} plates. All glassware was flame dried under an inert atmosphere of dry nitrogen. Chemical shifts for ^{1}H NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent resonance as the internal standard (chloroform: δ 7.26). Chemical shifts for ^{13}C NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent as the internal standard (deuteriochloroform: δ 77.0).

Materials. Unless stated otherwise, commercial reagents were used without purification. Solvents were purified by distillation under dry nitrogen: from CaH_2 (CH_2Cl_2, 1,2-dichloroethane, chloroform, DMF, Et_3N, pyridine); from 4 Å molecular sieves (DMSO, acetonitrile, nitromethane); from sodium (toluene); from potassium/benzophenone (THF); and from sodium/benzophenone (Et_2O). Norbornadiene (**22**), 1,4-dibromobutane, 1,5-dibromopentane, and 2-chloroethanol were purified by distillation from 4 Å molecular sieves under dry nitrogen. Substituted norbornadienes (**23**−**25**, **27**, **29**, **30**, **32**, **33**, **35**, **36**),[1b] **31**,[18] **56**−**58**,[5c] and acetylene **60**[13] were prepared according to literature procedures.

5-(2-Bicyclo[2.2.1]hepta-2,5-dien-2-yl)pentan-1-ol (26). Dimethyl sulfoxide (DMSO, 100 mL), water (25 mL) and sodium bicarbonate (5.0 g, 59.5 mmol) were added to a flask containing bromide **24**[1b] (4.6 g, 19.1 mmol). The reaction mixture was allowed to stir at 95 °C for 22 h. After the reaction mixture was quenched with water (200 mL), the aqueous layer

(14) HCOSY: ^{1}H−^{1}H correlated spectroscopy. HSQC: heteronuclear single quantum coherence. HMBC: heteronuclear multiple bond correlation. NOESY: nuclear Overhauser enhancement spectroscopy. See: Crews, P.; Rodriguez, J.; Jaspars, M. *Organic Structure Analysis*; Oxford University Press: Oxford, 1998.

(15) GOESY: gradient enhanced nuclear Overhauser enhancement spectroscopy. See: (a) Stonehouse, J.; Adell, P.; Keeler, J.; Shaka, A. J. *J. Am. Chem. Soc.* **1994**, *116*, 6037. (b) Stott, K.; Stonehouse, J.; Keeler, J.; Hwang, T.-L.; Shaka, A. J. *J. Am. Chem. Soc.* **1995**, *117*, 4199. (c) Dixon, A. M.; Widmalm, G.; Bull, T. E. *J. Magn. Reson.* **2000**, *147*, 266.

(16) As suggested by one of the referees, we have performed semiempirical molecular mechanics calculations (using AM1, PC Spartan Pro, Wavefunction, Inc., 1999) of the relative energies of the isomers of cycloadducts **49**, **49b**, **49c**, and **49d** (Figure 2). We found that cycloadduct **49**, which we obtained as the only regio- and stereoisomer in the cycloaddition, is the most stable isomer. Isomer **49** is approximately 27 kcal/mol more stable than **49b**, 29 kcal/mol more stable than **49c**, and 2 kcal/mol more stable than **49d**.

(17) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(18) Lautens M.; Tam, W.; Lautens, J. C. Edwards, L. G.; Crudden, C. M.; Smith, A. C. *J. Am. Chem. Soc.* **1995**, *117*, 6863.

was extracted with diethyl ether (5 × 100 mL), and the combined organic layers were washed sequentially with water (100 mL) and brine (100 mL) and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the crude product was purified by vacuum distillation (0.2 mmHg at 85 °C) to give **26** (2.9168 g, 16.36 mmol, 86%) as a colorless oil: R_f 0.33 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3326 (br s), 3117 (w), 3064 (m), 2967 (s), 2932 (s), 2863 (s), 1622 (w), 1555 (m), 1300 (s), 1055 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.74 (m, 2H), 6.11 (m, 1H), 3.60 (t, 2H, J = 6.8 Hz), 3.48 (br s, 1H), 3.26 (br s, 1H), 2.18 (m, 2H), 1.96 (d, 1H, J = 5.7 Hz), 1.93 (d, 1H, J = 5.7 Hz), 1.55 (m, 2H), 1.43 (m, 2H), 1.31 (m, 2H), 1.76 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.6, 143.7, 142.3, 133.3, 73.4, 62.8, 53.4, 49.9, 32.5, 31.3, 26.9, 25.3. Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 81.08; H, 9.89.

2-[2-(Bicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxy)propoxy]-tetrahydro-2*H*-pyran (42). To a flame-dried flask containing alcohol **29**[1b] (2.503 g, 20.49 mmol), THP-protected 3-iodopropan-1-ol (6.5362 g, 24.20 mmol), and tetrabutylammonium bromide (1.36 g, 4.09 mmol) was added 50% NaOH (6.3 g in 6.3 mL water, 158 mmol) at 0 °C. The reddish-brown reaction mixture was stirred at 70 °C for 51 h. After the reaction was quenched with saturated sodium chloride (20 mL) and water (50 mL), the aqueous layer was extracted with diethyl ether (3 × 50 mL), and the combined organic layers were washed sequentially with water (50 mL) and brine (50 mL) and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **42** (3.8331 g, 14.5 mmol, 71%, a 1:1 mixture of diastereomers) as a colorless oil: R_f 0.48 (EtOAc/hexanes = 1:9); IR (neat, NaCl) 3065 (w), 2939 (s), 2867 (s), 1555 (w), 1441 (m), 1200 (m), 1125 (s), 1021 (s), 733 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.78 (dd, 1H, J = 5.0, 3.0 Hz), 6.72 (dd, 1H, J = 5.0, 3.0 Hz), 6.42 (m, 1H), 4.55 (m, 1H), 4.08 (m, 2H), 3.82 (m, 2H), 3.53 (s, 1H), 3.37−3.50 (m, 5H), 2.01 (dm, 1H, J = 6.0 Hz), 1.96 (dm, 1H, J = 6.0 Hz), 1.74−1.88 (m, 3H), 1.68 (m, 1H), 1.48−1.58 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.2, 143.3, 142.5, 138.0, 98.8, 98.7, 73.58, 73.56, 69.3, 67.0, 66.9, 64.4, 62.19, 62.17, 51.24, 51.19, 50.1, 30.6, 30.0, 25.4, 19.5. Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.44; H, 9.13.

3-(2-Bicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxy)propan-1-ol (43). To a flame-dried flask containing **42** (3.05 g, 11.5 mmol) in MeOH (100 mL) was added pyridinium *p*-toluenesulfonate, PPTS (328.4 mg, 1.82 mmol) at room temperature. The reaction mixture was stirred at 55 °C for 50 min. After the reaction was quenched with water (200 mL), the aqueous layer was extracted with diethyl ether (3 × 50 mL), and the combined organic layers were washed sequentially with water (50 mL) and brine (50 mL) and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **43** (1.4926 g, 8.28 mmol, 72%) as a pale yellow oil: R_f 0.12 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3392 (br s), 3064 (w), 2934 (s), 2866 (s), 1635 (w), 1351 (m), 1087 (s), 1069 (s), 699 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.77 (dd, 1H, J = 5.1, 3.1 Hz), 6.71 (dd, 1H, J = 5.1, 3.0 Hz), 6.43 (s, 1H), 4.11 (d_{AB}, 1H, J = 12.8 Hz), 4.06 (d_{AB}d, 1H, J = 12.8, 1.3 Hz), 3.72 (t, 2H, J = 5.6 Hz), 3.46−3.55 (m, 3H), 3.41 (br s, 1H), 2.74 (br s, 1H), 2.01 (d, 1H, J = 6.0 Hz), 1.96 (d, 1H, J = 6.0 Hz), 1.79 (p, 2H, J = 5.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.6, 143.3, 142.4, 138.5, 73.7, 69.6, 69.1, 61.8, 51.2, 50.1, 31.9.

Bromobicyclo[2.2.1]hepta-2,5-dien-2-ylacetic Acid, Methyl Ester (45). Bromoacetyl bromide (0.59 mL, 6.77 mmol) was added to a flame-dried flask containing alcohol **29**[1b] (742 mg, 6.07 mmol), dichloromethane (20 mL), and pyridine (0.73 mL, 9.11 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. After the reaction mixture was quenched with water (20 mL), the aqueous layer was extracted with diethyl ether (3 × 30 mL), and the combined organic layers were washed sequentially with saturated copper(II) sulfate (30 mL), water (2 × 30 mL), and brine (30 mL) and dried over magnesium sulfate. The solvent was removed by rotary evaporation to give ester **45** (1.41 g, 5.80 mmol, 96%) as a colorless oil that was used in the next step without further purification: R_f 0.67 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3066 (w), 2982 (m), 2936 (m), 2868 (w), 1740 (s), 1285 (s), 1162 (m), 1108 (m), 965 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.79 (dd, 1H, J = 5.1, 3.0 Hz), 6.74 (dd, 1H, J = 5.0, 2.8 Hz), 6.58 (d, 1H, J = 1.5 Hz), 4.82 (d_{AB}d, 1H, J = 13.1, 1.4 Hz), 4.78 (d_{AB}d, 1H, J = 13.1, 1.5 Hz), 3.83 (s, 2H), 3.56 (br s, 1H), 3.44 (br s, 1H), 2.02 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.9, 151.6, 143.2, 142.4, 140.7, 73.8, 64.6, 51.3, 50.2, 25.7.

Iodobicyclo[2.2.1]hepta-2,5-dien-2-ylacetic Acid, Methyl Ester (46). Sodium iodide (1.6982 g, 11.3 mmol) was added to a flame-dried flask containing reagent-grade acetone (9 mL) and bromoester **45** (1.1812 g, 4.86 mmol) at room temperature. The reaction mixture was stirred at room temperature for 5 h. After the reaction mixture was filtered and the precipitate washed with dichloromethane, the organic layer was washed with a 10% $NaHSO_3$ solution (30 mL). The aqueous layer was extracted with dichloromethane (2 × 15 mL), and the combined organic layers were washed sequentially with water (30 mL) and brine (30 mL) and dried over sodium sulfate. The solvent was removed by rotary evaporation to give iodoester **46** (1.1683 g, 4.03 mmol, 83%) as a colorless oil that was used in the next step without further purification: R_f 0.74 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3059 (s), 2967 (s), 2886 (s), 1730 (s), 1631 (w), 1555 (w), 1413 (m), 1023 (m), 805 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.81 (dd, 1H, J = 5.0, 4.0 Hz), 6.74 (dd, 1H, J = 5.0, 3.1 Hz), 6.59 (d, 1H, J = 1.4 Hz), 4.80 (d_{AB}d, 1H, J = 13.1, 1.1 Hz), 4.74 (d_{AB}d, 1H, J = 13.1, 1.4 Hz), 3.69 (s, 2H), 3.57 (br s, 1H), 3.46 (br s, 1H), 2.05 (dm, 1H, J = 6.0 Hz), 1.99 (dm, 1H, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.5, 151.8, 143.2, 142.5, 140.6, 73.8, 64.4, 51.3, 50.2, −5.5.

(Nitrooxy)bicyclo[2.2.1]hepta-2,5-dien-2-ylacetic Acid, Methyl Ester (47). Sodium nitrate (0.8795 g, 5.18 mmol) was added to a flame-dried flask covered in aluminum foil containing dry acetonitrile (12 mL) and iodoester **46** (1.0381 g, 3.58 mmol) at room temperature. The reaction mixture was stirred at room temperature for 15.5 h. The reaction mixture was filtered, the remaining precipitate was washed with diethyl ether, and the organic layer was then washed with water (2 × 15 mL) and dried over magnesium sulfate. The solvent was removed by rotary evaporation to give nitrate **47** (0.7864 g, 3.49 mmol, 97%) as a colorless oil that was used in the next step without further purification: R_f 0.59 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3067 (w), 2974 (s), 2939 (s), 2870 (m), 1728 (s), 1632 (s), 1412 (s), 1387 (s), 846 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.79 (dd, 1H, J = 4.5, 3.1 Hz), 6.75 (dd, 1H, J = 4.5, 3.1 Hz), 6.60 (d, 1H, J = 1.5 Hz), 4.91 (s, 2H), 4.85 (dd, 2H, J = 6.1, 1.4 Hz), 3.59 (s, 1H), 3.42 (s, 1H), 2.05 (dt, 1H, J = 6.0, 1.5 Hz), 2.01 (dt, 1H, J = 6.0, 1.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.6, 151.2, 143.3, 142.4, 141.5, 74.0, 67.1, 64.5, 51.4, 50.3; HRMS calcd for $C_{10}H_{11}NO_5$ m/z 225.0637, found m/z 225.0636.

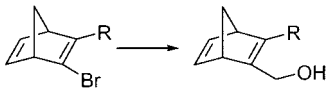
Oxobicyclo[2.2.1]hepta-2,5-dien-2-ylacetic Acid, Methyl Ester (48). Anhydrous sodium acetate (219.5 mg, 2.67 mmol) was added to a flame-dried flask containing dry dimethyl sulfoxide (15 mL) and nitrate **47** (590.3 mg, 2.62 mmol) at room temperature. The reaction mixture was stirred at room temperature for 20 min and changed from a cloudy pale yellow solution to a clear dark yellow solution. After the reaction mixture was quenched by pouring into ice-cold brine (50 mL), the aqueous layer was extracted with diethyl ether (3 × 20 mL), and the combined organic layers were washed sequentially with saturated sodium bicarbonate (20 mL) and water (30 mL) and dried over magnesium sulfate The solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (EtOAc/hexanes = 1:3) to give **48** (237 mg, 1.21 mmol, 46%) as an opaque oil. **48** was isolated as a 3:1 mixture of its glyoxylate form (hydrated aldehyde) and its aldehyde form: R_f 0.23 (EtOAc/hexanes = 3:7); IR (neat, NaCl) 3442 (br s), 3067 (m), 2974 (s), 2938 (s), 2870 (s), 1744 (s), 1556 (m), 1451 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.41 (s, 0.25H), 6.67−6.80 (m, 2H), 6.60 (dm, 0.25H, J = 1.3 Hz), 6.58 (m, 0.75H), 5.36 (m, 0.4H), 4.82−4.99 (m, 2H), 3.92 (m, 0.4H), 3.61 (m, 0.25H), 3.58 (m, 0.75H),

3.49 (m, 0.25H), 3.44 (m, 0.75H), 1.98−2.08 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 183.7, 168.7, 151.3, 150.8, 143.3, 142.5, 142.4, 142.3, 141.2, 141.0, 88.3, 74.0, 73.8, 65.0, 64.8, 51.4, 51.3, 50.4, 50.3.

3-Phenylbicyclo[2.2.1]hepta-2,5-diene-2-carboxylic Acid, Ethyl Ester (61). Phenylacetylene ester **60**[13] (3.4914 g, 20.04 mmol) and freshly distilled cyclopentadiene **59** (1.88 g, 28.4 mmol) were added to a Pyrex pressure tube under an atmosphere of nitrogen. The tube was sealed tightly and heated to 160 °C for 84 h. The crude product was purified by vacuum distillation (0.5 Torr at 110 °C−120 °C) to give **61** (2.3756 g, 9.89 mmol, 49%) as a clear colorless oil: R_f 0.39 (EtOAc/hexanes = 5:95); IR (neat, NaCl) 3054 (m), 2977 (s), 2869 (s), 1712 (s), 1558 (m), 1491 (m), 1444 (s), 1242 (s), 1100 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54 (m, 2H), 7.36 (m, 3H), 7.00 (dd, 1H, J = 5.0, 3.0 Hz), 6.93 (dd, 1H, J = 5.0, 3.1 Hz), 4.15 (q, 2H, J = 7.1 Hz), 4.08 (m, 1H), 3.87 (m, 1H), 2.27 (dt, 1H, J = 5.2, 1.4 Hz), 2.07 (dt, 1H, J = 6.6, 1.4 Hz), 1.23 (t, 3H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.3, 165.5, 143.7, 140.8, 139.3, 135.6, 128.4, 127.8, 127.6, 70.5, 60.0, 58.4, 53.0, 14.1; HRMS calcd for $C_{16}H_{16}O_2$ m/z 240.1150, found m/z 240.1145.

3-Phenylbicyclo[2.2.1]hepta-2,5-diene-2-methanol (63). Diisobutylaluminum hydride, DIBAL (1 M in hexane, 8.3 mL, 8.3 mmol), was added to a flame-dried flask containing norbornadiene ester **61** (1.0449 g, 4.345 mmol) and THF (20 mL) at −78 °C (acetone/dry ice bath). The reaction was stirred for 2 h at −78 °C, quenched at that temperature with water (10 mL) and saturated ammonium chloride (40 mL), and allowed to warm to room temperature. The aqueous layer was extracted with diethyl ether (3 × 20 mL), and the combined organic layers were washed sequentially with water (40 mL) and brine (40 mL) and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **63** (647.4 mg, 3.265 mmol, 75%) as a colorless viscous oil: R_f 0.35 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3353 (br s), 3058 (m), 2968 (s), 2936 (s), 2866 (s), 1598 (m), 1493 (s), 1296 (s), 1029 (s), 986 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35 (m, 2H), 7.24 (m, 3H), 6.95 (dd, 1H, J = 5.0, 3.0 Hz), 6.89 (dd, 1H, J = 5.0, 3.0 Hz), 4.45 (d, 1H, J = 12.0 Hz), 4.40 (d, 1H J = 12.0 Hz), 3.80 (m, 1H), 3.77 (m, 1H), 2.17 (dt, 1H, J = 6.4, 1.6 Hz), 2.03 (dt, 1H, J = 6.0, 1.6 Hz), 1.45 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.3, 148.2, 142.9, 142.2, 136.5, 128.3, 126.8, 126.3, 71.0, 59.7, 55.4, 53.2; HRMS calcd for $C_{14}H_{14}O$ m/z 198.1045, found m/z 198.1040.

General Procedure for the Synthesis of Alcohols 62, 64, and 65.



3-Methylbicyclo[2.2.1]hepta-2,5-diene-2-methanol (62). 2-Bromo-3-methylnorbornadiene **57**[5c] (1.9971 g, 10.79 mmol) was added to a flame-dried flask and cooled to −78 °C (acetone/dry ice bath) following the addition of THF (50 mL). *tert*-Butyllithium (12.7 mL, 1.7 M, 21.6 mmol) was added via syringe to the solution, maintaining the temperature below −65 °C. The reaction mixture was stirred at −78 °C for 15 min. Paraformaldyde (4.6971 g, ∼52.1 mmol) was then added to the flask and stirred at −78 °C for 1 h, and the solution was then allowed to warm to room temperature and stirred for 1 h. After the reaction mixture was quenched with water (20 mL), the aqueous layer was extracted with diethyl ether (2 × 30 mL). The aqueous layer was then acidified to a pH of 6 and extracted with diethyl ether (2 × 15 mL), and the combined organic layers were washed sequentially with water (40 mL) and brine (40 mL) and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **62** (1.1769 g, 8.64 mmol, 80%) as a colorless oil: R_f 0.30 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3362 (br s), 3064 (m), 2966 (s), 2934 (s), 2866 (s), 1440, (m), 1309 (m), 1291 (m), 993 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.81 (dd, 1H, J = 5.2, 2.8 Hz), 6.76 (dd, 1H, J = 5.2, 3.0 Hz), 4.23 (d, 1H, J = 12.2 Hz), 4.12 (d, 1H, J = 12.2 Hz), 3.53 (s, 1H), 3.27 (s, 1H), 1.95 (dt, 1H, J = 5.6, 1.6 Hz), 1.89 (dt, 1H, J = 5.6, 1.6 Hz), 1.78 (s, 3H), 1.17 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.9, 144.7, 143.3, 141.8, 71.3, 58.9, 55.7, 51.8, 14.3; HRMS calcd for $C_9H_{12}O$ m/z 136.0888, found m/z 136.0882.

3-Chlorobicyclo[2.2.1]hepta-2,5-diene-2-methanol (64). Following the above general procedure using bromide **58**[5c] (1.5757 g, 7.67 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **64** (0.7234 g, 4.62 mmol, 60%) as a colorless oil: R_f 0.33 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3365 (br s), 3069 (m), 2980 (s), 2940 (s), 2871 (s), 1637, (m), 1451 (m), 1298 (s), 1048 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.86 (m, 2H), 4.31 (d, 1H, J = 12.8 Hz), 4.18 (d, 1H, J = 12.8 Hz), 3.66 (m, 1H), 3.43 (m, 1H), 2.22 (dt, 1H, J = 6.0, 1.6 Hz), 2.07 (dt, 1H, J = 6.0, 1.6 Hz), 1.51 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.5, 143.8, 142.8, 141.5, 71.5, 58.3, 56.8, 51.6; HRMS calcd for C_8H_9OCl m/z 156.0342, found m/z 156.0348.

3-Bromobicyclo[2.2.1]hepta-2,5-diene-2-methanol (65). Following the above general procedure using dibromide **56**[5c] (1.2380 g, 4.95 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **65** (0.8498 g, 4.23 mmol, 85%) as a colorless oil: R_f 0.33 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3330 (br s), 3068 (m), 2977 (s), 2939 (s), 2869 (s), 1630 (m), 1558 (m), 1449 (m), 1297 (s), 1039 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.84 (dd, 1H, J = 4.8, 2.8 Hz), 6.80 (dd, 1H, J = 4.8, 2.8 Hz), 4.25 (d, 1H, J = 12.8 Hz), 4.09 (d, 1H, J = 12.8 Hz), 3.66 (m, 1H), 3.50 (m, 1H), 2.38 (br s, 1H), 2.21 (dt, 1H, J = 6.2, 1.6 Hz), 2.05 (dt, 1H, J = 6.2, 1.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.4, 142.4, 141.5, 132.3, 71.8, 59.4, 58.3, 51.9; HRMS calcd for C_8H_9OBr m/z 199.9837, found m/z 199.9842.

General Procedure for the Synthesis of THP-Protected Alcohols: 34, 66, 67, 68, and 69.

2-[2-(Bicyclo[2.2.1]hepta-2,5-dien-2-ylpropoxy)ethoxy]-tetrahydro-2*H*-pyran (34). To a flame-dried flask containing alcohol **31**[18] (2.2558 g, 15.02 mmol), THP-protected 2-chloroethanol (4.9537 g, 30.09 mmol), and tetrabutylammonium bromide (1.004 g, 3.010 mmol) was added 50% NaOH (4.6 g in 4.6 mL water, 115 mmol) at 0 °C. The reddish-brown reaction mixture was stirred at 66 °C for 63 h. After the reaction was quenched with saturated sodium chloride (10 mL) and water (20 mL), the aqueous layer was extracted with diethyl ether (4 × 20 mL), and the combined organic layers were washed sequentially with water (20 mL) and brine (20 mL) and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (EtOAc/hexanes = 3:97) to give **34** as an inseparable mixture of two diastereomers (4.0362 g, 14.49 mmol, 96%) as a colorless oil: R_f 0.63 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3063 (w), 2938 (s), 2866 (s), 1441 (m), 1201 (m), 1125 (s), 1036 (s), 989 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.72 (m, 2H), 6.11 (d, 1H, J = 1.5 Hz), 4.62 (t, 1H, J = 3.5 Hz), 3.82 (m, 2H), 3.54−3.60 (m, 3H), 3.46−3.51 (m, 2H), 3.42 (t, 2H, J = 6.7 Hz), 3.25 (s, 1H), 2.23 (m, 2H), 1.94 (d_{AB}t, 1H, J = 5.7, 1.5 Hz), 1.91 (d_{AB}t, 1H, J = 5.7, 1.5 Hz), 1.82 (m, 1H), 1.67−1.73 (m, 3H), 1.47−1.62 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.1, 143.7, 142.2, 133.5, 98.8, 73.4. 70.8, 69.9, 66.5, 62.1, 53.4, 49.9, 30.5, 27.9, 27.1, 25.4, 19.4.

2-(3-Methylbicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxyethoxy)tetrahydro-2*H*-pyran (66). Following the above general procedure using alcohol **62** (1.0049 g, 7.38 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **66** as an inseparable mixture of two diastereomers (1.6486 g, 6.24 mmol, 85%) as a colorless oil: R_f 0.55 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3064 (w), 2938 (s), 2866 (s), 1441 (m), 1353 (m), 1201, (m), 1125 (s), 1075 (s), 1036(s), 732 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.78 (dd,

1H, J = 8.0, 4.8 Hz), 6.72 (dd, 1H, J = 8.0, 4.8 Hz), 4.63 (t, 1H, J = 3.6 Hz), 4.16 (dd, 1H, J = 12.4, 2.0 Hz), 4.00 (d, 1H, J = 12.4 Hz), 3.83 (m, 2H), 3.58−3.36 (m, 4H), 3.49 (s, 1H), 3.26 (s, 1H), 1.94 (m, 1H), 1.86 (dm, 1H, J = 5.6 Hz), 1.77 (s, 3H), 1.82−1.47 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.6, 143.22, 143.17, 142.75, 142.72, 141.37, 98.79, 98.73, 71.05, 70.99, 68.2, 66.65, 66.61, 66.48, 66.45, 62.1, 55.7, 52.0, 51.9, 30.5, 25.4, 19.4, 14.4.

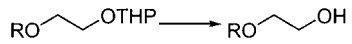
2-(3-Phenylbicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxyethoxy)tetrahydro-2*H*-pyran (67). Following the above general procedure using alcohol **63** (0.6450 g, 3.25 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **67** as an inseparable mixture of two diastereomers (0.6372 g, 1.95 mmol, 60%) as a colorless oil: R_f 0.51 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3060 (w), 2942 (s), 2869 (s), 1727 (w), 1442 (m), 1201, (m), 1125 (s), 1075 (s), 1035 (s), 909 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34 (m, 2H), 7.23 (m, 3H), 6.92 (dd, 1H, J = 5.2, 2.8 Hz), 6.89 (m, 1H), 4.63 (m, 1H), 4.41 (d, 1H, J = 12.6 Hz), 4.24 (d, 1H, J = 12.6 Hz), 3.83 (m, 4H), 3.57−3.48 (m, 4H), 2.17 (m, 1H), 2.01 (d, 1H, J = 6.0 Hz), 1.83 (m, 1H), 1.72 (m, 1H), 1.57 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.87, 151.81, 146.94, 146.90, 142.95, 142.88, 141.77, 141.74, 136.7, 128.2, 126.7, 126.4, 98.77, 98.71, 70.88, 70.84, 69.02, 68.98, 67.4, 66.6, 66.5, 62.05, 62.02, 55.4, 53.45, 53.40, 30.5, 25.4, 19.4.

2-(3-Chlorobicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxyethoxy)tetrahydro-2*H*-pyran (68). Following the above general procedure using alcohol **64** (0.6004 g, 3.83 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **68** as an inseparable mixture of two diastereomers (0.7917, 2.78 mmol, 73%) as a colorless oil: R_f 0.68 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 2942 (s), 2870 (s), 1636 (w), 1453 (w), 1441 (w), 1124 (s), 1075 (s), 1035 (s), 909 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.82 (m, 2H), 4.63 (t, 1H, J = 3.6 Hz), 4.21 (d, 1H, J = 12.8 Hz), 4.04 (dd, 1H, J = 12.8, 0.8 Hz), 3.84 (m, 2H), 3.64 (m, 1H), 3.57−3.41 (m, 5H), 2.22 (m, 1H), 2.05 (dt, 1H, J = 6.0, 1.6 Hz), 1.83 (m, 1H), 1.72 (m, 1H), 1.65−1.49 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.2, 143.83, 143.81, 142.8, 142.7, 141.08, 141.03, 98.76, 98.71, 71.38, 71.33, 68.8, 66.47, 66.43, 65.47, 62.05, 56.8, 51.70, 51.67, 30.5, 25.4, 19.4. Anal. Calcd for $C_{15}H_{21}O_3Cl$: C, 63.26; H, 7.43. Found: C, 62.91; H, 7.54.

2-(3-Bromobicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxyethoxy)tetrahydro-2*H*-pyran (69). Following the above general procedure using alcohol **65** (0.8519 g, 4.24 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **69** as an inseparable mixture of two diastereomers (1.0558, 3.21 mmol, 76%) as a colorless oil: R_f 0.53 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3068 (w), 2940 (s), 2868 (w), 1629 (m), 1557 (m), 1441 (m), 1297 (m), 1113 (s), 1036 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.82 (m, 2H), 4.63 (t, 1H, J = 3.6 Hz), 4.21 (d, 1H, J = 12.8 Hz), 4.02 (d, 1H, J = 12.8 Hz), 3.84 (m, 2H), 3.66 (s, 1H), 3.58−3.42 (m, 5H), 2.23 (m, 1H), 2.06 (dt, 1H, J = 6.4, 1.6 Hz), 1.84−1.49 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.84, 147.82, 142.4, 141.2, 134.1, 98.76, 98.72, 71.78, 71.73, 68.8, 66.9 66.5, 62.12, 62.06, 58.52, 58.46, 52.23, 52.13, 30.5, 25.4, 19.4. Anal. Calcd for $C_{15}H_{21}O_3$-Br: C, 54.72; H, 6.43. Found: C, 54.39; H, 6.66.

2-(3-Ethoxycarbonylbicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxyethoxy)tetrahydro-2*H*-pyran (70). To a flame-dried flask containing alcohol **69** (1.3430 g, 4.08 mmol) and THF (20 mL) that had been cooled to −78 °C in an acetone dry ice bath was added *tert*-butyllithium (4.8 mL, 1.7 M, 8.16 mmol) and the mixture stirred for 15 min. Using a cannula, ethyl chloroformate (1.56 mL, 16.3 mmol) in THF (10 mL) that had also been cooled to −78 °C was added, and the mixture was allowed to stir for 1 h. The reaction mixture was allowed to warm to room temperature and quenched with water (20 mL). The aqueous layer was extracted with diethyl ether (3 × 20 mL), and the combined organic layers were washed sequentially with water (25 mL) and brine (25 mL) and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **70** (0.8417 g, 2.61 mmol, 64%) as a colorless oil: R_f 0.44 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 2941 (s), 2871 (s), 1739 (vs), 1699 (s), 1369 (m), 1294 (s), 1125 (s), 1021 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.87 (dd, 1H, J = 4.8, 3.2 Hz), 6.77 (m, 1H), 4.71 (d, 1H, J = 14.8 Hz), 4.65 (t, 1H, J = 3.6 Hz), 4.48 (d, 1H, J = 14.8 Hz), 4.17 (m, 2H), 3.93 (m, 1H), 3.88 (m, 1H), 3.85 (m, 2H), 3.55 (m, 4H), 2.08 (m, 1H), 2.00 (dt, 1H, J = 6.4, 1.6 Hz), 1.84 (m, 1H), 1.73 (m,1H), 1.65−1.51 (m, 4H), 1.30 (t, 3H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.98, 168.95, 165.3, 143.40, 143.35, 141.55, 141.49, 98.86, 98.82, 71.66, 71.63, 69.7, 67.5, 66.46, 66.43, 62.1, 60.1, 53.5, 51.4, 30.5, 25.4, 19.4, 14.3.

General Procedure for the Synthesis of Alcohols: 37, 71, 72, 73, 74, and 75).



2-[2-(Bicyclo[2.2.1]hepta-2,5-dien-2-ylpropoxy)ethanol (37). To a flame-dried flask containing THP-protected alcohol **34** (1.2724 g, 4.57 mmol) in MeOH (40 mL) was added pyridinium *p*-toluenesulfonate, PPTS (126.5 mg, 0.503 mmol) at room temperature. The reaction mixture was stirred at 55 °C for 45 min. After the reaction was quenched with water (200 mL), the aqueous layer was extracted with diethyl ether (3 × 50 mL), and the combined organic layers were washed sequentially with water (50 mL) and brine (50 mL) and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (EtOAc/hexanes = 1:4) to give **37** (772.8 mg, 3.98 mmol, 87%) as a colorless oil: R_f 0.18 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3412 (br s), 3063 (m), 2964 (s), 2864 (s), 1692 (m), 1448 (s), 1358 (s), 1120 (s), 1059 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.75 (m, 2H), 6.14 (d, 1H, J = 1.5 Hz), 3.71 (m, 2H), 3.50−3.53 (m, 3H), 3.44 (t, 2H, J = 6.6 Hz), 3.28 (s, 1H), 2.26 (m, 2H), 2.06 (t, 1H, J = 5.8 Hz), 1.97 (d_{AB}m, 1H, J = 5.8 Hz), 1.94 (d_{AB}m, 1H, J = 5.8 Hz), 1.72 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.1, 143.8, 142.3, 133.7, 73.5, 71.7, 70.8, 61.8, 53.4, 50.0, 27.9, 27.2. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.41; H, 9.30.

(3-Methylbicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxy)-ethanol (71). Following the above general procedure using THP-protected alcohol **66** (1.4315 g, 5.42 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 15:85) to give **71** (595.4 mg, 3.30 mmol, 61%) as a colorless oil: R_f 0.15 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3399 (br s), 3061 (m), 2936 (s), 2867 (s), 1718 (s), 1454, (m), 1353 (m), 1269 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.79 (dd, 1H, J = 4.8, 2.8 Hz), 6.74 (dd, 1H, J = 4.8, 2.8 Hz), 4.14 (d, 1H, J = 12.0 Hz), 4.00 (d, 1H, J = 12.0 Hz), 3.69 (t, 2H, J = 4.6 Hz), 3.48 (s, 1H), 3.42 (dt, 1H, J = 10.2, 4.6 Hz), 3.35 (dt, 1H, J = 10.2, 4.6 Hz), 3.27 (s, 1H), 2.25 (br s, 1H), 1.95 (dt, 1H, J = 6.0, 1.6 Hz), 1.88 (d, 1H, J = 6.0 Hz), 1.78 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.0, 143.1, 142.4, 141.5, 71.2, 70.4, 66.5, 61.8, 55.7, 52.0, 14.4; HRMS calcd for $C_{11}H_{16}O_2$ m/z 180.1150, found m/z 180.1140.

(3-Phenylbicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxy)-ethanol (72). Following the above general procedure using THP-protected alcohol **67** (0.4915 g, 1.51 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 15:85) to give **72** (193.4 mg, 0.798 mmol, 53%) as a colorless oil: R_f 0.18 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3419 (br s), 3060 (m), 2975 (s), 2936 (s), 2866 (s), 1725 (w), 1598 (m), 1352 (m), 1296 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35 (m, 2H), 7.24 (m, 3H), 6.94 (dd, 1H, J = 5.0, 3.0 Hz), 6.89 (dd, 1H, J = 5.0, 3.4 Hz), 4.37 (d, 1H, J = 12.2 Hz), 4.23 (d, 1H, J = 12.2 Hz), 3.79 (m, 1H), 3.74 (m, 1H), 3.67 (t, 2H, J = 4.6 Hz), 3.40 (m, 2H), 2.55 (br s, 1H), 2.18 (dt, 1H, J = 6.0, 1.6 Hz), 2.03 (dt, 1H, J = 6.4, 1.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.2, 146.3, 142.7, 141.8, 136.4, 128.2, 126.7, 126.2, 71.0, 70.9, 67.3, 61.6, 55.4, 53.4; HRMS calcd for $C_{16}H_{18}O_2$ m/z 242.1307, found m/z 242.1304.

(3-Chlorobicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxy)-ethanol (73). Following the above general procedure using THP-protected alcohol **68** (0.3247 g, 1.14 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 15:85) to give **73** (185.3 mg, 0.923 mmol, 81%) as a

colorless oil: R_f 0.24 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3424 (br s), 2940 (s), 2870 (s), 1635 (w), 1454 (w), 1299 (m), 1107 (s), 1062 (s), 912 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.84 (m, 2H), 4.21 (d, 1H, J = 12.8 Hz), 4.05 (d, 1H, J = 12.8 Hz), 3.70 (t, 2H, J = 4.8 Hz), 3.62 (m, 1H), 3.44 (m, 1H), 3.42 (dt, 2H, J = 9.2, 4.8 Hz), 2.23 (dt, 1H, J = 6.2, 1.6 Hz), 2.08 (dt, 1H, J = 6.2, 1.6 Hz), 2.05 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.6, 143.4, 142.7, 141.2, 71.6, 70.8, 65.5, 61.8, 56.9, 51.8. Anal. Calcd for $C_{10}H_{13}O_2Cl$: C, 59.86; H, 6.53. Found: C, 60.17; H, 6.40.

(3-Bromobicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxy)ethanol (74). Following the above general procedure using THP-protected alcohol **69** (0.9562 g, 2.90 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 15:85) to give **74** (602.6 mg, 2.46 mmol, 85%) as a colorless oil: R_f 0.15 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3419 (br s), 3068 (w), 2973 (s), 2939 (s), 2868 (s), 1629 (m), 1558 (m), 1449 (m), 1351 (s), 1298 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.82 (m, 2H), 4.19 (d, 1H, J = 12.6 Hz), 4.02 (dd, 1H, J = 12.6, 1.2 Hz), 3.70 (t, 2H, J = 4.1 Hz), 3.63 (s, 1H), 3.54 (s, 1H), 3.45 (dt, 1H, J = 10.4, 4.8 Hz), 3.37 (dt, 1H, J = 10.4, 4.8 Hz), 2.23 (d, 1H, J = 6.2 Hz), 2.16 (br s, 1H), 2.07 (d, 1H J = 6.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.4, 142.3, 141.3, 134.5, 71.9, 70.9, 66.9, 61.7, 58.5, 52.3; HRMS calcd for $C_{10}H_{13}O_2Br$ m/z 244.0099, found m/z 243.9950.

(3-Ethoxycarbonylbicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxy)ethanol (75). Following the above general procedure using THP-protected alcohol **70** (0.5669 g, 1.76 mmol) and using EtOH instead of MeOH, the crude product was purified by column chromatography (EtOAc/hexanes = 15:85) to give **75** (288.7 mg, 1.21 mmol, 69%) as a colorless oil: R_f 0.17 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3458 (br s), 3070 (w), 2979 (s), 2939 (s), 2872 (s), 1699 (vs), 1627 (s), 1449 (m), 1239 (s), 1101 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.88 (dd, 1H, J = 4.8, 3.2 Hz), 6.77 (dd, 1H, J = 4.8, 3.2 Hz), 4.68 (d, 1H, J = 14.4 Hz), 4.48 (d, 1H, J = 14.4 Hz), 4.17 (m, 2H), 3.93 (m, 1H), 3.82 (m, 1H), 3.74 (m, 2H), 3.52 (dt, 1H, J = 10.4, 4.4 Hz), 3.46 (dt, 1H, J = 10.4, 4.6 Hz), 2.11 (br s, 1H), 2.09 (dt, 1H, J = 6.6, 1.6 Hz), 2.01 (dt, 1H J = 6.6, 1.6 Hz), 1.29 (t, 3H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.1, 165.2, 143.4, 141.9, 141.4, 71.8, 71.5, 67.3, 61.8, 60.1, 53.6, 51.4, 14.3.

General Procedure for Swern Oxidations (Synthesis of Aldehydes 28, 38−40, 44, and 76−80).

5-(2-Bicyclo[2.2.1]hepta-2,5-dien-2-yl)pentan-1-al (28). Dimethyl sulfoxide (DMSO, 1.4 mL, 19.7 mmol) was added to a flame-dried flask containing oxalyl chloride (0.9 mL, 10.3 mmol) and dichloromethane (15 mL) at −78 °C (dry ice/acetone bath). Five minutes after the addition, alcohol **26** (1.546 g, 8.672 mmol) in dichloromethane (8 mL) was added slowly to the reaction mixture via a cannula. The reaction mixture was stirred at −78 °C for 30 min. Freshly distilled triethylamine (5.6 mL, 40.2 mmol) was added to the reaction mixture at −78 °C. The reaction was stirred at −78 °C for 15 min and at room temperature for 1.5 h. After the reaction mixture was quenched with saturated NH_4Cl (20 mL), the aqueous layer was extracted with diethyl ether (3 × 30 mL), and the combined organic layers were washed sequentially with water (100 mL) and brine (100 mL) and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the crude product was purified by bulb-to-bulb distillation (0.5 mmHg, 110 °C) to give **28** (1.0782 mg, 6.12 mmol, 71%) as a colorless viscous oil: R_f 0.69 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3064 (m), 2967 (s), 2932 (s), 2863 (s), 2830 (m), 2718 (m), 1725 (s), 1555 (m), 1622 (w), 1300 (s), 695 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.73 (t, 1H, J = 1.8 Hz), 6.73 (m, 2H), 6.11 (d, 1H, J = 1.6 Hz), 3.47 (br s, 1H), 3.25 (br s, 1H), 2.40 (td, 2H, J = 7.3, 1.8 Hz), 2.19 (m, 2H), 1.95 (dt, 1H, J = 5.7, 1.5 Hz), 1.92 (dt, 1H, J = 5.7, 1.6 Hz), 1.59 (p, 2H, J = 7.3 Hz), 1.44 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 202.6, 158.0, 143.7, 142.2, 133.7, 73.4, 53.3, 49.9, 43.6, 31.0, 26.5, 21.6. Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.56; H, 9.43.

2-Bicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxyacetaldehyde (38). Following the above general procedure using alcohol **35**[1b] (1.6164 g, 9.72 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **38** (1.3868 g, 8.45 mmol, 87%) as a colorless viscous oil: R_f 0.50 (EtOAc/hexanes = 3:7); IR (neat, NaCl) 3065 (s), 2979 (s), 2935 (s), 2867 (s), 1736 (s), 1628 (m), 1555 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.69 (s, 1H), 6.78 (dd, 1H, J = 5.2, 3.0 Hz), 6.73 (dd, 1H, J = 5.2, 3.0 Hz), 6.53 (m, 1H), 4.25 (d_{AB}, 1H, J = 12.8 Hz), 4.17 (d_{AB}, 1H, J = 12.8 Hz), 3.95 (s, 2H), 3.56 (br s, 1H), 3.48 (br s, 1H), 2.02 (d_{AB}, 1H, J = 6.0 Hz), 1.99 (d_{AB}, 1H, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 200.8, 153.5, 143.3, 142.5, 140.6, 74.7, 73.8, 69.9, 51.2, 50.2; HRMS calcd for $C_{10}H_{12}O_2$ m/z 164.0837, found m/z 164.0850.

2-Bicyclo[2.2.1]hepta-2,5-dien-2-ylethoxyacetaldehyde (39). Following the above general procedure using alcohol **36**[1b] (753.6 mg, 4.18 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **39** (316.6 mg, 1.78 mmol, 43%) as a colorless viscous oil: R_f 0.62 (EtOAc/hexanes = 2:3); IR (neat, NaCl) 3117 (m), 3063 (s), 2967 (s), 2866 (s), 1731 (s), 1694 (s), 1555 (m), 1306 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.72 (s, 1H), 6.75 (m, 2H), 6.25 (d, 1H, J = 1.5 Hz), 4.06 (s, 2H), 3.62 (t, 2H, J = 6.9 Hz), 3.51 (m, 1H), 3.34 (m, 1H), 2.52 (m, 2H), 1.99 (dt, 1H, J = 5.8, 1.5 Hz), 1.95 (dt, 1H, J = 5.8, 1.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.0, 154.7, 143.9, 142.3, 135.6, 76.2, 73.7, 70.3, 53.5, 50.2, 31.6; HRMS calcd for $C_{11}H_{14}O_2$ m/z 178.0994, found m/z 178.0988.

2-Bicyclo[2.2.1]hepta-2,5-dien-2-ylpropoxyacetaldehyde (40). Following the above general procedure using alcohol **37** (550.3 mg, 2.83 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 1:4) to give **40** (301.2 mg, 1.57 mmol, 56%) as a colorless viscous oil: R_f 0.39 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3062 (m), 2969 (s), 2866 (s), 1724 (s), 1642 (w), 1622 (w), 1447 (m), 1325 (m), 912 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.72 (s, 1H), 6.75 (m, 2H), 6.15 (d, 1H, J = 1.1 Hz), 4.05 (s, 2H), 3.53 (br s, 1H), 3.49 (t, 2H, J = 6.6 Hz), 3.28 (br s, 1H), 2.28 (m, 2H), 1.98 (dm, 1H, J = 5.7 Hz), 1.95 (dm, 1H, J = 5.7 Hz), 1.77 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.1, 143.8, 142.3, 134.4, 133.9, 76.3, 73.5, 71.6, 53.5, 50.1, 27.8, 27.1; HRMS calcd for $C_{12}H_{16}O_2$ m/z 192.1150, found m/z 192.1166.

3-(2-Bicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxy)propanal (44). Following the above general procedure using alcohol **43** (510.3 mg, 2.83 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 1:9) to give **44** (385 mg, 2.16 mmol, 76%) as a colorless viscous oil: R_f 0.44 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3064 (w), 2961 (s), 2933 (s), 2870 (s), 1725 (s), 1641 (m), 1354 (m), 913 (m), 731 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.77 (t, 1H, J = 1.9 Hz), 6.78 (dd, 1H, J = 4.8, 3.1 Hz), 6.73 (dd, 1H, J = 4.8, 3.1 Hz), 6.46 (d, 1H, J = 1.4 Hz), 4.14 (d_{AB}d, 1H, J = 12.9, 1.2 Hz), 4.08 (d_{AB}d, 1H, J = 12.9, 1.5 Hz), 3.67 (m, 2H), 3.55 (br s, 1H), 3.43 (br s, 1H), 2.64 (td, 2H, J = 6.0, 1.9 Hz), 2.02 (dt, 1H, J = 6.0, 1.4 Hz), 1.98 (dm, 1H, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.3, 154.5, 143.3, 142.5, 138.9, 73.7, 69.6, 63.4, 51.2, 50.2, 43.8; HRMS calcd for $C_{11}H_{14}O_2$ m/z 178.0994, found m/z 178.0989.

(3-Methylbicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxy)acetaldehyde (76). Following the above general procedure using alcohol **71** (205.3 mg, 1.14 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **76** (122.4 mg, 0.687 mmol, 60%) as a colorless viscous oil**,** R_f 0.32 (EtOAc/hexanes = 1:4). Spectral data indicated a mixture of the aldehyde with its glycolate (hydrated aldehyde), which was used in the next step without further purification and characterization.

(3-Phenylbicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxy)acetaldehyde (77). Following the above general procedure using alcohol **72** (96.3 mg, 0.397 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **77** (58.1 mg, 0.242 mmol, 61%) as a colorless viscous oil**,** R_f 0.34 (EtOAc/hexanes = 1:4). Spectral data indicated a mixture of the aldehyde with its glycolate (hydrated aldehyde), which was used in the next step without further purification and characterization.

(3-Chlorobicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxy)acetaldehyde (78). Following the above general procedure using alcohol **73** (96.5 mg, 0.481 mmol), the crude product was

purified by column chromatography (EtOAc/hexanes = 5:95) to give **78** (73.0 mg, 0.367 mmol, 76%) as a colorless viscous oil, R_f 0.32 (EtOAc/hexanes = 1:4). Spectral data indicated a mixture of the aldehyde with its glycolate (hydrated aldehyde), which was used in the next step without further purification and characterization.

(3-Bromobicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxy)acetaldehyde (79). Following the above general procedure using alcohol **74** (169.5 mg, 0.692 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **79** (92.4 mg, 0.380 mmol, 55%) as a colorless viscous oil, R_f 0.38 (EtOAc/hexanes = 1:4). Spectral data indicated a mixture of the aldehyde with its glycolate (hydrated aldehyde), which was used in the next step without further purification and characterization.

(3-Ethoxycarbonylbicyclo[2.2.1]hepta-2,5-dien-2-ylmethoxy)acetaldehyde (80). Following the above general procedure using alcohol **75** (130.1 mg, 0.546 mmol). The crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give **80** (93.0 mg, 0.394 mmol, 72%) as a colorless viscous oil, R_f 0.20 (EtOAc/hexanes = 1:4). Spectral data indicated a mixture of the aldehyde with its glycolate (hydrated aldehyde), which was used in the next step without further purification and characterization.

General Procedure for in Situ Formation of Nitrones from the Corresponding Aldehydes and Subsequent Intramolecular 1,3-Dipolar Cycloadditions (Synthesis of Cycloadducts 49, 50, 51, 52, 53, 54, 55, 81, 82, 83, 84, and 85).

(3a*R,5a*R**,6*R**,9*S**,9a*R**)-2,3,3a,4,5a,6-Hexahydro-4-methyl-6,9-methano-1*H*,9*H*-benzo[*d*]cyclopent[*c*]isoxazole (Cycloadduct 49).** Aldehyde **27**[1b] (101 mg, 0.624 mmol) in toluene (10 mL) was added to a flame-dried flask containing 4 Å molecular sieves (15 mg). Pyridine (0.2 mL, 2.50 mmol) followed by *N*-methylhydroxylamine (103 mg, 1.25 mmol) was added to the reaction mixture at room temperature. The reaction mixture was stirred at room temperature for 15 h, and TLC indicated the disappearance of the aldehyde **27**. The reaction mixture was stirred at 90 °C for 69 h. The solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (EtOAc/hexanes = 1:4) to give cycloadduct **49** (60.8 mg, 0.318 mmol, 51%) as a colorless viscous oil: R_f 0.43 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3063 (w), 2954 (s), 2857 (s), 1440 (m), 1328 (s), 1136 (w), 1046 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.24 (dd, 1H, J = 5.7, 3.0 Hz), 6.00 (dd, 1H, J = 5.7, 3.2 Hz), 3.72 (s, 1H), 2.76 (br s, 1H), 2.61 (s, 3H), 2.55 (d, 1H, J = 4.6 Hz), 2.45 (br s, 1H), 1.99 (d, 1H, J = 8.8 Hz), 1.82 (m, 1H), 1.44−1.60 (m, 5H), 1.27 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.3, 134.3, 91.1, 78.8, 69.4, 48.7, 46.5, 46.3, 43.8, 36.5, 30.6, 25.0; HRMS calcd for $C_{12}H_{17}NO$ *m*/*z* 191.1310, found *m*/*z* 191.1309.

(1*S,4*R**,4a*R**,6a*R**,10a*R**)-4,4a,6,6a,7,8,9,10-octahydro-6-methyl-1,4-methano-1*H*-dibenz[*c*,*d*]isoxazole (Cycloadduct 50).** Following the above general procedure using aldehyde **28** (217.8 mg, 1.21 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 5:95) to give cycloadduct **50** (46.2 mg, 0.225 mmol, 19%) as a colorless viscous oil: R_f 0.32 (EtOAc/hexanes = 1:4); IR (neat, NaCl) 3061 (m), 2938 (s), 2863 (s), 2771 (m), 1456 (s), 1432 (s), 1326 (s), 1034 (s), 716 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.28 (dd, 1H, J = 5.6, 3.0 Hz), 6.02 (dd, 1H, J = 5.6, 3.2 Hz), 3.56 (s, 1H), 2.75 (s, 1H), 2.67 (s, 3H), 2.50 (s, 1H), 2.32 (t, 1H, J = 5.4 Hz), 2.13 (d, 1H, J = 9.1 Hz), 1.65−1.33 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.9, 133.2, 88.9, 71.4, 59.4, 46.3, 45.7, 45.3, 43.5, 29.3, 23.7, 19.9, 18.5. Anal. Calcd for $C_{13}H_{19}NO$: C, 76.06; H, 9.33. Found: C, 75.71; H, 9.37.

(3a*S,5a*R**,6*R**,9*S**,9a*R**)-3a,4,5a,6-Tetrahydro-4-methyl-6,9-methano-1*H*,3*H*,9*H*-furo[3,4-c][1,2]benzisoxazole (Cycloadduct 51).** Following the above general procedure using aldehyde **38** (132.3 mg, 0.806 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 1:1) to give cycloadduct **51** (110.8 mg, 0.573 mmol, 71%) as a colorless viscous oil: R_f 0.24 (EtOAc = 100%); IR (neat, NaCl) 3068 (m), 2968 (s), 2851 (s), 2781 (m), 1471 (m), 1460 (m), 1329 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.26 (dd, 1H, J = 5.7, 2.9 Hz), 6.11 (dd, 1H, J = 5.7, 3.3 Hz), 4.01 (s, 1H), 3.83 (d, 1H, J = 10.0 Hz), 3.81 (d, 1H, J = 9.4 Hz), 3.62 (dd, 1H, J = 10.0, 3.4 Hz), 3.35 (d, 1H, J = 9.4 Hz), 2.88 (s, 1H), 2.80 (s, 1H), 2.71 (s, 3H), 2.68 (s, 1H), 2.08 (d, 1H, J = 9.0 Hz), 1.67 (dd, 1H, J = 9.0, 1.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.9, 135.9, 91.1, 78.4, 76.7, 71.3, 70.7, 46.53, 46.50, 46.35, 44.0. Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82. Found: C, 68.52; H, 7.83.

(4a*S,6a*R**,7*R**,10*S**,10a*R**)-1,2,4a,5,6a,7-Hexahydro-5-methyl-7,10-methano-4*H*,10*H*-pyrano[3,4-*c*][1,2]benz-isoxazole (Cycloadduct 52).** Following the above general procedure using aldehyde **39** (97.4 mg, 0.545 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 1:3) to give cycloadduct **52** (68.1 mg, 0.329 mmol, 60%) as a colorless viscous oil: R_f 0.17 (EtOAc/hexanes = 2:3); IR (neat, NaCl) 3091 (m), 2955 (s), 2848 (s), 2772 (m), 1434 (s), 1338 (s), 1136 (s), 1064 (s), 1040 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.28 (dd, 1H, J = 5.7, 3.0 Hz), 6.05 (dd, 1H, J = 5.7, 3.3 Hz), 3.86 (dt, 1H, J = 10.9, 4.6 Hz), 3.77 (d_{AB}d, 1H, J = 13.0, 1.9 Hz), 3.67 (d_{AB}d, 1H, J = 13.0, 4.0 Hz), 3.61 (s, 1H), 3.42 (td, 1H, J = 11.2, 3.0 Hz), 2.76 (s, 1H), 2.67 (s, 3H), 2.68 (s, 1H), 2.23 (s, 1H), 2.12 (d, 1H, J = 9.2 Hz), 1.96 (m, 1H), 1.70 (dd, 1H, J = 9.2, 1.4 Hz), 1.46 (dt, 1H, J = 14.5, 3.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.2, 133.9, 89.5, 70.7, 64.1, 63.6, 57.0, 45.7, 45.4, 45.1, 43.5, 31.6; HRMS calcd for $C_{12}H_{17}NO_2$ *m*/*z* 207.1259, found *m*/*z* 207.1260.

(4a*R,6a*R**,7*R**,10*S**,10a*R**)-3,4,4a,5,6a,7-Hexahydro-5-methyl-7,10-methano-1*H*,10*H*-pyrano[4,3-*c*][1,2]-benzisoxazole (Cycloadduct 53).** Following the above general procedure using aldehyde **44** (71.4 mg, 0.401 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 2:3) to give cycloadduct **53** (39.0 mg, 0.188 mmol, 47%) as a colorless viscous oil: R_f 0.32 (EtOAc); IR (neat, NaCl) 3063 (w), 2961 (s), 2861 (s), 2774 (w), 1459 (m), 1430 (m), 1110 (s), 954 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.36 (dd, 1H, J = 5.7, 3.0 Hz), 6.04 (dd, 1H, J = 5.7, 3.3 Hz), 3.73 (ddd, 1H, J = 11.0, 5.9, 2.7 Hz), 3.59 (d_{AB}, 1H, J = 12.1 Hz), 3.54 (d_{AB}, 1H, J = 12.1 Hz), 3.52 (dd, 1H, J = 11.3, 3.5 Hz), 3.48 (s, 1H), 2.76 (br s, 1H), 2.72 (br s, 1H), 2.68 (s, 3H), 2.47 (m, 1H), 2.17 (d, 1H, J = 9.2 Hz), 1.71 (d, 1H, J = 9.2 Hz), 1.97 (m, 1H), 1.61 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.6, 134.1, 86.8, 70.8, 68.0, 62.9, 58.9, 45.7, 45.4, 44.5, 43.3, 24.5. Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27. Found: C, 69.82; H, 8.31.

Cycloadduct 54. Following the above general procedure using aldehyde **40** (75.9 mg, 0.395 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 2:3) to give cycloadducts **54** (45.6 mg, 0.206 mmol, 52%, as a mixture of two major and one minor isomers) as a colorless viscous oil: R_f 0.09 (EtOAc/hexanes = 2:3); IR (neat, NaCl) 3059 (w), 2951 (s), 2845 (s), 2774 (w), 1434 (m), 1331 (m), 1296 (m), 1262 (m), 1242 (m), 1122 (m), 886 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.25 (dd, 1H, J = 5.6, 2.8 Hz), 6.21 (dd, 1H, J = 5.6, 2.8 Hz), 6.08 (dd, 1H, J = 5.4, 3.0 Hz), 5.97 (dd, 1H, J = 5.4, 3.1 Hz), 3.98 (m, 2H), 3.86 (m, 2H), 3.60 (m, 2H), 3.30 (m, 2H), 2.95 (s, 1H), 2.88 (s, 1H), 2.83 (s, 3H), 2.80 (s, 3H), 2.76 (s, 2H), 2.71 (s, 2H), 2.13 (m, 2H), 2.00 (m, 2H), 1.80−1.94 (m, 3H), 1.53−1.63 (m, 3H), 1.46 (m, 2H), 1.27 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.3, 140.6, 133.3, 133.2, 66.7, 66.4, 65.4, 52.4, 48.5, 48.4, 48.0, 47.8, 46.3, 46.1, 45.6, 45.2, 41.5, 40.3, 35.5, 25.4, 24.6; HRMS calcd for $C_{13}H_{19}NO_2$ *m*/*z* 221.1416, found *m*/*z* 221.1420.

(3a*R,5a*S**,6*S**,9*R**,9a*S**)-3a,4,5a,6-Tetrahydro-4-methyl-6,9-methano-1*H*,3*H*,9*H*-furo[3,4-*c*][1,2]benzisoxazol-3-one (Cycloadduct 55).** Following the above general procedure using aldehyde **48** (93.5 mg, 0.477 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 15:85) to give cycloadduct **55** (42.0 mg, 0.203 mmol, 43%) as white solids. Recrystallization from 20% EtOAc/hexanes provided crystals suitable for X-ray analysis:[12] R_f 0.49 (EtOAc/hexanes = 2:3); IR (neat, NaCl) 3077 (w), 2971 (m), 2913 (m), 2877 (w), 2852 (w), 1774 (s), 1382 (w), 1328 (w), 1205 (w), 1179 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.35 (dd, 1H, J = 5.6, 2.9 Hz), 6.21 (dd, 1H, J = 5.6, 3.3 Hz), 4.37 (d, 1H, J = 9.8 Hz), 4.10 (s, 1H), 3.99 (d, 1H, J = 9.8 Hz), 3.03 (s, 1H), 2.89 (s, 2H), 2.85 (s, 3H), 2.10 (m, 1H), 1.80 (m, 1H); ^{13}C NMR ($CDCl_3$, 100

MHz) δ 172.3, 137.11, 137.08, 92.4, 74.7, 45.9, 45.8, 44.4. Anal. Calcd for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.32. Found: C, 63.82; H, 6.30.

(3a*S,5a*R**,6*R**,9*S**,9a*R**)-3a,4,6-Trihydro-4,5a-dimethyl-6,9-methano-1*H*,3*H*,9*H*-furo[3,4-*c*][1,2]benzisoxazole (Cycloadduct 81).** Following the above general procedure using aldehyde **76** (60.2 mg, 0.338 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 1:3) to give cycloadduct **81** (37.3 mg, 0.180 mmol, 53%) as a clear, light brown oil: R_f 0.28 (EtOAc/hexanes = 2:3); IR (neat, NaCl) 3062 (w), 2965 (s), 2865 (s), 2776 (w), 1454 (s), 1364, (m), 1325 (m), 1160 (m), 1081 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.17 (m, 2H), 3.84 (d, 1H, J = 10.0 Hz), 3.69 (d, 1H, J = 10.0 Hz), 3.56 (dd, 1H, J = 10.0, 3.4 Hz), 3.21 (d, 1H, J = 10.0 Hz), 2.89 (d, 1H, J = 3.4 Hz), 2.71 (s, 1H), 2.69 (s, 1H), 2.68 (s, 3H), 2.20 (d, 1H, J = 8.8 Hz), 1.57 (dm, 1H, J = 8.8 Hz), 1.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.3, 136.0, 93.2, 79.5, 73.2, 72.2, 71.1, 51.2, 48.8, 46.4, 44.0, 19.9. Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27. Found: C, 69.53; H, 8.06.

(3a*S,5a*R**,6*R**,9*S**,9a*R**)-3a,4,6-Trihydro-4-methyl-5a-phenyl-6,9-methano-1*H*,3*H*,9*H*-furo[3,4-*c*][1,2]-benzisoxazole (Cycloadduct 82).** Following the above general procedure using aldehyde **77** (45.6 mg, 0.190 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 1:3) to give cycloadduct **82** (20.8 mg, 0.0772 mmol, 41%) as a clear, light brown oil: R_f 0.58 (EtOAc/hexanes = 2:3); IR (neat, NaCl) 3059 (w), 2959 (s), 2869 (s), 2847 (s), 2778 (w), 1498 (m), 1446 (m), 1241 (m), 912 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67 (m, 2H), 7.32 (m, 2H), 7.25 (m, 1H), 6.34 (dd, 1H, J = 5.6, 3.2 Hz), 6.24 (dd, 1H, J = 5.6, 3.2 Hz), 3.95 (d, 1H, J = 10.0 Hz), 3.72 (dd, 1H, J = 9.6, 4.0 Hz), 3.70 (d, 1H, J = 10.0 Hz), 3.28 (d, 1H, J = 9.6 Hz), 3.25 (m, 1H), 3.08 (d, 1H, J = 4.0 Hz), 2.88 (m, 1H), 2.76 (s, 3H), 2.41 (dm, 1H, J = 8.8 Hz), 1.76 (dt, 1H, J = 8.8, 1.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.3, 138.1, 135.9, 128.0, 127.9, 127.1, 97.1, 80.2, 75.7, 73.6, 71.0, 50.8, 49.3, 46.9, 44.1. Anal. Calcd for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11. Found: C, 76.02; H, 7.01.

(3a*S,5a*R**,6*R**,9*S**,9a*R**)-3a,4,6-Trihydro-5a-chloro-4-methyl-6,9-methano-1*H*,3*H*,9*H*-furo[3,4-*c*][1,2]-benzisoxazole (Cycloadduct 83).** Following the above general procedure using aldehyde **78** (73.0 mg, 0.367 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 1:3) to give cycloadduct **83** (38.7 mg, 0.170 mmol, 46%) as a clear, light brown oil: R_f 0.24 (EtOAc/hexanes = 2:3); IR (neat, NaCl) 3073 (w), 2988 (s), 2962 (s), 2878 (s), 2850 (s), 2782, (w), 1467 (m), 1325 (m), 1141 (m), 1098 (m), 1061 (s), 912 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.27 (dd, 1H, J = 6.0, 3.2 Hz), 6.22 (dd, 1H, J = 6.0, 3.2 Hz), 4.12 (d, 1H, J = 10.0 Hz), 3.96 (d, 1H, J = 10.0 Hz), 3.63 (dd, 1H, J = 10.0, 3.2 Hz), 3.35 (d, 1H, J = 10.0 Hz), 3.25 (m, 1H), 3.08 (d, 1H, J = 3.2 Hz), 2.82 (m, 1H), 2.80 (s, 3H), 2.07 (dm, 1H, J = 9.2 Hz), 1.77 (dt, 1H, J = 9.2, 1.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.0, 136.1, 117.8, 79.5, 76.2, 74.9, 70.9, 53.7, 47.6, 46.3, 44.1; HRMS calcd for $C_{11}H_{14}NClO_2$ m/z 227.0713, found m/z 227.0710.

(3a*S,5a*R**,6*R**,9*S**,9a*R**)-3a,4,6-Trihydro-5a-bromo-4-methyl-6,9-methano-1*H*,3*H*,9*H*-furo[3,4-*c*][1,2]-benzisoxazole (Cycloadduct 84).** Following the above general procedure using aldehyde **79** (68.8 mg, 0.283 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 1:3) to give cycloadduct **84** (11.5 mg, 0.0423 mmol, 15%) as a clear, light brown oil that was found to be a mixture of two isomers in a ratio of 60:40: R_f 0.23 (EtOAc/hexanes = 2:3); IR (neat, NaCl) 3073 (m), 2986 (s), 2961 (s), 2876 (s), 2853 (s), 2784, (w), 1467 (m), 1325 (m), 1061 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.24 (m, 2H), 4.28 (d, 0.6H, J = 10.0 Hz), 4.22 (d, 0.4H, J = 10.0 Hz), 4.01 (d, 0.6H, J = 10.4 Hz), 3.98 (d, 0.4H, J = 10.4 Hz), 3.64 (dt, 1H, J = 10.4, 3.4 Hz), 3.44 (d, 0.6H, J = 10.0 Hz), 3.41 (m, 0.6H), 3.37 (d, 0.4H, J = 10.0 Hz), 3.26 (m, 0.4H), 3.12 (d, 0.6H, J = 3.4 Hz), 3.09 (d, 0.4H, J = 3.4 Hz), 2.83 (s, 1.8H), 2.82 (s, 1.2H), 2.78 (m, 1H), 2.08 (d, 1H, J = 9.6 Hz), 1.78 (d, 1H, J = 9.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.8, 137.1, 136.2, 136.0, 79.8, 79.5, 77.2, 74.9, 71.0, 55.2, 53.7, 47.7, 47.1, 46.4, 46.3, 44.2, 44.1; HRMS calcd for $C_{11}H_{14}NBrO_2$ m/z 271.0208, found m/z 271.0200.

(3a*S,5a*R**,6*R**,9*S**,9a*R**)-3a,4,6-Trihydro-5a-ethoxycarbonyl-4-methyl-6,9-methano-1*H*,3*H*,9*H*-furo[3,4-*c*]-[1,2]benzisoxazole (Cycloadduct 85).** Following the above general procedure using aldehyde **80** (93.0 mg, 0.394 mmol), the crude product was purified by column chromatography (EtOAc/hexanes = 1:3) to give cycloadduct **85** (61.1 mg, 0.230 mmol, 57%) as a clear, light brown oil: R_f 0.15 (EtOAc/hexanes = 2:3); IR (neat, NaCl) 3068 (w), 2981 (s), 2872 (s), 2872 (s), 2848 (s), 2779, (w), 1719 (vs), 1454 (m), 1264 (s), 1098 (s), 1058 (s), 915 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.20 (dd, 1H, J = 5.6, 2.8 Hz), 6.18 (dd, 1H, J = 5.6, 2.8 Hz), 4.18 (m, 2H), 4.11 (d, 1H J = 10.0 Hz), 3.84 (d, 1H, J = 10.0 Hz), 3.58 (dd, 1H, J = 10.0, 4.0 Hz), 3.21 (d, 1H, J = 10.0 Hz), 2.96 (s, 1H), 2.93 (d, 1H, J = 4.0 Hz), 2.77 (s, 1H), 2.73 (s, 3H), 2.16 (d, 1H, J = 9.2 Hz), 1.63 (d, 1H, J = 9.2 Hz), 1.24 (t, 3H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 137.0, 135.6, 94.7, 79.3, 77.1, 72.9, 70.7, 61.0, 50.0, 48.7, 46.5, 44.2, 14.1. Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22. Found: C, 63.58; H, 7.29.

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Supporting Information Available: ^{1}H and ^{13}C (APT) NMR spectra for compounds **34**, **38**, **39**, **43**−**49**, **52**, **54**, **61**−**66**, **70**−**72**, **74**, **75**, **83**, and **84**; X-ray structure of **55**; ^{1}H, ^{13}C (APT) NMR, HCOSY, HSQC, and GOESY spectra for cycloadduct **81**. This material is available free of charge via the Internet at http://pubs.acs.org.

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