was evaporated, yielding 16 g of crude $T^0_{OH}(NO_2\text{-NS})$ and 19.5 g of crude T^0_{OH}(Cl-NS). The crude products were purified by column chromatography with silica and hexane–ethyl acetate as eluent. The nitro alcohols derived from NS and Cl-NS were ≥98% pure on the basis of the proton NMR; the one derived from NO_2-NS was ≥96%. The latter has mp 65–69 °C; the others remained as pale oils.

Triethylamine and DABCO were obtained from Aldrich. The former was refluxed over CaH_2 and distilled under nitrogen while the latter was recrystallized from hexanes. The other buffers were analytical grade and were used without further purification.

Reactions Solutions and pH Measurements. The methodology was similar to the one used before.[3d,f] pH measurements were conducted in thermally equilibrated solutions (20 °C) by using an Orion 611 pH meter with a Corning No. 476022 glass electrode and a Beckman No. 39400 calomel reference electrode. The pH meter was calibrated with Hallé[18] buffers.

Kinetic Measurements. Fast reactions were monitored in a Durrum-Gibson stopped-flow apparatus, slow reactions were monitored in a Perkin-Elmer 559A spectrophotometer, and both were equipped for computerized data acquisition and analysis. In reactions where T^-_{OH} was used as starting material, T^-_{OH} was generated by placing the substrate into a 0.5 M KOH solution; this base concentration assured rapid, complete formation of T^-_{OH} before signficant conversion to products occurred. This solution was then diluted to 5×10^{-3} M KOH before it was used in pH-jump experiments.

Spectrophotometric and HPLC Product-Ratio Determinations. The ratio $[T^-_{OH}]/[CH_2NO_2^-] = [T^-_{OH}]/[ArCHO]$ (eq 18) was obtained after reacting T^0_{OH} in KOH solution by measuring the apparent extinction coefficient, ϵ_{app}, of the resulting solution at a wavelength where the extinction coefficient of T^-_{OH} ($\epsilon_{T^-_{OH}}$) and the sum of the extinction coefficients of ArCHO and $CH_2NO_2^-$ (ϵ_P) show a maximum difference (250 nm for NS, 265 nm for Cl-NS, and 268 nm for NO_2-NS). From eq 28 and 29, where x and y are the mole fractions of T^-_{OH} and products,

$$\epsilon_{app} = x\epsilon_{T^-_{OH}} + y\epsilon_P \quad (28)$$

$$x + y = 1 \quad (29)$$

respectively, $[T^-_{OH}]/[CH_2NO_2^-] = x/y$ is easily found. Since x/y was relatively small, at least for NS (0.181) and Cl-NS (0.224), and the fact that both T^-_{OH} and P absorb, the x/y ratios may be subject to relatively high experimental error. We therefore also used an HPLC method to determine these ratios, which circumvents the problem that both T^-_{OH} and P are absorbing. All experiments were done on a Hewlett-Packard 1090M chromatograph, using a Hypersil ODS 5-μm (100 × 45 mm) column and a 30% methanol–70% water mobile phase. Unfortunately, the gain in precision with the HPLC method was more than counteracted by the necessity to use higher substrate concentrations, which in basic solution leads to some condensation of $CH_2NO_2^-$ with the substrate despite precautionary measures. Nevertheless, the spectrophotometric and HPLC results were in fair agreement with each other.

In a similar way, the k_2^H/k_{-1}^H ratios were found as $[T^0_{OH}]/[S]$ after acidifying a solution of T^-_{OH}. Here the fact that only S had a significant extinction coefficient at λ_{max} of S facilitated the spectrophotometric measurements. The HPLC results were again in fair agreement with the spectrophotometric ones, but they are deemed less reliable than the latter.

Acknowledgment. This research was supported by Grant CHE-8617370 from the National Science Foundation.

Supplementary Material Available: Tables S1–S13 listing kinetic data (13 pages). Ordering information is given on any current masthead page.

Palladium-Catalyzed Trimethylenemethane Reaction To Form Methylenetetrahydrofurans. Aldehyde and Ketone Substrates and the Tin Effect[1]

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Abstract: The palladium-catalyzed trimethylenemethane (TMM) cycloaddition of carbonyl compounds has been shown to have a strong dependence upon the presence of cocatalysts such as tri-*n*-butyltin acetate, di-*n*-butyltin diacetate, or trimethyltin acetate. High-yielding annulations of aldehydes were accomplished either by using TMM precursors that contain the elements of trialkyltin acetate (which is then generated in situ) or by using silicon-based precursors and an exogenous cocatalyst. Synthetically, the latter was greatly preferable. Trimethyltin acetate was the best cocatalyst found, being effective at levels of 3–5 mol %. Under these conditions, aldehydes were cleanly converted to 2-substituted 4-methylenetetrahydrofurans in 88–99% yield. Stereogenic aldehydes have good diastereoselectivity. Polyoxygenated α-alkoxy aldehydes generated a single diastereomer in excellent yield. Although many ketones were unreactive (e.g., *tert*-butylcyclohexanone), the 5-oxacyclohexenones, 5-oxacyclohexanones, a 2-acylfuran, and an alkynyl ketone were also shown to be subject to carbonyl cycloaddition when sterically unencumbered. The starting materials for the first two types of substrates were prepared either in optically active form from commercially available glucose derivatives or as racemic mixtures by oxidation of 2-(hydroxymethyl)furans. Some generated a single diastereomer in good yields when a tin cocatalyst was present. In simple systems, the stereochemistry of the major isomer was shown by nuclear Overhauser effect difference spectroscopy to be that derived from axial attack on the carbonyl group. The enones were also subject to methylenecyclopentane formation by olefin cycloaddition. In every case these products are a single diastereomer. The mechanism of the cocatalysis by trialkyltin acetate is briefly discussed and a stannyl ether is suggested as the critical intermediate.

Five-membered oxygen heterocycles are among the most common structures in biologically active compounds. The stable form of many sugars, including many antineoplastic and antiviral agents including the AIDS drug azidothymidine (AZT),[3] is or contains a polyhydroxylated tetrahydrofuran. Nearly the entire class of compounds called ionophores,[4] because of their ion-chelating ability, include at least one tetrahydrofuran ring. Monensin,[5] for

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(2) NSF Graduate Fellow, 1985–1988.

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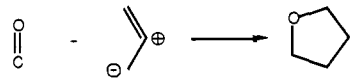
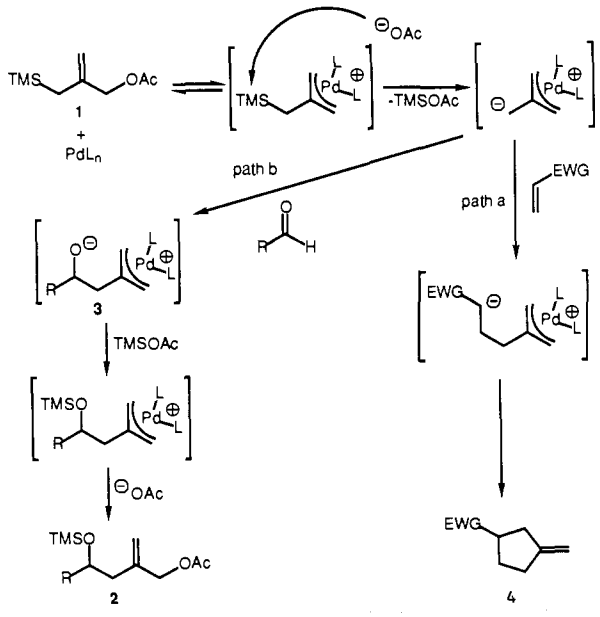


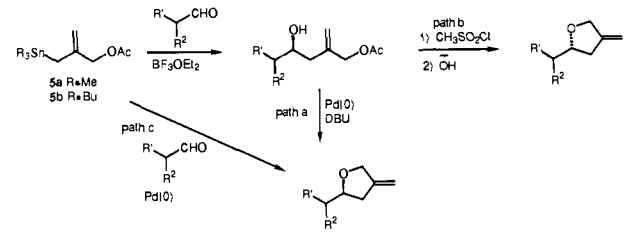
Figure 1. Tetrahydrofuran annulation.

Scheme I. Dichotomy in Pd-Catalyzed Cycloadditions to Electron-Deficient Olefins and Carbonyl Groups

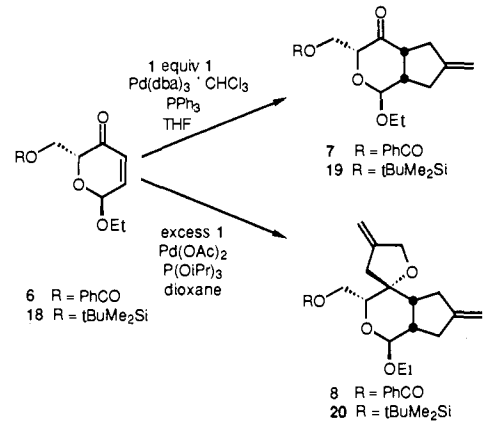


example, is a clinically active ionophore antibiotic. In addition, a variety of miscellaneous biologically active materials are based upon tetrahydrofuran skeletons. Muscarine[6] is a toxic alkaloid and prostacyclin,[7] otherwise known as PGI_2, is a powerful inhibitor of platelet aggregation and a vasodilator.[8] Such potent and diverse activity is sure to attract the interest of synthetic chemists, and a variety of methods now exist for dihydro- and tetrahydrofuran synthesis.[9] However, few of these are based upon an annulation strategy,[10] and of those that are, single-step procedures[11] are uncommon. Conceptually, an all-carbon 1,3-dipole equivalent is an attractive agent for tetrahydrofuran formation. The reaction

Scheme II. Carbonyl Cycloaddition and Its Equivalent



Scheme III. Cycloadditions of a 5-Oxacyclohexenone



of such a species with a carbonyl group could allow a one-step synthesis of five-membered oxygen heterocycles by [3 + 2] cycloaddition onto the carbon oxygen double bond[12] (Figure 1).

Nearly 10 years ago,[13] we showed that tetrakis(triphenylphosphine)palladium(0)-induced ionization of 3-acetoxy-2-[(trimethylsilyl)methyl]-1-propene (**1**) provides an intermediate that serves as the desired all-carbon 1,3-dipole. The original work showed that reactions with Michael acceptors gave products annulated by a functionalized five-membered carbocycle.[14] The originally proposed mechanism for this process, involving a palladium-bound trimethylenemethane (Pd–TMM) complex as the crucial dipolar intermediate, has withstood the test of time (Scheme I, path a).[15] Detailed stereochemical and kinetic study of this cycloaddition process has recently been completed[16] and several total syntheses have utilized the trimethylenemethane (TMM) cycloaddition as a key step.[17] A virtue of this cycloaddition is the creation of an exocyclic methylene group as a handle for further structural elaboration.

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Despite our success regarding methylenecyclopentane formation, the further goal of an effective methylenetetrahydrofuran synthesis remained elusive. Early in the game of deciphering the chemistry of the Pd–TMM complex,[18] its reactivity with aldehydes was investigated. The reaction of cinnamaldehyde is illustrative. A mixture of a palladium(0) catalyst, cinnamaldehyde, and bifunctional conjunctive reagent **1** yielded the addition product **2** in low yield. No cycloadducts derived from carbonyl or olefin addition (i.e., **4**) were detected. These products were envisioned (Scheme I, path b) to come about from the TMM intermediate by nucleophilic addition to the aldehyde and formation of the alkoxide **3**. Since alkoxides are poor nucleophiles for π-allylpalladium species,[19] closure to the tetrahydrofuran is quite slow and formation of the silyl ether by reaction with trimethylsilyl acetate thwarts the cycloaddition pathway.

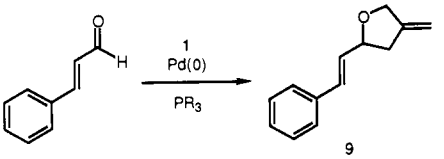
Because of these disappointing results in the area of a one-step carbonyl cycloaddition, we developed a two-step method that can be applied to the synthesis of methylenetetrahydrofurans, as illustrated in Scheme II.[20] An advantage of this strategy is the ability to partition this intermediate to either diastereomeric tetrahydrofuran. This sequence is also suitable for ketones, and under slightly modified conditions, imines are converted to pyrrolidines. To our surprise, when the tin reagents **5** were reacted with aldehydes in the presence of a Pd(0) catalyst (but no Lewis acid), methylenetetrahydrofuran cycloadducts were cleanly formed in a single step (Scheme II, path c).[21] Yield and diastereoselectivity are good and are maintained or improved in comparison with the two-step process.

Further exploration of the one-step cycloaddition of the TMM intermediate with carbonyl compounds thus became an important challenge. Of particular interest are the differing reactivities of **1** and **5**. Not only is this behavior mysterious in the context of a mechanism involving the Pd–TMM complex, but from a synthetic point of view, the apparently less effective silicon reagent is a considerably more desirable starting material. Its large-scale preparation and purification are somewhat simpler, and cost, stability,[22] and toxicity are of less concern relative to the organostannane. This paper begins to describe our work in detail, which has generated a broad understanding of the synthetic potential of the palladium(0)-catalyzed trimethylenemethane carbonyl cycloaddition process and of the divergent reactivity of **1** and **5**.[23]

Results and Discussion

Cycloadducts from the Silicon-Based TMM Precursor and Aldehydes. The unexpected observation that the glucose derivative **6** reacts with an excess of TMM precursor (4 equiv) overnight in dioxane at reflux to give a 49% yield of the bisadduct **8** (see Scheme III) initiated our investigation into carbonyl group additions. Because in our earlier work we had observed the formation of the (acyclic) addition products **2**, it seemed likely that the problems encountered in obtaining cycloadducts using **1** as the TMM precursor were not a result of the addition step. Rather, as indicated in Scheme I, difficulties probably stemmed from poor cyclization of **3**. In our two-step carbonyl cycloaddition approach,[20] it had been found that the higher temperatures of refluxing dioxane encouraged cyclization. Therefore, three representative aldehydes were subjected to the usual TMM cycloaddition conditions [**1**, tetrakis(triphenylphosphine)palladium generated in situ] in refluxing dioxane. While undecylenic aldehyde showed no evidence of yielding an identifiable product, crude reaction mixtures from naphthaldehyde and cinnamaldehyde showed clear signals for the desired cycloadduct in the crude NMR spectra. The carbonyl cycloadducts were easily discernible in the ^{1}H NMR spectra by their two sets of characteristic AB quartets for the allylic protons in the tetrahydrofuran rings, one centered around δ 4.40 [typically δ 4.46 (d, J = 13.0 Hz, 1 H), 4.32 (d, J = 13.0 Hz, 1 H)] and the other around δ 2.60 [typically δ 2.77 (dd, J = 15.4, 6.9 Hz, 1 H), 2.45 (dd, J = 15.4, 7.4 Hz, 1 H)].

Due to the ease of identifying the products by the chemical shift of the styryl protons, the cycloaddition of cinnamaldehyde to produce **9** was adopted as the model system. Numerous attempts



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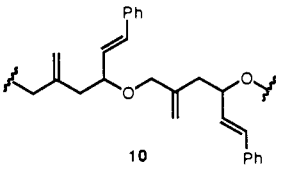
under yet more forcing conditions, such as refluxing toluene and sealed tube experiments, failed to improve results. It was found, however, that syringe pump addition of 1.5 equiv of TMM precursor allowed the reaction to go to 95% completion. Under all conditions uncyclized products such as **2** remained present, and moreover, the desired product was contaminated by what appeared to be an oligomer. Closer inspection revealed that this material is characterizable by its ^{1}H NMR spectrum, which shows greatly broadened absorptions downfield from δ 2.25 that correspond nicely to the chemical shifts of the uncyclized product **2**. It is, therefore, suggested to consist of the structural fragment shown in **10**. Obviously, the slow cyclization of **3** was allowing pro-



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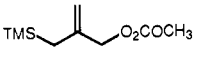
duction of products derived from intermolecular reaction. By use of the syringe pump conditions, 65% of a mixture of the desired product and the uncyclized product contaminated by ~10% of the oligomer was isolable.

Given that cyclization of **3** was slow, the only recourse for improving the yields and cleanliness of the reaction appeared to be scavenging the silyl acetate, which was leading to production of the uncyclized product. Many attempts using several fluoride sources met with failure. Use of in situ generated alkoxide as the silicon scavenger in the form of methoxide ion derived from palladium-induced ionization of carbonate **11** met with failure.



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A possible procedure was to run the reaction under the syringe pump conditions in refluxing dioxane and then attempt to desilylate and close the uncyclized product.[20] This, in fact, was a viable process. Addition of 0.25 equiv of water and 0.25 equiv of DBU to the reaction mixture followed by gentle refluxing gave respectable yields of the cycloadducts of cinnamaldehyde (entry 1, Table I) and perillaldehyde (entry 2, Table I), which were distilled in a bulb-to-bulb apparatus to remove the oligomeric products. Naphthaldehyde proved somewhat more well-behaved, and with the syringe pump conditions generated little of the uncyclized product. Table I summarizes these results. Also shown in Table I is a tertiary aldehyde, **12**. A yield of 75% of cycloadduct **13** was cleanly obtained in refluxing THF by the slow-addition technique. Evidently, the sterically hindered nature of the carbonyl group in this substrate either speeds cyclization, slows silylation of the alkoxide, or both.

During these initial experiments it was discovered that, in reactions involving aldehydes, no external reductant is necessary

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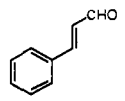
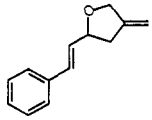
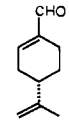
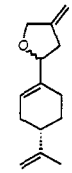
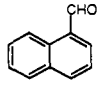
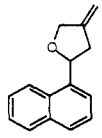
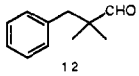
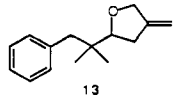
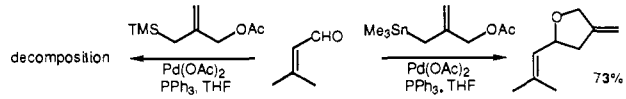
Table I. Aldehyde Adducts without the Influence of Organotin Species

entry	aldehyde	TMM adduct	isolated yield[a]
1			75%
2			71%[b]
3			88%
4	 12	 13	75%

[a] All reactions run under slow addition conditions in dioxane at reflux except entry 4, which was run in refluxing THF. [b] Diastereomeric ratio is 1:1.

Scheme IV. Example of Dependence of Cycloaddition on Precursor



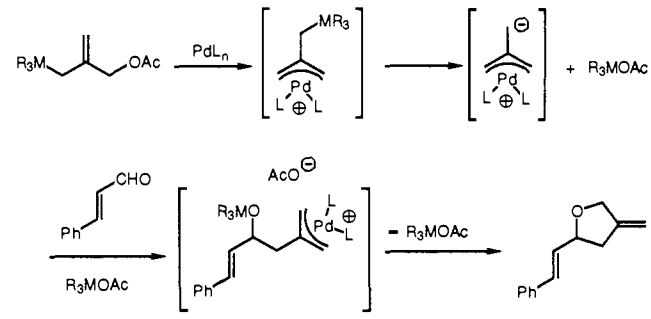
to produce an active zero-valent palladium catalyst. It seems that aldehydes are capable of the redox chemistry necessary to generate Pd(0) from palladium(II) acetate. A brief examination of this phenomenon could not provide any conclusions regarding the nature of the organic products. Nevertheless, this affords a considerable amount of convenience when using aldehydes as TMM substrates since readily available, air-stable palladium acetate can be used as a source of palladium(0) and adventitious oxidation of the catalyst is removed as a potential experimental difficulty.

Conspicuously absent from Table I is an aldehyde that possesses kinetically acidic protons. Attempted cycloaddition of saturated aldehydes uniformly gave intractable reaction mixtures with no evidence of methylenetetrahydrofuran formation. Even the unsaturated prenylaldehyde decomposed under the reaction conditions, showing no less than three aldehyde resonances in the crude proton NMR spectrum.

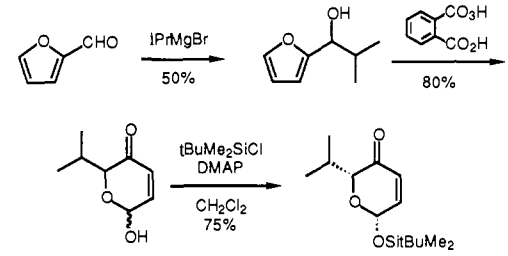
Analysis of the Tin Effect. While demonstrating the ability of the silicon-based TMM precursor **1** to undergo cycloaddition with certain aldehydes rather than simply produce addition products was a step in the right direction, the reactivity differences between **1** and the tin reagents **5** remained a puzzle. The extraordinary contrast was highlighted as illustrated (see Scheme IV) by reaction of 1.2 equiv of **5a** with prenylaldehyde, which cleanly produced 73% of the cycloadduct with no evidence of side products. Clearly these results had to be caused by the variation of the group IV metal in the TMM precursor. Scheme V follows the silicon or tin atom (M) through the presumed trimethylenemethane mechanism.

The formation of R_3MOAc free in solution suggested the following experiment. Cinnamaldehyde was reacted with **1** and 10 mol % of readily available tri-*n*-butyltin chloride in refluxing

Scheme V. A Mechanistic Proposal



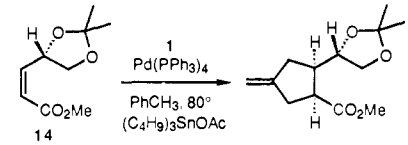
Scheme VI. Preparation of 2-[(*tert*-Butyldimethyl)siloxy]-6-isopropyloxacyclohex-3-en-5-one



THF without the use of a syringe pump. While the reaction proceeded only to ~25% completion before losing its healthy bright yellow color, the sole product formed was the desired methylenetetrahydrofuran. No addition product or oligomer was detected. Moreover, the presence of residual TMM precursor confirmed that the source of the reaction failure was decomposition of the catalyst. Believing that the trialkyltin halide was having the deliterious effects on the catalyst, commercially available tri-*n*-butyltin acetate[25,26] was next tested as an additive. *This time 1.1 equiv of TMM precursor completely converted cinnamaldehyde to its trimethylenemethane cycloadduct in 89% yield!* It was found that 10–25 mol % was best for clean results and ease of purification.

For the tin cocatalysts to impart to the silicon TMM precursors the full synthetic potential of **5**, satisfactory yields must be obtained with a variety of aldehydes. As hoped, prenylaldehyde and several others provided good to excellent yields with tri-*n*-butyltin acetate as cocatalyst in refluxing THF. Among the examples in Table II are primary, secondary, and α-alkoxy aldehydes. The last provided good to excellent diastereoselectivity.[27]

Several other types of electrophiles were briefly studied under these new conditions as well. *tert*-Butylcyclohexanone and imines[28] failed to react, and the cycloaddition of cyclohexenone was not improved. The presence of tin acetate did not affect the stereoselectivity of cis unsaturated ester **14**, which continued to conserve the cis geometry in the product.[29]



It was postulated that qualities that would make the stannane kinetically more reactive would improve its overall effectiveness

(25) Tributyltin acetate is available from Alfa Chemical Cc.

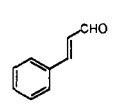
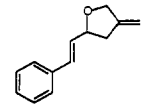
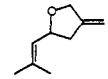
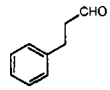
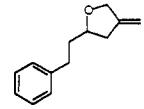
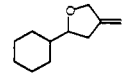
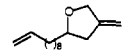
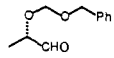
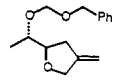
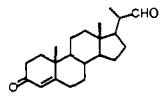
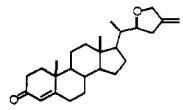
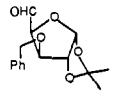
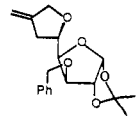
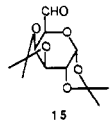
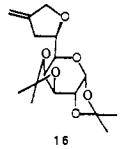
(26) For reviews of tin chemistry, see: Davies, A. G.; Smith, P. J. Tin In *Comprehensive Organometallic Chemistry*; Wilkinson, G. W., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982. Okawara, R.; Wada, M. In *Organotin Compounds*; Sawyer, A. K., Ed.; Dekker: New York, 1971; Vol. 2, p 253.

(27) The major diastereomer was identified by comparison to the products of our previously published two-step cycloaddition approach. See: Reference 20.

(28) See, however: Jones, M. D.; Kemmitt, D. W. *J. Chem. Soc., Chem. Commun.* **1986**, 1201.

(29) Trost, B. M.; Mignani, S. M. *Tetrahedron Lett.* **1986**, *27*, 4137.

Table II. Aldehyde Cycloadducts with Tin Acetate Cocatalysis

Entry	Aldehyde	TMM adduct	Isolated Yield $(nC_4H_9)_3SnOAc$	Isolated Yield $(CH_3)_3SnOAc$
1			89%	95%
2			80%	--
3			71%	99%
4			88%	88%
5			--	89%
6			74% (4:1)[b]	--
7			94% (3:1)[b]	--
8			62%	--
9	 15	 16	--	84%

[a] All reactions were run for 2–4 h in THF at reflux with $Pd(0)Ac)_2/PPh_3$ as catalyst and with 20–40 mol % Bu_3SnOAc or 5–10 mol % Me_3SnOAc as cocatalyst. [b] Syn/anti ratio.

as a cocatalyst in the cycloaddition reaction. Thus, it was believed that yet better results could be obtained with more electrophilic and/or less sterically hindered tin reagents. However, di-*n*-butyltin oxide and di-*n*-butyltin diacetate proved to be no more effective than tri-*n*-butyltin acetate, and di-*n*-butyltin bis(trifluoroacetate) rapidly destroyed the catalyst in much the same way as tri-*n*-butyltin chloride.

The increased electrophilicity of the trimethyltin moiety relative to tri-*n*-butyltin is established.[30,31] Trimethyltin acetate is most easily prepared from commercially available trimethyltin hydroxide by acid–base exchange with acetic acid in water. Azeotroping in benzene removes the water and provides the soluble form as a crystalline solid [mp 192–193 °C (lit.[31] mp soluble form 191–192 °C)].

As hoped, far superior results were obtained when trimethyltin acetate was used as cocatalyst. Both yields and cleanliness of the reaction were improved, and the reaction time was far shorter. Whereas tri-*n*-butyltin acetate gave complete reactions in ~4 h in refluxing THF, trimethyltin acetate generally led to reaction completion within 1 h. Table II shows the excellent results obtained with this cocatalyst and TMM precursor **1**. Most notably, the galactose-derived aldehyde **15** gives a single stereoisomer **16** in 99% yield.

Trimethyltin acetate is a crystalline solid of rather low volatility whose toxicity[32,33] requires its careful handling. Nevertheless, it is a far more active cocatalyst than tri-*n*-butyltin acetate, and as such, much less is required. The trimethyltin residue can be removed easily and completely from the crude reaction mixture by simple filtration through a silica gel plug. This is not true with the di- and tri-*n*-butyltin cocatalysts, whose elimination requires chromatography.

Reactive Ketones as Acceptors. Although the reactivity of aldehydes in the cycloaddition had been delineated at this point, the glucose derivative **6**, available from tri-*O*-acetyl-D-glucal,[24] still contained the only ketonic carbonyl group that had provided a cycloadduct even in the absence of tin additives. (*tert*-Butylcyclohexanone is completely unreactive.) The sterically hindered nature of the carbonyl group apparently induces clean cyclization

(30) Okawara, R.; Webster, D. E.; Rochow, E. G. *J. Am. Chem. Soc.* **1960**, *82*, 3287. Luijten, J. G. A.; van der Kerk, G. J. M. *Investigations in the Field of Organotin Chemistry*; Tin Research Institute: England, 1955.

(31) Simons, P. B.; Graham, W. A. G. *J. Organomet. Chem.* **1967**, *8*, 479. McFarlane, W.; Wood, R. J. *J. Organomet. Chem.* **1972**, *40*, C17. Chih, H.; Penfold, B. R. *J. Cryst. Mol. Struct.* **1973**, *3*, 285.

(32) Ascher, K. R. S.; Nissim, S. *World Rev. Pest Control* **1964**, *3*, 188. Barnes, J. M.; Magos, L. *Organomet. Chem. Rev.* **1968**, *3*, 137. Smith, P. J. *Toxicological Data on Organotin Compounds*; International Tin Research Institute: London, 1978.

(33) Aldridge, W. N.; *Adv. Chem. Ser.* **1976**, *157*, 186. Elliot, B. M.; Aldridge, W. N.; Bridges, J. W. *Biochem. J.* **1979**, *177*, 461. Taketa, F.; Siebenlist, K.; Kasten-Jolly, J.; Palosaari, N. *Arch. Biochem. Biophys.* **1980**, *203*, 466.

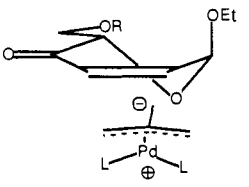
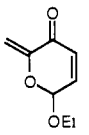


Figure 2. Proposed transition state for enone addition.

as with the tertiary aldehyde, **12**, in Table I. It had attracted interest in the first place because, as an olefin cycloaddition substrate, the presence of the ring oxygen should remove some amount of steric hindrance to axial attack and, in conjunction with the axial oxygen appendage, provide an inductive activation of the olefin toward nucleophilic addition in contrast to the sluggishness of the reactions of cyclohexenones. The formation of **8** in 54% yield more than confirmed these suspicions.[34]

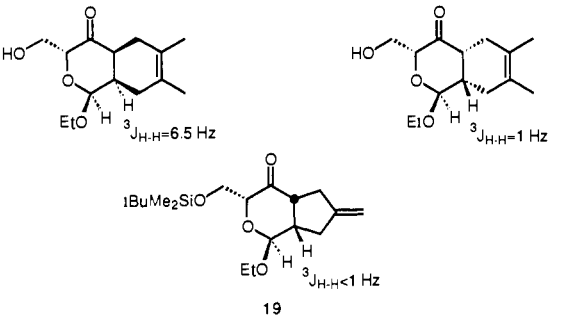
While 5-oxacyclohexenones and 5-oxacyclohexanones have been examined theoretically in some detail, empirical study has been limited to simple nucleophiles (vide infra). By studying the structural features necessary for formation of carbocycles and/or heterocycles, it became our aim to establish the reactivity of this class of electrophiles with a more complex nucleophile, namely the Pd–TMM complex. Furthermore, we hoped that chemo- and stereocontrolled cycloadditions of these substrates could lead to considerable synthetic utility given the array of functionality present in the products.

Variation of the oxygen protecting group on the side chain α' to the carbonyl group was first explored. This was largely a matter of practicality since the benzoate moiety of **6** was subject to elimination and formation of **17** when unknown impurities were



17

present [**17** was identified by its proton NMR spectrum: (270 MHz, $CDCl_3$) δ 6.85 (dd, J = 11.1, 2.2 Hz, 1 H), 6.28 (d, J = 11.1 Hz, 1 H), 5.59 (s, 1 H), 5.40 (d, J = 2.2 Hz, 1 H), 4.95 (s, 1 H), 3.95 (dq, J = 9.8, 7.0 Hz, 1 H), 3.64 (dq, J = 9.8, 7.0 Hz, 1 H), 1.22 (t, J = 7.0 Hz, 3 H)]. Synthesis of the *tert*-butyldimethylsilyl-protected **18** was straightforward. Cycloaddition in refluxing THF using triphenylphosphine and dibenzylideneacetone–palladium(0)–chloroform complex as catalyst and an excess of **1** gave a 70% yield of the cycloadduct **19** (Scheme III). Use of the dibenzylideneacetone–palladium(0) complex proved most convenient for these reactions since it is an air-stable source of palladium(0) and the ketones are not capable of reducing palladium acetate. As might be expected, an unfortunate side product with this catalyst system is the TMM cycloadducts of dibenzylideneacetone, but these are, in general, less polar than the highly oxygenated ketones and are easily removed by chromatography. The structure of **19** was assigned as the olefin adduct since mass spectral evidence indicated that only one TMM fragment had been incorporated and IR and ^{13}C NMR spectroscopy showed resonances indicative of the presence of a carbonyl group (IR, 1720 cm^{-1}; ^{13}C, δ 208.6). The rest of the structure was assigned by proton NMR spectroscopy with benzene-d_6 as solvent, which showed terminal methylene resonances [δ 4.84 (br s)], the silicon group at δ 0.94 (s, 9 H), 0.06 (s, 6 H), the ethoxy substituent [δ 3.70, 3.28, 1.07 (ABX_3)], and the α side chain [δ 4.14, 3.96 (AB of ABX)]. The stereochemistry of the ring juncture was shown to be trans to the ethoxide substituent by comparison of the coupling constant of the acetal proton (J < 1 Hz) with the Diels–Alder cycloadducts of similar molecules as illustrated.[35]



19

While the trans vicinal coupling constant of 1 Hz to the acetal proton is similar to the value for the TMM adduct, the cis coupling constant of 6.5 Hz is somewhat larger. Reported dipolar cycloaddition products also correspond nicely, but in this case data for both epimers are not available.[36] The assignment of trans stereochemistry is very reasonable based on the ground-state conformation of the enolone **19** shown in Figure 2, which should also correspond to the reactive conformation. Due to the anomeric effect,[37] the ethoxy substituent is axial and guards the β face of the olefin. Thus, steric approach control combines with the stereoelectronic bias for pseudoaxial attack of nucleophiles to produce the observed adduct.

Unlike the benzoate, the silyl-protected oxacyclohexenone refused to form the bisadduct. Numerous attempts under forcing conditions with large excesses of **1**, starting from either **18** or **19**, showed no evidence for the formation of bisannulated products **20** and led eventually to decomposition. The reactivity difference between the two differently protected, but otherwise identical molecules is striking. In fact, the benzoate **6** (Scheme III) forms the bisadduct so readily that the second cycloaddition is competitive with the first. The monoadduct **7** can be isolated in 50% yield (70% based on recovered starting material) if the reaction is followed closely, but starting material (29%) and small amounts of bisadduct are present, as well, at this point. The stereochemistry of **7** is again assigned by the small coupling constant displayed by the acetal proton. The bisadduct **8** is assigned as attack from the exo face of the bicyclic [4.3.0] monoadduct.

To gain further insight into the reactivity and synthetic utility of **6** and **18**, each was hydrogenated (hydrogen gas, palladium/carbon) to give the saturated ketones **21** and **22** (Table III). While **21** provided a 60% yield of a mixture of carbonyl cycloadducts, **22** yielded no identifiable products. Each of these experiments was conducted with and without tin cocatalysis. In the presence of tri-*n*-butyltin acetate, the yield of a 3:2 mixture of the cycloadducts **23** and **24** is improved to 80%. The major isomer **23** was assigned to that arising from axial attack by the Pd–TMM complex. This assignment was made by spectral comparison with **8**. In particular, **24** shows proton NMR signals for the (benzoyloxy)methyl side-chain spin system [δ 4.67 (dd, J = 11.7, 2.5 Hz, 1 H), 4.29 (dd, J = 11.7, 7.9 Hz, 1 H), 4.12 (dd, J = 7.9, 2.5 Hz, 1 H)] that are nearly superimposable with those of **8** [δ 4.62 (dd, J = 11.3, 2.1 Hz, 1 H), 4.20 (dd, J = 11.3, 8.1 Hz, 1 H), 4.06 (dd, J = 8.1, 2.1 Hz, 1 H)] and so is assigned to the corresponding product, i.e., that arising from equatorial attack on the ketone. Meanwhile, **23** shows an ABX system with two of the signals as a complex multiplet at δ 4.40 and the other at δ 4.20 (dd, J = 8.4, 2.3 Hz).

The isopropyl-substituted oxacyclohexenone **25**, which is readily available as a racemate from furfural[38] by addition of isopropylmagnesium bromide and oxidation with monoperphthalic

(34) The same effect has been noticed with the Diels–Alder reaction: Fraser-Reid, B.; Underwood, R.; Ousterhout, M.; Grossman, J. A.; Liotta, D. *J. Org. Chem.* **1986**, *51*, 2152.

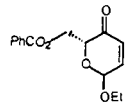
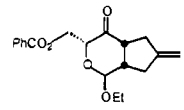
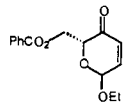
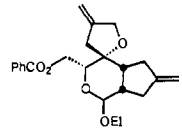
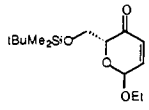
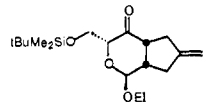
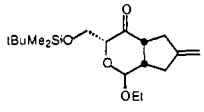
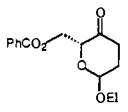
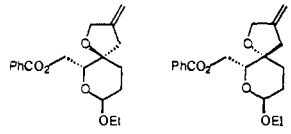
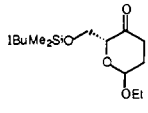
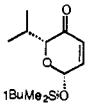
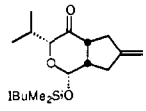
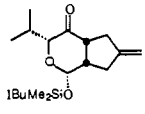
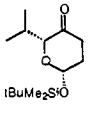
(35) Gnichtel, H.; Gumbrecht, C.; Luger, P. *Liebigs Ann. Chem.* **1984**, 1531. Chew, S.; Ferrier, R. J. *J. Chem. Soc., Chem. Commun.* **1984**, 911. Primequ, J. L.; Anderson, R. C.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1983**, *105*, 5874.

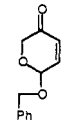
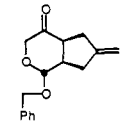
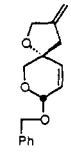
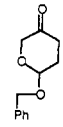
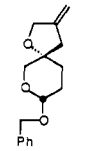
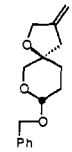
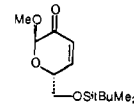
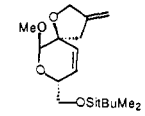
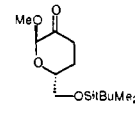
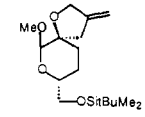
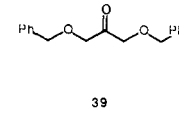
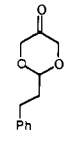
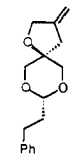
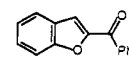
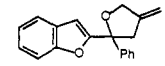
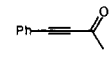
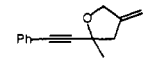
(36) Gnichtel, H.; Autenrieth-Ansorge, L. *Liebigs Ann. Chem.* **1985**, 2217.

(37) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer Verlag: New York, 1983.

(38) Achmatowicz, O., Jr.; Bukowski, P. *Can. J. Chem.* **1975**, *53*, 2524. Achmatowicz, O., Jr., Szechner, B. *Tetrahedron* **1976**, *32*, 1051. DeShong, P.; Ramesh, S.; Elango, V.; Perez, J. J. *J. Am. Chem. Soc.* **1985**, *107*, 5219.

Table III. Summary of Results Obtained with Ketone Acceptors

entry	ketone	reaction time	product(s)	isolated yield[a]
1		4 h		70%
2		16 h		54%
3		2 h		70%
4			none	
5		4 h		80%
6			none	
7		4 h		94%
8			none	
9			none	

entry	ketone	reaction time	product(s)	isolated yield[a]
10		6 h	 2:1 	54%
11		2 h	 2:1 	84%
12		1 h		91%
13		1 h		81%
14			none	
15		1 h		55%
16		22 h		80%
17		8 h		61%

[a] See text and Experimental Section for detailed procedures.

acid followed by protection of the hemiacetal [*tert*-butyldimethylsilyl chloride, triethylamine, and 30 mol % (dimethylamino)pyridine in dichloromethane; see Scheme VI] was also explored. The use of monoperphthalic acid in chloroform proved to be the reagent of choice for transformation of the furan to the hemiacetal. The insolubility of both the peracid and the acid compared to other oxidants[39] permits a nonaqueous workup for the water-unstable hemiacetal. The stereochemistry at the acetal center reflects the kinetic selectivity of silylation of the equatorial epimer and is demonstrated by the spectral data. The coupling constants between the acetal proton and the vinyl protons are 1.0

(39) Samnes, P. G.; Street, L. J. *J. Chem. Soc., Chem. Commun.* **1983**, 666.

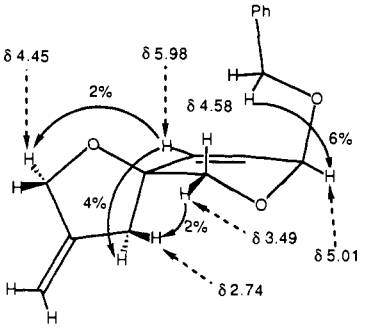
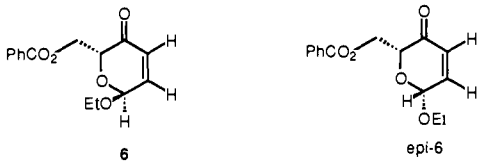


Figure 3. NOE data of cycloadduct **31**.

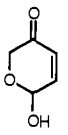
Hz for the vicinal coupling and 1.5 Hz for the allylic coupling, in good agreement with the data for epi-**6**,[40] whereas **6** displays



6 epi-**6**

no allylic coupling and a vicinal coupling of 3.4 Hz. The enone **25** is an excellent substrate, which forms the olefin cycloadduct in 94% yield as a single stereoisomer shown in Table III. The introduction of tri-*n*-butyltin acetate had no effect on this reaction. The product is again derived from pseudoaxial attack on the olefin as demonstrated by coupling constant information. The monoadduct **26** refused to form the corresponding bisadduct and was stable to the reaction conditions even in refluxing dioxane. The corresponding saturated ketone **27** was also inert. This reactivity is identical with that of the α'-(silyloxy)methyl-substituted heterocycles, **18**, **19**, and **22**, but different from that of the α'-(benzoyloxy)methyl-substituted heterocycles, **6**, **7**, and **21**.

Since the α' side chain appeared to have such a large influence on the cycloaddition chemistry, it seemed logical to make an α'-unsubstituted oxacyclohexenone. The hemiacetal **28** is readily



28

available by oxidation of commercially available 2-(hydroxymethyl)furan.[41] Again the oxidation was best carried out with monoperphthalic acid. Transacetalization with benzyl alcohol in methylene chloride containing tin tetrachloride as catalyst gives the protected "parent" oxacyclohexenone **29**. This molecule reacts satisfactorily under the standard TMM cycloaddition conditions when tri-*n*-butyltin acetate is included. A 58% yield of a 2:1 mixture of olefin to carbonyl cycloadducts is obtained. Rapid decomposition was observed without a tin cocatalyst present. This result is quite different from the cycloaddition of **25**, which proceeds smoothly without tin present. This behavior is attributed to the steric encumbrance of the α' position, which apparently precludes carbonyl addition and base-catalyzed decomposition pathways. Both cycloadducts of **25** are a single stereoisomer, as determined on pure samples obtained by preparative thin layer chromatography. The olefin cycloadduct, **30**, displayed ketone absorptions in the IR (1720 cm^{-1}) and ^{13}C NMR (δ 208.6) spectra, and the familiar small coupling constant (J = 2.6 Hz) for the acetal proton, which implies pseudoaxial attack on the olefin. The carbonyl cycloadduct, **31**, possessed proton [δ 5.98, 5.75 (J = 10.2 Hz)] and ^{13}C NMR (δ 146.5, 137.9) resonances for the olefin, as well as the typical methylenetetrahydrofuran signals [δ 5.06

(40) Achmatowicz, O.; Bielski, R. *Carbohydr. Res.* **1977**, *55*, 165.
(41) Piancatelli, G.; Scettri, A.; D'Auria, M. *Tetrahedron* **1980**, *36*, 661. Hendrickson, J. B.; Farina, J. S. *J. Org. Chem.* **1980**, *45*, 3359.

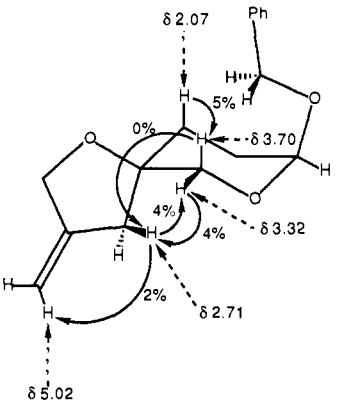


Figure 4. NOE data for cycloadduct **33**.

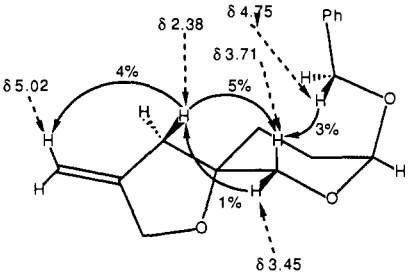


Figure 5. NOE data for cycloadduct **34**.

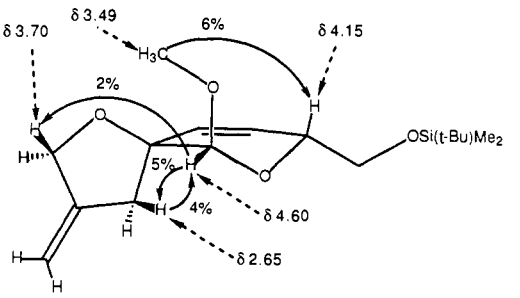


Figure 6. NOE data for cycloadduct **36**.

(br s, 1 H), 4.98 (br s, 1 H), 4.45 (br d, J = 13.1 Hz, 1 H), 4.32 (dd, J = 13.1, 1.9 Hz, 1 H), 2.74 (br d, J = 15.6 Hz, 1 H), 2.47 (br d, J = 15.6 Hz, 1 H)]. The stereochemistry at the spiro center was determined by nuclear Overhauser effect difference spectroscopy (NOEDS) as summarized in Figure 3 and by comparison of these data for the related adducts **33** and **34**.

Hydrogenation of **29** gives **32** in 98% yield. Reaction of **32** and **1** with a palladium(0) catalyst and tri-*n*-butyltin acetate as cocatalyst gives a 2:1 ratio of carbonyl cycloadducts **33** and **34** in 52% total yield. Use of trimethyltin acetate improved the yield to 84%, and the ratio of stereoisomers remained at 2:1. The development of trimethyltin acetate as a cocatalyst superior to tri-*n*-butyltin acetate came after much of the oxacyclohexenone work was completed. Consequently, this example is illustrative of the excellent properties of trimethyltin acetate for all carbonyl addition reactions. Possession of both stereoisomers allows assignment of stereochemistry at the spiro center via NOEDS, summarized in Figures 4 and 5.

The striking contrast in reactivity toward cycloaddition between enolones like **6** and **18** and the "reversed" enolone **35**[34] made a comparison using the TMM–PdL_2 as the cycloadding species of high interest. Consonant with the failure of the reversed enolone to serve as a dienophile in a Diels–Alder reaction, or a dipolarophile in a 1,3 dipolar cycloaddition,[34] it also fails to produce the carbocycle in its reaction with our trimethylenemethane species. Nevertheless, reaction of **35** with an excess of **1** in the presence of trimethyltin acetate rapidly provided 91% of an annulated product as a single stereoisomer. This material was assigned as the carbonyl cycloadduct **36** since IR and ^{13}C data showed no

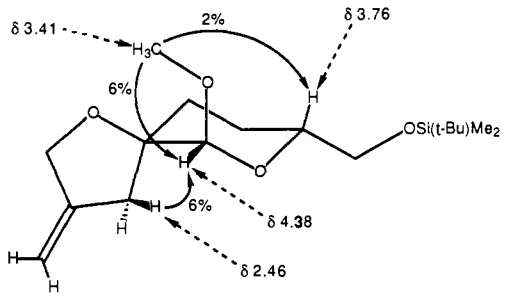
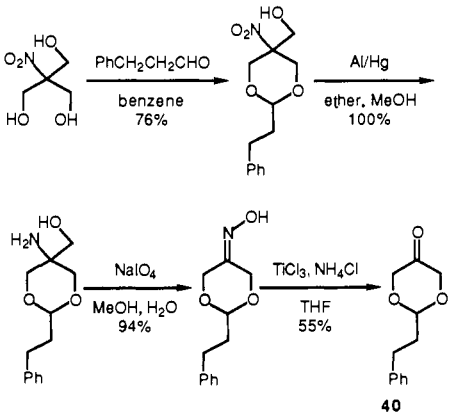


Figure 7. NOE data for cycloadduct **38**.

Scheme VII. Synthesis of 4-Phenethyl-3,5-dioxacyclohexanone (**40**)



carbonyl resonances and the endocyclic olefin was clearly present in the proton [δ 5.80 (s, 2 H)] and carbon (δ 127.2 and 127.9) NMR spectra. Once again, NOE data were relied upon to make the stereochemical assignment of **36**, as illustrated in Figure 6. The data show a large NOE between the equatorial six-membered ring acetal proton, and the high-field allylic signals. The structure is, therefore, assigned to axial attack by the Pd–TMM fragment. This is certainly what would be expected based upon steric shielding of the equatorial face of the carbonyl group by the methoxy substituent. Analogously, the saturated ketone **37** gave an 81% yield of the cycloadduct **38**. Again in this case trimethyltin acetate is a particularly helpful additive. This reaction with tributyltin acetate generated several unidentified side products and yielded less than 50% of the desired material. Its stereochemical assignment also corresponds to axial attack and is shown in Figure 7.

In order to study the effect of α-oxygen substituents more directly, two α,α'-dialkoxy ketones were prepared. The acyclic system **39** is available as described in the literature.[42] A route to the cyclic ketone **40**, shown in Scheme VII, was developed[43] that utilized tris(hydroxymethyl)nitromethane as starting material. Formation of the acetal of hydrocinnamaldehyde put in place the desired dioxacyclohexane skeleton. Reduction to the amine (aluminum amalgam)[44] and oxidative cleavage with sodium metaperiodate[45] gave an oxime that was reduced to the desired material via the method of Corey.[46] As can be seen, the aluminum amalgam reduction is an excellent process for deoxygenation of

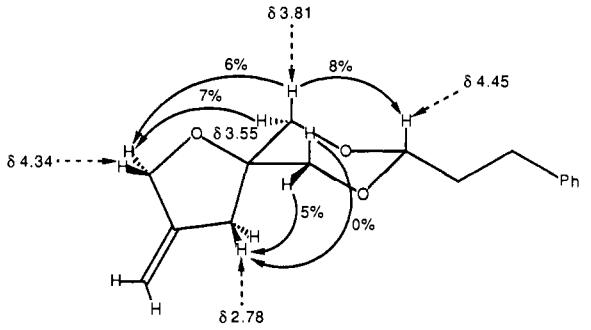


Figure 8. NOE data for cycloadduct **41**.

aliphatic nitro groups. Ketone **40** was unstable to storage for more than a few days even below 0 °C. Reaction of **39** and **40** with excess TMM precursor was conducted without tin cocatalysis; nevertheless, the results are clear. While **39** provided no cycloadduct and was, in fact, stable to the reaction conditions, **40** provided a 59% yield of cycloadduct in rapid fashion. The stereochemical assignment of **41** by NOEDS, as shown in Figure 8, demonstrated that the product was again derived from axial attack on the ketone. The enhanced reactivity of the cyclic dioxygenated ketone can only be explained by the conformational rigidity of the six-membered ring, which properly aligns the π system of the carbonyl group with the β-carbon–oxygen σ bonds of the ring.

In ancillary studies, we explored the utilization of conjugated ketones as acceptors. While the α-alkoxy ketone **42** does not have conformational rigidity to maximize the oxygen effect, the absence of any competing deprotonation reactions apparently permits cycloaddition to occur in excellent yield (80%), even in the absence of any tin cocatalyst. Addition of tri-*n*-butyltin acetate slightly lowers the isolated yield to 63%—a fact that may stem from the need to separate the tin cocatalyst from the product.

What other types of ketone substrates that may participate remains to be defined. That other substrates will be found is illustrated by the observation that the ynone **42** cycloadds exclusively with the carbonyl group to give a 61% yield of the methylenetetrahydrofuran **43**. The failure to add to the acetylene confirms our earlier failed attempts to add to an acetylenic ester.[13] The low steric hindrance associated with an alkyne may make it look like an aldehyde with respect to carbonyl addition. An alternative explanation invokes an interaction of the palladium catalyst with the acetylenic linkage. That such an interaction occurs is clearly demonstrated by our observation that acetylenic ketones like **46** isomerize to dienes with the palladium catalysts employed herein.[47] Indeed, this isomerization competes with the cycloaddition to the carbonyl group when we employ substrates like **46**.

Discussion. The direct cycloaddition of a trimethylenemethane fragment to a carbonyl group represents a convenient stereocontrolled approach to substituted tetrahydrofurans. In accord with the notion that the initial step is a nucleophilic addition to a carbonyl group, the stereoselectivity of addition to aldehydes is quite analogous to that of typical nucleophiles. For example, the formation of the 22-S isomer in the steroid substrate (Table II, entry 7) arises from a typical Felkin–Anh model represented in **47**. Optimization of the diastereoselectivity was not attempted. Electronic effects induce nucleophilic addition to α-alkoxy aldehydes such as a lactaldehyde (Table II, entry 6) through **48**

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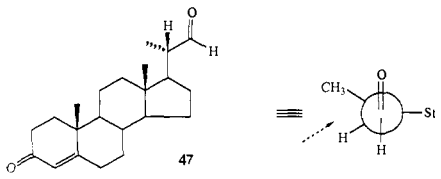
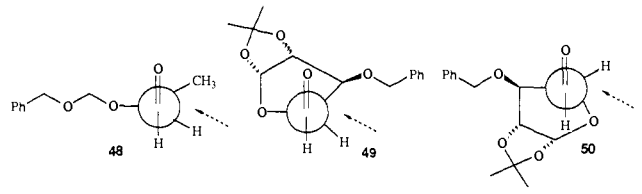


as the reactive conformer, which accounts for the major adduct here, too.[48] A similar argument may apply to the sugar-derived



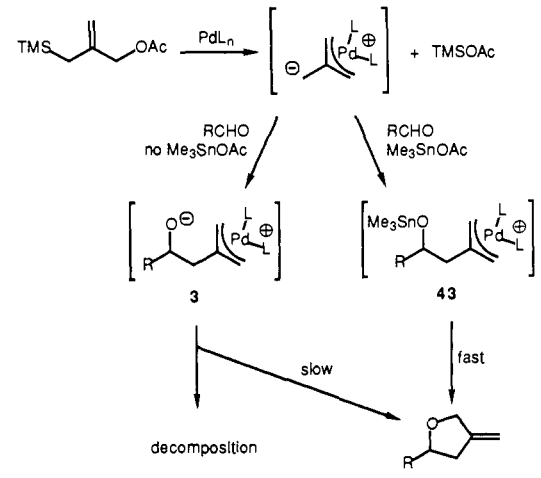
aldehydes (Table II, entries 8 and 9) as depicted in drawing **49**, although an alternative conformer **50** has been invoked to explain the diastereoselectivity.[49] Again, the diastereoselectivity of the annulation follows the same path with extraordinary control.

The behavior of the carbohydrate-derived enones and their saturated analogues further characterizes the (trimethylenemethane)palladium complex as a nucleophilic species. The enones undergo excellent olefin annulation in contrast to simple cyclohexenones.[13] Satisfactory cycloaddition in the latter case requires either double activation[50] or use of less basic substituted trimethylenemethane complexes.[14e] Invoking an asynchronous mechanistic interpretation[16] in which the nucleophilic addition proceeds by 1,4-axial attack, we suggest that diminished steric strain for axial attack, because of the ring oxygen, and the enhanced electrophilicity of the acceptors due to the oxygen substituents accounts for the excellent reactivity. Synthetically, the highly diastereoselective cyclopentannulation translates into a valuable cyclopentanone synthesis with functionalized diastereomerically pure side chains as shown in **51**.

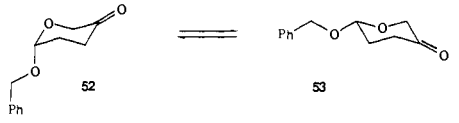
At first glance, a similarity between the Diels–Alder reaction of electron-rich dienes[24] and the TMM–PdL_2 complex in their behavior toward the enones like **6** or **18** and the inverse enone **35** suggests similar pathways (i.e., concerted cycloadditions?). That is, **35** is totally unreactive in the condensation with electron-rich dienes and fails to react at the olefin with TMM–PdL_2. However, the ability of the latter to be a nucleophile allows an alternative pathway to proceed, i.e., simple carbonyl addition.

Attack by sterically nondemanding nucleophiles on carbonyl groups in six-membered rings proceeds preferentially in an axial fashion to minimize torsional strain.[51-57] This trend is accentuated

Scheme VIII. A Mechanistic Interpretation of Cocatalysis



in six-membered rings that possess (1) a conjugating double bond[52,57] and (2) a β-oxygen substituent.[53,55] The TMM–PdL_2 complex falls into the class of nucleophiles that follows this trend. The major exception, Table III, entry 2, reflects overriding steric hindrance to attack in an axial fashion by the fused methylenecyclopentyl ring. Steric hindrance by the α substituent with substrate **21** (Table III, entry 5) accounts for its lower axial selectivity. The importance of similar steric hindrance is revealed in comparing ketones **27** and **32**, where α substitution in the former case simply shuts down cycloaddition. The diminished diastereoselectivity of cycloaddition to ketone **32** (Table III, entry 11) appears surprising in light of the other results. A possible explanation may reside in its conformational mobility in contrast to all our other substrates. The conformational mobility of substrate **51** may derive from the steric strain destabilizing the electronically favored conformer **52**. By this reasoning, both



adducts may derive by axial attack since this mode of addition to conformer **52** generates adduct **33** and similar attack on conformer **53** gives adduct **34**. Reduction of the steric strain in **52** by introducing a 3,4 double bond, i.e., enone **29**, locks the conformation, and to the extent that enone **29** leads to carbonyl addition, it does so by axial attack. Thus, the TMM–PdL_2 complex demonstrates a high bias for axial attack in the absence of overwhelming steric strain.

Substrate **29** is the only case of those recorded herein where carbonyl and olefin addition competes. Both processes appear to be two steps: nucleophilic attack followed by ring closure. Normally, "hard" nucleophiles prefer 1,2-addition and "soft" nucleophiles prefer 1,4-addition. Our complex, then, falls somewhere between the two, but more toward the latter than the former. An alternative explanation proposes that the first bond formation in a 1,2-fashion is preferred kinetically with α,β-unsaturated aldehydes and ketones. The proportion of carbonyl addition versus olefin addition then depends upon the degree of reversibility of this first step, which then would proceed via the kinetically slower but thermodynamically more favored conjugate

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(57) Wu, Y.-D.; Houk K. N.; Trost, B. M. *J. Am. Chem. Soc.* **1987**, *109*, 5560.

addition path. Performing appropriate experiments to test this latter pathway has been unsuccessful to date.

The major question of the current studies addresses the issue of the "tin effect". Clearly trialkyltin acetate cocatalysis greatly enhances the generality and yield of the palladium-catalyzed trimethylenemethane annulation of carbonyl compounds. Two individual effects seem responsible for the overall improvement. First, the presence of tin compounds results in clean formation of five-membered ring products. Acyclic byproducts, which are pervasive in the absence of cocatalysis, are eliminated. Second, decomposition of carbonyl starting materials is suppressed. Tin cocatalysts are, in fact, crucial for cycloaddition of most aldehydes (as illustrated in Scheme IV) and the easily enolizable ketones (e.g., **29** and **32**).

While a detailed discussion is deferred, we suggest now, as depicted in Scheme VIII, that these effects can be mechanistically attributed to the existence of stannyl ether **43** in the reaction pathway. It is this highly nucleophilic species[58] that, rather than an alkoxide **3**, is the long-lived intermediate. Stannyl ethers react excellently with π-allylpalladium cations,[59] while alkoxides are especially poor nucleophiles for these electrophiles.[19] In the cycloaddition reaction then, formation of **54** would provide an intermediate relatively prone to cyclization to the methylenetetrahydrofuran since its rapid collapse would favor intramolecular over intermolecular reaction.

Certainly the most dramatic effect of the catalytic presence of trialkyltin acetate is the improvement in the annulation of substrates bearing acidic protons. While the Pd–TMM complex is probably basic enough[14f] to deprotonate these aldehydes and ketones, the reaction is kinetically slow. It seems more likely that in the reaction without tin additives, it is the alkoxide **2** that is acting as the base responsible for decomposition. Capping of the oxygen nucleophile by the trialkylstannyl moiety and rapid cyclization would greatly lessen both the basicity and concentration of the intermediate and, thus, suppress deleterious processes such as enolization. The desired cycloaddition is left as the only remaining favorable process. In summary, a stannyl ether would seem to play a central role in the tin effect.

Experimental Section

General Procedures. All anhydrous reactions were performed in oven-dried glassware under a positive pressure of dry nitrogen. All reactions were magnetically stirred unless otherwise indicated. Anhydrous solvents were transferred by oven-dried syringes. Solvents were distilled before use. Hexane, ethyl acetate, benzene, methylene chloride, chloroform, tetramethylethylenediamine, dimethyl sulfoxide, and triethylamine were distilled from calcium hydride. Tetrahydrofuran, dioxane, and diethyl ether were distilled from sodium benzophenone ketyl. Tetrakis(triphenylphosphine)palladium(0)[60] was stored in an inert-atmosphere glovebox and transferred rapidly in air for use. Dibenzylideneacetone–palladium(0)–chloroform complex was prepared as described by Ishii[61] and stored in air. Chromatographic[62] and spectral procedures are outlined in the supplementary material.

A Simplified Procedure for the Preparation of 2-[(Trimethylsilyl)methyl]-3-[(trimethylsilyl)oxy]-1-propene (1). A 2-L three-neck flask is equipped with a mechanical stirrer, a nitrogen inlet, and a rubber stopper. The apparatus is flushed with nitrogen. After cooling, 500 mL of ether (on this scale it is most convenient to use an unopened anhydrous can) is added by quick removal and replacement of the septum. The flask is cooled in an ice bath and *n*-butyllithium (10.4 M from Aldrich, 100 mL, 1.04 mol) added via syringe. Care should be taken as the reagent is somewhat pyrophoric. Tetramethylethylenediamine (distilled from calcium hydride, 160 mL) is added and 2-methyl-2-propen-1-ol (34 mL, 29.14 g, 0.404 mol) is added dropwise via syringe over 20 min to give a vigorous reaction and a white precipitate. Anhydrous THF (350 mL) is added and the mixture becomes clear or nearly so. The septum is replaced with a glass stopper and the reaction mixture vigorously stirred. The yield is similar if the reaction is quenched after 24–36 h at room temperature. At this time the reaction mixture may be yellow to dark red with a gummy precipitate. The reaction vessel is cooled to about −30 °C and trimethylsilyl chloride (distilled from calcium hydride or tributylamine, 230 mL, 1.81 mol) is added rapidly from an addition funnel. The solution becomes clear, is allowed to warm to room temperature, and is stirred for 15 min. The reaction mixture is added to 3 L of ether, 1 L of 10% sodium bicarbonate is carefully introduced, and the mixture is shaken vigorously. The aqueous mixture is separated and extracted with ether. The combined organic layers are washed with 2 × 1 L of saturated aqueous copper sulfate, 500 mL of distilled water, and 500 mL of saturated aqueous sodium chloride. The solution is dried over potassium carbonate, the solvent removed in vacuo, and the residue carefully distilled, bp 57–59 °C (4 mm), to give the 44.2 g of the desired product (48%).[63] Analogous procedures can be used to make a variety of other TMM precursors (vide infra).

2-[(*E*)-2-Phenylethenyl]-4-methylenetetrahydrofuran (9). Method A. 2-[(Trimethylsilyl)methyl]-3-acetoxy-1-propene, 1 (280 mg, 320 μL, 1.50 mmol), was dissolved in dioxane (1.0 mL) and placed in a 1-mL syringe affixed to a syringe pump. Palladium acetate (9.3 mg, 42 μmol) was placed in an oven-dried test tube and thoroughly flushed with nitrogen. Dioxane (2.0 mL) was added and the mixture heated at 70 °C until homogeneous. Triisopropyl phosphite (55 mg, 65 μL, 264 μmol) was added rapidly and the solution became nearly clear. Cinnamaldehyde (156 mg, 136 μL, 1.0 mmol) was added, and syringe pump addition of the TMM precursor was begun. The addition was set to be completed in 4 h. At this time the mixture was diluted with ether (2 mL) and filtered through a silica gel plug. After concentration in vacuo, the residue was flash chromatographed (95:5 hexane–ethyl acetate). Bulb-to-bulb distillation [160 °C (1 mm Hg)] of the chromatographed material gave a clear oil and yielded 140 mg (75%) of the desired product identical with that prepared earlier:[21] ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.40–7.20 (m, 5 H), 6.62 (d, J = 15.9 Hz, 1 H), 6.22 (dd, J = 15.9, 6.9 Hz, 1 H), 5.02 (br s, 1 H), 4.94 (br s, 1 H), 4.57 (q, J = 7.1 Hz, 1 H), 4.46 (d, J = 13.0 Hz, 1 H), 4.32 (d, J = 13.0 Hz), 1 H), 2.77 (dd, J = 15.4, 6.9 Hz, 1 H), 2.45 (dd, J = 15.4, 7.4 Hz, 1 H).

Analogous procedures to the above were employed for the remaining entries of Table I. The details are reported in the supplementary material and the spectral data of the adducts below.

2-(2-Naphthyl)-4-methylenetetrahydrofuran: ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.11–7.40 (m, 7 H), 5.68 (t, J = 7.4 Hz, 1 H), 5.06 (m, 2 H), 4.75 (d, J = 15.9 Hz, 1 H), 4.59 (t, J = 15.9 Hz, 1 H), 3.23 (dd, J = 13.1, 7.4 Hz, 1 H), 2.69 (dd, J = 15.1, 7.4 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 147.6, 137.5, 133.7, 130.5, 128.7, 127.8, 125.8, 125.4, 125.4, 123.3, 122.3, 104.6, 77.6, 71.2, 40.4; IR ($CDCl_3$) 1600, 1510, 1450, 1380 cm^{-1}; MS calculated for $C_{15}H_{14}O$ m/e 210.1041, found 210.1038.

2-[4(*S*)-Isopropenylcyclohex-1-enyl]-4-methylenetetrahydrofuran: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70 (br s, 1 H), 4.94 (t, J = 2.2 Hz, 1 H), 4.87 (t, J = 2.2 Hz, 1 H), 4.70 (br s, 2 H), 4.40 (d, J = 13.2 Hz, 1 H), 4.35–4.15 (m, 2 H), 2.70–1.75 (m, 9 H), 1.73 (s, 3 H), 1.49 (m, 1 H), 1.0 (m, 1 H). Major isomer: ^{13}C NMR (50 MHz, $CDCl_3$) δ 149.7, 148.3, 136.7, 121.8, 108.6, 103.9, 82.7, 70.9, 41.1, 37.0, 30.4, 27.5, 24.3, 20.7. Minor isomer: ^{13}C NMR (50 MHz, $CDCl_3$) δ 149.5, 148.5, 142.6, 123.2, 108.5, 103.9, 82.7, 70.9, 41.2, 37.3, 30.5, 27.3, 24.5, 20.7.

2-(1,1-Dimethyl-2-phenylethyl)-4-methylenetetrahydrofuran (13): ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.29–7.15 (m, 5 H), 4.95 (t, J = 2.1 Hz, 1 H), 4.88 (t, J = 2.1 Hz, 1 H), 4.42 (br d, J = 13.0 Hz, 1 H), 4.24 (br d, J = 13.0 Hz, 1 H), 3.65 (t, J = 2.1 Hz, 1 H), 2.70 (d, J = 12.9 Hz, 1 H), 2.43 (br s, 1 H), 2.40 (br s, 1 H), 0.90 (s, 3 H), 0.80 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.7, 138.6, 130.8, 127.6, 125.8, 103.8, 85.7, 71.4, 45.1, 37.3, 33.4, 22.8, 22.0; IR ($CDCl_3$) 1610, 1595, 1486, 1460, 1443, 1380 cm^{-1}; MS calculated for $C_{15}H_{20}O$ m/e 216.1514, found 216.1520.

2-[(*E*)-2-Phenylethenyl]-4-methylenetetrahydrofuran (9). Method B. A solution of palladium acetate (5 mg, 22 μmol), triphenylphosphine (30 mg, 114 μmol), and tributyltin acetate (35 mg, 100 μmol) under nitrogen in 1.0 mL of THF was heated at 70 °C until homogeneous. Cinnamaldehyde (66 mg, 63 μL, 0.50 mmol) and 2-[(trimethylsilyl)methyl]-3-acetoxy-1-propene (**1**; 93 mg, 110 μL, 0.50 mmol), were added and heating continued at 70 °C for 4 h. The reaction mixture was cooled, diluted with 80:20 hexane–ethyl acetate (2 mL), and filtered through a silica gel plug. After evaporation of solvent the residue was flash chromatographed (97:3 hexane–ethyl acetate) to give 83 mg (89%) of 2-[(*E*)-2-phenylethenyl]-4-methylenetetrahydrofuran identical with that previously prepared (vide supra).

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Analogous procedures were employed for the following three cycloadducts. The spectral data follow and the experimental details of each run appear in the appendix.

2-(2-Methyl-2-propenyl)-4-methylenetetrahydrofuran: ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.24 (dq, J = 8.6, 1.2 Hz, 1 H), 4.97 (quint, J = 2.2 Hz, 1 H), 4.89 (dt, J = 2.2, 2.0 Hz, H), 4.60 (dt, J = 8.6, 6.0 Hz, 1 H), 4.40 (d, J = 13.1 Hz, 1 H), 4.23 (d, J = 13.1 Hz, 1 H), 2.63 (dd, J = 15.5, 6.0 Hz, 1 H), 2.27 (dd, J = 15.5, 6.0 Hz, 1 H), 1.74 (d, J = 1.2 Hz, 3 H), 1.71 (d, J = 1.2 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 148.7, 124.9, 116.8, 103.8, 76.3, 70.6, 39.5, 25.7, 18.2; IR ($CDCl_3$) 1663, 1427, 1371 cm^{-1}; MS calculated for $C_9H_{14}O$ m/e 138.1045, found 138.1040.

2(R)-[1(S)-(Benzyloxymethoxy)ethyl]-4-methylenetetrahydrofuran (anti product, major) and 2(S)-[1(S)-(benzyloxymethoxy)ethyl]-4-methylenetetrahydrofuran (syn product, minor). High R_f, assigned anti stereochemistry: ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.36–7.27 (m, 5 H), 4.99 (t, J = 2.2 Hz, 1 H), 4.91 (t, J = 2.2 Hz, 1 H), 4.84–4.82 (m, 2 H), 4.63 (s, 2 H), 4.39 (br d, J = 12.9 Hz, 1 H), 4.28 (br d, J = 12.9 Hz, 1 H), 4.28 (br d, J = 12.9 Hz, 1 H), 3.90 (m, 2 H), 2.57 (m, 2 H), 1.21 (d, J = 14.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.7, 137.9, 128.4, 127.8, 127.6, 104.3, 93.4, 87.7, 74.2, 71.3, 69.4, 34.0, 16.7; IR ($CDCl_3$) 2916, 2879, 2845, 1100, 1091, 1030, 1018 cm^{-1}. Low R_f, assigned syn stereochemistry: ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.36–7.26 (m, 5 H), 4.98 (t, J = 2.2 Hz, 1 H), 4.91 (t, J = 2.2 Hz, 1 H), 4.88 (s, 2 H), 4.66–4.65 (m, 2 H), 4.43 (br d, J = 13.2 Hz, 1 H), 4.28 (br d, J = 13.2 Hz, 1 H), 3.95 (dt, J = 8.7, 6.4 Hz, 1 H), 3.83 (quint, J = 6.3 Hz, 1 H), 2.55 (dd, J = 15.5, 6.3 Hz, 1 H), 2.38 (ddd, J = 8.7, 6.4, 2.2 Hz, 1 H), 1.20 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.7, 138.0, 128.4, 127.9, 127.6, 104.2, 93.7, 83.0, 74.9, 71.3, 69.5, 35.1, 16.8; MS (of the mixture) calculated for $C_{15}H_{19}O_3$ m/e 247.1334, found 247.1324.

Trimethylenemethane Annulation of 3-Oxopreg-4-ene-20β-carboxaldehyde. This product mixture was identical with that previously prepared:[21] ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.66 (s, 1 H), 4.92 (s, 1 H), 4.82 (s, 1 H), 4.31 (d, J = 13 Hz, 1 H), 4.16 (d, J = 13 Hz, 1 H), 4.00 (t, J = 8 Hz, 1 H), 2.40–0.85 (m, 26 H), 1.16 (s, 3 H), 0.70 (2 singlets, 3 H). Major isomer: ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.4, 171.4, 148.7, 123.7, 103.6, 81.7, 71.4, 55.6, 53.8, 53.6, 53.1, 42.4, 39.5, 39.3, 38.5, 35.7, 35.6, 33.9, 32.9, 31.9, 27.8, 24.1, 21.0, 17.3, 12.5, 11.7.

5,8-Anhydro-3-*O*-benzyl-6,7-dideoxy-1,2-*O*-isopropylidene-7-methylene-α-D-*gluco*-1,4-octofuranulose. A mixture of dibenzylideneacetone–palladium(0)–chloroform complex (20 mg, 19 μmol), triphenylphosphine (60 mg, 229 μmol), and tri-*n*-butyltin acetate (35 mg, 100 μmol) under a nitrogen atmosphere was dissolved in 3 mL of THF. Of this solution, 1 mL was added to 5-anhydro-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-gluco-1,4-furanose (45 mg, 0.112 mmol). The mixture was brought to reflux and 2-[(trimethylsilyl)methyl]-3-acetoxy-1-propene (**1**; 55 mg, 60 μL, 0.27 mmol), was added. After 5 h, TLC showed no starting material remained, and the reaction was diluted and filtered through a silica gel plug with 10 mL of a 4:1 mixture of hexane–ethyl acetate. Removal of solvent yielded a yellow oil, which was flash chromatographed (92:8 hexane–ethyl acetate) to give the adduct (32 mg, 62%) as a single stereoisomer identical with that previously prepared:[21] ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.36–7.26 (m, 5 H), 5.91 (d, J = 3.7 Hz, 1 H), 5.01 (br s, 1 H), 4.94 (br s, 1 H), 4.67 (s, 2 H), 4.59 (d, J = 3.7 Hz, 1 H), 4.39 (br d, J = 11.9 Hz, 1 H), 4.34–4.26 (m, 2 H), 4.11–4.03 (m, 2 H), 2.75 (br dd, J = 16.0, 6.8 Hz, H), 2.67 (br dd, J = 16.0, 6.8 Hz, 1 H), 1.49 (s, 3 H), 1.31 (s, 3 H).

Trimethyltin Acetate. Trimethyltin hydroxide (1.65 g, 9.13 mmol) was vigorously stirred in distilled water (2 mL). After complete dissolution, acetic acid (0.60 g, 0.57 mL, 10.0 mmol) was added, and the mixture was stirred at room temperature for 3 h. Benzene (20 mL) was added, and the water was removed azeotropically into a Dean–Stark trap. After the refluxing vapor became clear, the solution was cooled and the resulting solid collected. The product was recrystallized from benzene and dried to give 1.42 g (70%) of the soluble form of trimethyltin acetate,[31] identical with that previously reported: mp 192–193 °C (lit.[31] mp soluble form 191–192 °C, mp insoluble form 196.5–197.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.06 (s, 3 H), 0.55 (s, 9 H, $^2J_{Sn-H}$ = 32 Hz). Anal. Calcd for $C_5H_{12}O_2Sn$: C, 26.94; H, 5.43. Found: C, 27.24, H, 5.79.

2-[(E)-2-Phenylethenyl]-4-methylenetetrahydrofuran (9). Method C. Palladium acetate (5 mg, 22 μmol), triphenylphosphine (30 mg, 114 μmol), and trimethyltin acetate (5 mg, 22 μmol) in 1.0 mL of THF under nitrogen were heated at 70 °C until homogeneous. Cinnamaldehyde (66 mg, 63 μL, 0.50 mmol) and 2-[(trimethylsilyl)methyl]-3-acetoxy-1-propene (**1**; 93 mg, 110 μL, 0.50 mmol) were added and heating continued at 70 °C for 1 h. The reaction mixture was cooled, diluted with 80:20 hexane–ethyl acetate (2 mL), and filtered through a silica gel plug. After evaporation of solvent, the residue was flash chromatographed (97:3 hexane–ethyl acetate) to give 88 mg (95%) of 2-[(E)-2-phenylethenyl]-4-methylenetetrahydrofuran, identical with that previously prepared (vide supra).

Analogous procedures were employed for the preparation of the following four cycloadducts. The spectral data follow and the experimental details for each run appear in the supplementary material.

2-(2-Phenylethyl)-4-methylenetetrahydrofuran: ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.30–7.14 (m, 5 H), 4.96 (t, J = 2.1 Hz, 1 H), 4.89 (t, J = 2.1 Hz, 1 H), 4.39 (d, J = 13.1 Hz, 1 H), 4.22 (d, J = 13.1 Hz, 1 H), 3.91 (quint, J = 1.0 Hz, 1 H), 2.79–2.58 (m, 3 H), 2.21 (dd, J = 13.5, 8.5 Hz, 1 H), 2.00–1.70 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.2, 141.8, 128.3 (4), 125.7, 104.0, 79.1, 70.7, 38.6, 36.7, 32.3; IR ($CDCl_3$) 2920, 2840, 1040 cm^{-1}; MS calculated for $C_{13}H_{17}O$ m/e 189.1279, found 189.1286.

2-Cyclohexyl-4-methylenetetrahydrofuran: ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.92 (t, J = 1.8 Hz, 1 H), 4.84 (br s, 1 H), 4.32 (d, J = 13.1 Hz, 1 H), 4.16 (dd, J = 13.1, 1.4 Hz, 1 H), 3.56 (q, J = 8.4 Hz, 1 H), 2.52 (dd, J = 15.6, 5.5 Hz, 1 H), 2.23 (m, 1 H), 1.92 (d, J = 13.1 Hz, 1 H), 1.72–1.55 (m, 4 H), 1.37 (m, 1 H), 1.26–1.20 (m, 3 H), 1.17–0.88 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.6, 103.7, 84.5, 70.8, 42.7, 36.6, 29.7, 29.1, 26.5, 26.0, 25.8; IR ($CDCl_3$) 2905, 2853, 1441, 1038 cm^{-1}; MS calculated for $C_{11}H_{18}O$ m/e 166.1357, found 166.1351.

2-(9-Decenyl)-4-methylenetetrahydrofuran: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 (ddt, J = 17.0, 6.6 Hz, 1 H), 5.01–4.87 (m, 4 H), 4.37 (d, J = 13.1 Hz, 1 H), 4.21 (dm, J = 13.1 Hz, 1 H), 3.90 (m, 1 H), 2.60 (dd, J = 15.7, 5.5 Hz, 1 H), 2.19 (m, 1 H), 2.03 (q, J = 8.1 Hz, 2 H), 1.62 (m, 1 H), 1.60–1.20 (m, 13 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 139.2, 114.0, 103.8, 80.0, 70.7, 38.8, 35.1, 33.8, 29.6, 29.5, 29.4, 29.1, 28.9, 26.0; IR (neat) 1679, 1650, 1473, 1441, 891 cm^{-1}; MS calculated for $C_{15}H_{26}O$ m/e 222.1984, found 222.1974. Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.98; H, 11.79.

Galactose-Derived Cycloadduct 16: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.49 (d, J = 5.1 Hz, 1 H), 5.00 (br s, 1 H), 4.91 (br s, 1 H), 4.60 (dd, J = 8.0, 2.4 Hz, 1 H), 4.38 (dd, J = 8.0, 1.8 Hz, 1 H), 4.32 (br s, 2 H), 4.29 (dd, J = 5.0, 2.5 Hz, 1 H), 4.20 (td, J = 8.6, 6.8 Hz, 1 H), 3.57 (dd, J = 8.6, 1.8 Hz, 1 H), 2.74 (dd, J = 16.0, 9.0 Hz, 1 H), 2.53 (dd, J = 16.0, 5.8 Hz, 1 H), 1.48 (s, 3 H), 1.44 (s, 3 H), 1.35 (s, 3 H), 1.31 (s, 3 H); ^{13}C NMR (MHz, $CDCl_3$) δ 147.2, 109.2, 108.6, 104.9, 96.3, 76.7, 71.2, 70.8, 70.6, 70.4, 69.2, 36.1, 26.0, 25.9, 24.9, 24.3; IR ($CDCl_3$) 2985, 2935, 2858, 1382, 1255, 1212, 1169, 1069, 1001, 902 cm^{-1}; MS calculated for $C_{26}H_{24}O_6$ m/e 312.1587, found 312.1571.

5(S)-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-7(S)-ethoxy-2-methylene-4-oxo-6-oxa-3a(R),7a(S)-perhydroindane (19). Dibenzylideneacetone–palladium(0)–chloroform complex (7 mg, 17 μmol) and triphenylphosphine (24 mg, 92 μmol) in 1.0 mL of THF were heated at 70 °C until homogeneous and added to 2(S)[[(*tert*-butyldimethylsilyl)oxy]methyl]-4(S)-ethoxy-3-oxacyclohex-5-en-1-one (**18**; 47 mg, 0.16 mmol). 2-[(Trimethylsilyl)methyl]-3-acetoxy-1-propene (**1**; 47 mg, 55 μL, 0.25 mmol) was added and the reaction heated at 70 °C for 2 h. The reaction mixture was cooled, diluted with 80:20 hexane–ethyl acetate (2 mL), and filtered through a silica gel plug. After evaporation of solvent, the residue was flash chromatographed (95:5 hexane–ethyl acetate) to give 38 mg (70%) of the title compound: R_f 0.60 (80:20 hexane–ethyl acetate); ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.85 (br s, 3 H), 4.15 (t, J = 3.3 Hz, 1 H), 3.90 (m, 3 H), 3.85 (m, 1 H), 3.54 (m, 1 H), 3.02–2.85 (m, 2 H), 2.58 (m, 1 H), 2.46–2.28 (m, 3 H), 1.22 (t, J = 7.0 Hz, 3 H), 0.84 (s, 9 H), 0.03 (s, 6 H); ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.84 (br s, 2 H), 4.58 (s, 1 H), 4.14 (t, J = 4.1 Hz, 1 H), 3.96 (m, 2 H), 3.70 (m, 1 H), 3.28 (m, 1 H), 3.09 (d, J = 17.0 Hz, 1 H), 2.73 (m, 1 H), 2.38 (m, 2 H), 2.12 (m, 2 H), 1.07 (t, J = 7.0 Hz, 3 H), 0.94 (s, 9 H), 0.06 (s, 6 H); ^{12}C NMR (125 MHz, $CDCl_3$) δ 208.6, 148.2, 106.7, 98.2, 75.7, 47.8, 45.8, 36.1, 33.4, 25.9, 18.4, 15.0, −5.4; IR ($CDCl_3$) 1720, 1663, 1471, 1375, 1361, 887, 836 cm^{-1}; MS calculated for $C_{14}H_{23}SiO_4$ ($M^+ - C_4H_9$) m/e 283.1366, found 283.1372.

Spiro[[5(S)-[(benzoyloxy)methyl]-7(S)-ethoxy-2-methylene-6-oxa-3a(R),7a(S)-perhydroindane]-4,2′(R)-(4′-methylenetetrahydrofuran)] (8). Palladium acetate (4 mg, 18 μmol) and 2-[[benzoyloxy)methyl]-4-ethoxy-3-oxacyclohex-5-en-1-one[24] (**6**; 86 mg, 0.31 mmol) in THF (1 mL) was heated at reflux until homogeneous. Triisopropyl phosphite (20 mg, 24 μL, 97 μmol) was rapidly introduced and the solution became nearly clear. 2-(Trimethylsilyl)-3-acetoxy-1-propene (**1**; 113 mg, 130 μL, 0.61 mmol) was then added in three equal portions over a period of 4 h. After refluxing overnight, the solution was cooled and diluted with 80:20 hexane–ethyl acetate (2 mL). Filtration through a silica gel plug, solvent removal, and flash chromatography (90:10 hexane–ethyl acetate) of the residue provided two products. The most polar (4 mg, 4%) of these was the monoadduct (see next experimental procedure). Collection of the high R_f spot yielded 65 mg (54%) of the title compound: R_f 0.41 (90:10 hexane–ethyl acetate: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 6.8 Hz, 1 H), 7.53 (m, 1 H), 7.40 (m, 1 H), 5.03 (br s, 1 H), 4.97 (br s, 1 H), 4.83 (s, 1 H), 4.81 (br s, 1 H), 4.62 (dd, J = 11.3, 2.1 Hz, 1 H), 4.43

(br d, J = 12.9 Hz, 1 H), 4.39 (br d, J = 12.9 Hz, 1 H), 4.20 (dd, J = 11.3, 8.1 Hz, 1 H), 4.06 (dd, J = 8.1, 2.1 Hz, H), 3.75 (dq, J = 9.8, 7.0 Hz, 1 H), 3.44 (dq, J = 9.8, 7.0 Hz, 1 H), 2.71 (br d, J = 16.8 Hz, 1 H), 2.68 (br t, J = 15.0 Hz, 1 H), 2.58 (br d, J = 16.8 Hz, 1 H), 2.45–2.30 (m, 2 H), 2.18 (dt, J = 12.9, 7.4 Hz, 1 H), 1.10 (t, J = 7.3 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz) 166.3, 151.4, 147.4, 132.8, 104.9, 104.3, 98.2, 83.0, 74.2, 72.9, 64.9, 62.7, 44.4, 44.0, 40.6, 36.1, 34.6, 15.6; IR ($CHCl_3$) 1715 cm^{-1}.

5(*S*)-[(Benzoyloxy)methyl]-7(*S*)-ethoxy-2-methylene-4-oxo-6-oxa-3a(*R*),7a(*S*)-perhydroindane (7). Tetrakis(triphenylphosphine)palladium (2 mg, 17 μmol), triphenylphosphine (10 mg, 38 μmol), and 2-[(benzoyloxy)methyl]-4-ethoxy-3-oxacyclohex-5-en-1-one[24] (**6** 66 mg, 0.25 mmol) in THF (0.5 mL) were heated at reflux until homogeneous. 2-(Trimethylsilyl)-3-acetoxy-1-propene (**1**; 56 mg, 65 μL, 0.30 mmol) was then added and reflux maintained. The reaction was followed very carefully by TLC and stopped as soon as the bisadduct became visible (~4 h). The solution was cooled and diluted with 80:20 hexane–ethyl acetate (2 mL). Filtration through a silica gel plug, solvent removal in vacuo, and flash chromatography (97:3 hexane–ethyl acetate) of the residue provided 19 mg of starting material (29%) and 42 mg (50%, 70% based on recovered starting material) of the desired product: R_f 0.18 (90:10 hexane–ethyl acetate; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.1 Hz, 2 H), 7.54 (t, J = 7.4 Hz, 1 H), 7.40 (t, J = 7.3 Hz, 2 H), 4.92 (br s, 2 H), 4.90 (s, 1 H), 4.73 (dd, J = 11.4, 2.7 Hz, 1 H), 4.58 (dd, J = 11.4, 5.6 Hz, 1 H), 4.54 (m, 1 H), 3.83 (dq, J = 9.8, 7.0 Hz, 1 H), 3.59 (dq, J = 9.8, 7.0 Hz, 1 H), 3.06 (m, 2 H), 3.69 (dt, J = 12.2, 10.9 Hz, 1 H), 2.49 (dd, J = 16.0, 7.9 Hz, 1 H), 2.40 (m, 2 H), 1.25 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.0, 170.3, 147.5, 133.0, 129.8, 129.6, 128.3, 107.4, 97.8, 72.1, 63.5, 63.0, 47.8, 46.0, 35.3, 33.2, 15.0; IR ($CDCl_3$) 1722, 1605, 1451, 1378, 1317, 889 cm^{-1}; Ms calculated for $C_{19}H_{22}O_5$ m/e 330.1467, found 330.1450.

Spiro[[2-(*R*)-[(benzoyloxy)methyl]-4-(*R*)-ethoxy-3-oxacyclohexane]-1,2′-(*S*)-(4′-methylenetetrahydrofuran)] (23, Major Isomer) and Spiro[[2-(*R*)-[(benzoyloxy)methyl]-4-(*R*)-ethoxy-3-oxacyclohexane]-1,2′-(*R*)-(4′-methylenetetrahydrofuran)] (24, Minor Isomer). To 2-(*R*)-[(benzyloxy)methyl]-4-(*R*)-ethoxy-3-oxacyclohexan-1-one (**21**; 104 mg, 0.374 mmol) was added a solution of dibenzylideneacetone–palladium(0)–chloroform complex (10 mg, 10 μmol), triphenylphosphine (30 mg, 115 μmol), and tributyltin acetate (35 mg, 100 μmol) in THF (1.5 mL) followed by 2-[(trimethylsilyl)methyl]-3-acetoxy-1-propene (**1**; 75 μL, 70 mg, 0.40 mmol). Twice during the reflux period of 5 h, additional TMM precursor (30 μL) was added. At this time TLC showed the reaction was complete. The solution was diluted with a 4:1 mixture of hexane–ethyl acetate and filtered through a silica gel plug, and the solvent was removed. Careful flash chromatography (95:5 hexane–ethyl acetate) gives the separated adducts; major isomer, 59 mg (48%); minor isomer, 39 mg (32%). Major isomer: R_f 0.32 (90:10 hexane–ethyl acetate); ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.05 (d, J = 7.1 Hz, 2 H), 7.54 (t, J = 7.1 Hz, 1 H), 7.44 (t, J = 7.1 Hz, 2 H), 5.01 (t, J = 2.1 Hz, 1 H), 4.97 (t, J = 2.1 Hz, 1 H), 4.92 (d, J = 2.1 Hz, 1 H), 4.67 (dd, J = 11.7, 2.5 Hz, 1 H), 4.42 (br s, 2 H), 4.29 (dd, J = 11.7, 7.9 Hz, 1 H), 4.12 (dd, J = 7.9, 2.5 Hz, 1 H), 3.74 (m, 1 H), 3.49 (m, 1 H), 2.80 (d, J = 16.1 Hz, 1 H), 2.37 (d, J = 16.1 Hz, 1 H), 2.11 (m, 1 H), 1.90 (m, 1 H), 1.78 (m, 1 H), 1.62 (m, 1 H), 1.20 (t, J = 2.1 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 146.5, 132.9, 130.1, 129.6, 129.5, 128.3, 105.5, 96.1, 80.5, 72.3, 71.0, 64.4, 62.5, 41.0, 29.4, 26.4, 15.1; IR ($CDCl_3$) 1716, 1600, 1448, 1271, cm^{-1}; MS calculated for $C_{19}H_{24}O_5$ m/e 332.1624, found 332.1638. Minor isomer: R_f 0.34 (90:10 hexane–ethyl acetate); ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.02 (d, J = 7.0 Hz, 2 H), 7.54 (t, J = 7.0 Hz, 1 H), 7.42 (t, J = 7.0 Hz, 2 H), 5.02 (t, J = 2.0 Hz, 1 H), 4.94 (t, J = 2.0 Hz, 1 H), 4.82 (d, J = 3.2 Hz, 1 H), 4.50–4.32 (m, 3 H), 4.20 (dd, J = 8.4, 2.3 Hz, 1 H), 3.79 (m, 1 H), 3.45 (m, 1 H), 2.81 (br d, J = 16.0 Hz, 1 H), 2.47 (br d, J = 16.0 Hz, 1 H), 2.07 (m, 1 H), 1.90 (m, 1 H), 1.80–1.61 (m, 2 H), 1.21 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 146.9, 132.8, 130.1, 129.5, 128.2, 105.7, 95.7, 81.3, 71.8, 70.7, 63.8, 62.1, 36.4, 31.8, 29.1, 15.0; IR ($CDCl_3$) 1710, 1599, 1448, 1274 cm^{-1}; MS calculated for $C_{19}H_{24}O_5$ m/e 332.1324, found 332.1636. Anal. Calcd for $C_{19}H_{24}O_5$: C, 68.65; H, 7.18. Found: C, 68.79; H, 7.33.

7(*R)-[(*tert*-Butyldimethylsilyl)oxy]-5-(*R**)-isopropyl-2-methylene-4-oxo-6-oxa-3a(*R**),7a(*S**)-perhydroindane (26).** To a homogeneous solution of palladium acetate (4.8 mg, 21.4 μmol) and triphenylphosphine (34 mg, 130 μmol) in THF (1.2 mL) was added *n*-butyllithium (25 μL, 1.4 M in hexane, 35 μmol).[17] After 5 min, the mixture was added to 4(*S**)-[(*tert*-butyldimethylsilyl)oxy]-2(*R**)-isopropyl-3-oxacyclohex-5-en-6-one (**25**; 103 mg, 0.373 mmol). 2-[(Trimethylsilyl)methyl]-3-acetoxy-1-propene (**1**; 110 μL, 0.50 mmol) was added and the solution refluxed until TLC showed no starting material remained. An additional portion of the TMM precursor (20 μL, 0.1 mmol) was necessary to force the reaction to completion (4 h total reaction time). The reaction mixture was worked up by cooling to room temperature, diluting with 80:20 hexane–ethyl acetate, and filtrating through a silica gel plug. Concentration and flash chromatography (95:5 hexane–ethyl acetate) gave 116 mg (94%) of the title compound as a clear oil: R_f 0.40 (90:10 hexane–ethyl acetate); ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.34 (d, J = 2.3 Hz, 1 H), 4.86 (m, 2 H), 3.68 (d, J = 4.2 Hz, 1 H), 2.92 (d, J = 16.2 Hz, 1 H), 2.78–2.70 (m, 2 H), 2.51–2.25 (m, 4 H), 1.00 (d, J = 6.8 Hz, 3 H), 0.90 (s, 9 H), 0.87 (d, J = 6.8 Hz, 3 H), 0.13 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.7, 148.8, 100.5, 95.3, 84.6, 49.4, 47.3, 34.1, 31.5, 28.2, 25.8, 19.8, 17.9, 17.0, −3.9, −5.4; IR ($CDCl_3$) 1713, 1460, 1380, 1367, 832 cm^{-1}; MS calculated for $C_{18}H_{32}SiO_3$ m/e 324.2121, found 324.2110.

7-(Benzyloxy)-2-methylene-4-oxo-6-oxaperhydroindane (30) and Spiro[[4(*R)-(benzyloxy)-3-oxacyclohex-5-ene]-1,2′(*S**)-(4-methylenetetrahydrofuran)] (31).** Following the procedure for the cycloaddition to **21**, dibenzylideneacetone–palladium(0)–chloroform complex (5 mg, 4.8 μmol), triphenylphosphine (15 mg, 57 μmol), tributyltin acetate (20 mg, 57 μmol), 4-(benzyloxy)-3-oxacyclohex-5-en-1-one (**29**; 56 mg, 0.254 mmol), and 2-[(trimethylsilyl)methyl]-3-acetoxy-1-propene (**1**; 93 mg, 110 μL, 0.50 mmol) in 1.0 mL of tetrahydrofuran were heated at 70 °C for 6 h. At this time TLC showed no starting material remained. The reaction mixture was cooled, diluted with 80:20 hexane–ethyl acetate (2 mL), and flash chromatographed (95:5 hexane–ethyl acetate) to give 47 mg (58%) of a 2:1 mixture of olefin cycloadduct and carbonyl cycloadduct. These were separated by preparative thin layer chromatography (90:10 hexane–ethyl acetate). Olefin cycloadduct: R_f 0.42 (90:10 hexane–ethyl acetate); ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.38–7.28 (m, 5 H), 4.89 (m, 2 H), 4.85 (d, J = 2.0 Hz, 1 H), 4.80 (d, J = 12.0 Hz, 1 H), 4.58 (d, J = 12.0 Hz, 1 H), 4.23 (d, J = 16.3 Hz, 1 H), 3.92 (d, J = 16.3 Hz, 1 H), 3.03 (td, J = 8.4, 3.2 Hz, 1 H), 2.92 (br d, J = 16.7 Hz, 1 H), 2.70 (q, J = 8.0 Hz, 1 H), 2.54–2.26 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.6, 147.7, 137.2, 128.5, 127.9, 127.8, 107.2, 97.9, 69.6, 66.8, 47.6, 45.0, 35.6, 33.7; IR ($CDCl_3$) 3010, 2910, 1720, 1055, 1025, 892 cm^{-1}; MS calculated for $C_{16}H_{18}O_3$ m/e 258.1256, found 258.1248. Carbonyl cycloadduct: R_f 0.45 (90:10 hexane–ethyl acetate); ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.39–7.27 (m, 5 H), 5.98 (d, J = 10.2 Hz, 1 H), 5.75 (dd, J = 10.2, 2.6 Hz, 1 H), 5.06 (br s, 1 H), 5.01 (d, J = 2.6 Hz, 1 H), 4.98 (br s, 1 H), 4.80 (d, J = 12.0 Hz, 1 H), 4.58 (d, J = 12.0 Hz, 1 H), 4.45 (br d, J = 13.1 Hz, 1 H), 4.32 (dd, J = 13.1, 1.9 Hz, 1 H), 3.87 (d, J = 10.7 Hz, 1 H), 3.49 (dd, J = 10.7, 1.5 Hz, 1 H), 2.74 (br d, J = 15.6 Hz, 1 H), 2.47 (br d, J = 15.6 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.5, 137.9, 134.3, 128.4, 127.9, 127.6, 126.2, 105.9, 93.0, 77.7, 70.5, 69.8, 64.2, 41.1; IR ($CDCl_3$) 3000, 2905, 1035, 1022 cm^{-1}; MS calculated for $C_{16}H_{18}O_3$ m/e 258.1256, found 258.1258.

Spiro[[4-(*R)-(benzyloxy)-3-oxacyclohexane]-1,2′-(*R**)-(4-methylenetetrahydrofuran)] (33, Major Isomer) and Spiro[[4-(*R**)-(benzyloxy)-3-oxacyclohexane]-1,2′(*S**)-(4-methylenetetrahydrofuran)] (34, Minor Isomer).** To a homogeneous solution of tetrakis(triphenylphosphine)palladium(0) (10 mg, 9 μmol), triphenylphosphine (5 mg, 19 μmol), and trimethyltin acetate (5 mg, 22 μmol) in 0.5 mL of THF were added 4-(benzyloxy)-3-oxacyclohexan-1-one (**32**; 26 mg, 0.126 mmol), and 2-[(trimethylsilyl)methyl]-3-acetoxy-1-propene (**1**; 24 mg, 28 mL, 0.13 mmol). After heating at 70 °C for 2 h, the reaction mixture was cooled, diluted with 80:20 hexane–ethyl acetate (4 mL), and filtered through a silica gel plug. After evaporation of solvent, the residue was flash chromatographed (95:5 hexane–ethyl acetate) to give 20 mg (56%) of the isomer derived from axial attack and 10 mg (28%) of the isomer derived from equatorial attack. Major isomer: R_f 0.45 (90:10 hexane–ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.26 (m, 5 H), 5.02 (quint, J = 2.2 Hz, 1 H), 4.94 (quint, J = 2.2 Hz, 1 H), 4.76 (d, J = 12.0 Hz, 1 H), 4.75 (s, 1 H), 4.47 (d, J = 12.0 Hz, 1 H), 4.40 (br d, J = 13.1 Hz, 1 H), 4.33 (dd, J = 13.1, 1.7 Hz, 1 H), 3.70 (d, J = 11.0 Hz, 1 H), 3.32 (dd, J = 11.0, 2.2 Hz, 1 H), 2.71 (br d, J = 14.5 Hz, 1 H), 2.37 (br d, J = 14.5 Hz, 1 H), 2.07 (td, J = 12.0, 4.4 Hz, 1 H), 1.90 (m, 1 H), 1.59–1.74 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 129.0, 128.4, 127.9, 127.6, 105.6, 95.8, 79.6, 7.0, 68.7, 65.8, 40.3, 30.1, 28.7; IR ($CDCl_3$) 3060, 2960, 1600, 1448, 1271, 1215, 1045, 1003 cm^{-1}; MS calculated for $C_{16}H_{20}O_3$ m/e 260.1422, found 260.1407. Minor isomer: R_f 0.38 (90:10 hexane–ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.25 (m, 5 H), 4.98 (t, J = 2.2 Hz, 1 H), 4.93 (t, J = 2.2 Hz, 1 H), 4.85 (t, J = 2.9 Hz, 1 H), 4.75 (d, J = 12.0 Hz, 1 H), 4.52 (d, J = 12.0 Hz, 1 H), 4.39 (br s, 2 H), 3.71 (d, J = 11.6 Hz, 1 H), 3.45 (dd, J = 11.6, 2.2 Hz, 1 H), 2.38 (br d, J = 15.8 Hz, 1 H), 2.31 (br d, J = 15.8 Hz, 1 H), 2.05 (m, 1 H), 1.91 (td, J = 13.1, 4.2 Hz, 1 H), 1.70 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 128.4, 127.8, 127.6, 105.2, 96.3, 79.4, 69.8, 69.0, 65.6, 41.2, 28.5, 26.9; IR ($CDCl_3$) 3030, 2960, 2921, 2866, 1600, 1457, 1440, 1128, 1035 cm^{-1}; MS calculated for $C_{16}H_{20}O_3$ m/e 260.1422, found 260.1427.

Spiro[[4(*R*)-[[(*tert*-butyldimethylsilyl)oxy]methyl]-2(*R*)-methoxy-3-oxacyclohex-5-ene]-1,2′[*R*)-(4′-methylenetetrahydrofuran)] (36). Fol-

lowing the procedure for the cycloaddition to **21** dibenzylideneacetone–palladium(0)–chloroform complex (5 mg, 5 μmol), triphenylphosphine (15 mg, 57 μmol), trimethyltin acetate (10 mg, 45 μmol), 4(*S**)-[(*tert*-butyldimethylsilyl)oxy]-2(*R**)-methoxy-3-oxacyclohex-5-en-1-one[34] (**35**; 35 mg, 0.14 mmol), and 2-[(trimethylsilyl)methyl]-3-acetoxy-1-propene (**1**; 37 mg, 43 μL, 0.20 mmol) in 0.5 mL of benzene were heated 2 h until TLC showed no starting material remained. After the usual workup and flash chromatography, there was obtained 36 mg (91%) of the title compound: R_f 0.12 (90:10 hexane–ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (s, 2 H), 4.99 (t, *J* = 2.2 Hz, 1 H), 4.93 (t, *J* = 2.2 Hz, 1 H), 4.60 (s, 1 H), 4.46 (br d, *J* = 13.4 Hz, 1 H), 4.37 (dd, *J* = 13.4, 1.6 Hz, 1 H), 4.15 (t, *J* = 5.5 Hz, 1 H), 3.68 (dd, *J* = 10.4, 5.5 Hz, 1 H), 3.59 (dd, *J* = 10.4, 5.5 Hz, 1 H), 3.49 (s, 3 H), 2.65 (br d, *J* = 15.8 Hz, 1 H), 2.50 (br d, *J* = 15.8 Hz, 1 H), 0.89 (s, 9 H), 0.06 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.5, 127.9, 127.2, 105.2, 100.3, 79.1, 70.6, 69.5, 65.6, 56.0, 43.7, 25.9, 18.3, −5.2; IR ($CDCl_3$) 2952, 2930, 2860, 1470, 1362, 1258, 1120, 1071, 1050, 839, 780 cm^{-1}; MS calculated for $C_{13}H_{21}O_4Si$ *m/e* 269.1210, found 269.1212.

4(*R*)-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-2(*R*)-methoxy-3-oxacyclohexan-1-one (37). 4-(*R*)-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-2-(*R*)-methoxy-3-oxacyclohex-2-en-1-one[34] (**35**; 65 mg, 0284 mmol) and Pd/C (10 mg) in 2 mL of ethyl acetate were stirred overnight under a balloon pressure of hydrogen. The reaction mixture was filtered through Celite, concentrated in vacuo, and flash chromatographed (90:10 hexane–ethyl acetate) to yield 61 mg (94%) of the title compound: R_f 0.50 (70:30 hexane–ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.51 (s, 1 H), 4.17 (dtd, *J* = 11.3, 5.6, 2.4 Hz, 1 H), 3.70 (dd, *J* = 10.7, 5.6 Hz, 1 H), 3.59 (dd, *J* = 10.7, 5.6 Hz, 1 H), 3.44 (s, 3 H), 2.75 (ddd, *J* = 15.0, 13.2, 6.5 Hz, 1 H), 2.41 (ddd, *J* = 15.0, 4.9, 1.7 Hz, 1 H), 2.07 (m, 1 H), 1.86 (tdd, *J* = 13.2, 11.3, 4.9 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 100.3, 69.9, 65.3, 55.1, 34.9, 29.2, 25.8, 18.3, −5.4; IR (neat) 1747, 1465, 1269, 825 cm^{-1}; MS calculated for $C_{13}H_{26}O_4Si$ *m/e* 274.1600, found 274.1601.

Spiro[4-(*R*)-[[(*tert*-butyldimethylsilyl)oxy]methyl]-2-(*R*)-methoxy-3-oxacyclohexane]-1,2′(*R*)-(4′-methylenetetrahydrofuran)] (38). Palladium acetate (3 mg, 13 μmol) and triphenylphosphine (18 mg, 68 μmol) in benzene (0.5 mL) were added to 4(*S**)-[(*tert*-butyldimethylsilyl)oxy]-2(*R**)-methoxy-3-oxacyclohexan-1-one (**37**; 27 mg, 0.10 mmol). 2-[(Trimethylsilyl)methyl]-3-acetoxy-1-propene (**1**; 26 mg, 30 μL, 0.14 mmol), was added and the solution refluxed 1 h until TLC showed no starting material remained. The reaction mixture was worked up by cooling to room temperature, diluting with 80:20 hexane–ethyl acetate, and filtering through a silica gel plug. Concentration and flash chromatography (95:5 hexane–ethyl acetate) gave 27 mg (81%) of the title compound: R_f 0.60 (70:30 hexane–ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.99 (t, *J* = 2.2 Hz, 1 H), 4.91 (t, *J* = 2.2 Hz, 1 H), 4.38 (m, 2 H), 3.76 (m, 1 H), 3.61 (dd, *J* = 10.5, 5.6 Hz, 1 H), 3.52 (dd, *J* = 10.5, 4.9 Hz, 1 H), 3.41 (s, 3 H), 2.71 (br d, *J* = 16.3 Hz, 1 H), 2.46 (br d, *J* = 16.3 Hz, 1 H), 2.08 (td, *J* = 12.8, 4.5 Hz, 1 H), 1.70 (br d, *J* = 13.5 Hz, 1 H), 1.61 (br d, *J* = 12.3 Hz, 1 H), 1.35 (m, 1 H), 0.89 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 106.5, 100.4, 70.0, 69.5, 66.3, 65.6, 55.1, 40.9, 29.3, 26.4, 25.7, 18.5, −5.5; IR ($CDCl_3$) 2957, 2935, 2873, 1476, 1369, 1258, 1141, 1078, 1027, 831, 760 cm^{-1}; MS calculated for $C_{13}H_{23}O_4Si$ ($M^+ - C_4H_9$) *m/e* 271.1366, found 271.1372.

Spiro[(4(*R)-(2-phenylethyl)-3,5-dioxane)1,2′(*R**)-(4′-methylenetetrahydrofuran)] (41).** A 1-mL aliquot of a catalyst solution prepared from dibenzylideneacetone–palladium(0)–chloroform complex (30 mg, 29 μmol) and triphenylphosphine (76 mg, 300 μmol) in THF (2.5 mL) was added to 4-(2-phenethyl)-3,5-dioxan-1-one (**40**; 79 mg, 0.385 mmol). 2-[(Trimethylsilyl)methyl]-3-acetoxy-1-propene (**1**; 93 mg, 110 μL, 0.50 mmol) was added and the mixture stirred for 30 min. After the usual workup and flash chromatography, there was obtained 59 mg (59%) of the title compound as a clear liquid: R_f 0.41 (90:10 hexane–ethyl acetate); ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.31–7.17 (m, 5 H), 5.08 (t, *J* = 2.2 Hz, 1 H), 4.97 (t, *J* = 2.2 Hz, 1 H), 4.45 (t, *J* = 5.1 Hz, 1 H), 4.34 (br s, 2 H), 3.81 (d, *J* = 10.1 Hz, 1 H), 3.55 (d, *J* = 10.1 Hz, 1 H), 2.78 (br s, 2 H), 2.72 (dd, *J* = 9.7, 9.0 Hz, 2 H), 1.93 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.2, 141.5, 137.5, 128.4, 125.8, 106.3, 101.4, 75.8, 73.4, 70.8, 40.8, 35.9, 30.2; IR ($CDCl_3$) 2951, 2851, 1446, 1242, 1121, 1053, 1033 cm^{-1}; MS calculated for $C_{16}H_{20}O_3$ *m/e* 260.1412, found 260.1416.

2-(2′-Benzofuryl)-2-phenyl-4-methylenetetrahydrofuran (43). Following our usual procedure, palladium acetate (1.7 mg, 7.5 μmol), triphenylphosphine (13.9 mg, 53 μmol), 2-benzoylfuran (33.3 mg, 0.15 mmol), and 2-[(trimethylsilyl)methyl]-3-acetoxy-1-propene (43.5 mg, 0.23 mmol) in 0.5 mL of toluene at 100 °C were stirred 22 h, although TLC monitoring revealed reaction was almost complete after 4 h. After the usual workup and flash chromatography, there was obtained 33 mg (80%) of the title compound: ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.58–7.17 (m, 9 H), 6.58 (s, 1 H), 5.11–5.07 (m, 1 H), 4.97–4.93 (m, 1 H), 4.94–4.60 (AB system, J_{AB} = 14.3 Hz, 2 H), 3.64–3.10 (AB system, J_{AB} = 13.7, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.2, 155.2, 146.6, 142.4, 128.2 (2 C), 128.0, 127.6, 125.7 (2 C), 124.1, 122.6, 121.0, 111.4, 105.0, 104.3, 84.5, 70.6, 44.5; IR ($CDCl_3$) 3043, 3018, 2901, 2848, 1662, 1448, 1248, 1160, 1035 cm^{-1}; MS calculated for $C_{19}H_{16}O_2$ *m/e* 276.1150, found 276.1147.

2-Methyl-2-(phenylethynyl)-4-methylenetetrahydrofuran (45). Following our usual procedure, palladium acetate (1.7 mg, 7.5 μmol), triphenylphosphine (13.9 mg, 53 μmol), 1-phenyl-1-butyn-3-one (21.6 mg, 0.15 mmol), tri-*n*-butyltin acetate (20.0 mg, 57 μmol), and 2-[(trimethylsilyl)methyl]-3-acetoxy-1-propane (33.5 mg, 0.18 mmol) in 0.5 mL of dioxane at 100 °C were heated for 8 h, although monitoring the reaction revealed it was almost complete after 3.5 h. Direct flash chromatography of the reaction mixture (9:1 hexane–ethyl acetate) gave 18 mg (61%) of the pure title compound: R_f 0.42 (9:1 hexane–ethyl acetate; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.43–7.38 (m, 2 H, Ph), 7.33–7.24 (m, 3 H, Ph), 5.05–5.02 (narrow m, 1 H), 4.98–4.95 (narrow m, 1 H), 4.57–4.41 (AB system, J_{AB} = 13.0 Hz, 2 H), 2.96–2.56 (AB system, J_{AB} = 15.0 Hz, 2 H), 1.67 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 147.3, 131.7 (2 C), 128.2, 128.1 (2 C), 122.7, 104.9, 91.1, 83.5, 76.8, 70.3, 46.9, 27.2; IR ($CDCl_3$) 3082, 2979, 2951, 2922, 2861, 2241, 1489, 1290, 1026 cm^{-1}. Anal. Calcd for $C_{14}H_{14}O$: C, 84.80; H, 7.10; MW, 198.1045. Found: C, 85.07, H, 7.14; MW, 198.1045.

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Supplementary Material Available: General experimental procedures, reaction details for cycloadditions for Table I, entries 2–4, and Table II, entries 2–7 and 9, and preparation of substrates **21**, **25**, **29**, **32**, **40**, and **42** (8 pages). Ordering information is given on any current masthead.