An Approach toward the Illudin Family of Sesquiterpenes Using the Tandem Cyclization−Cycloaddition Reaction of Rhodium Carbenoids

Albert Padwa,* Erin A. Curtis, and Vincent P. Sandanayaka[†]

Department of Chemistry, Emory University, Atlanta, Georgia 30322

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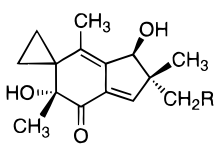
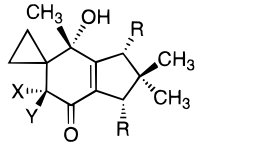
The Rh(II)-catalyzed reaction of 1-acetyl-1-(diazoacetyl)cyclopropane with 5,5-dimethylcyclopentenone afforded the product of a 1,3-dipolar cycloaddition in high yield. The reaction involves formation of a rhodium carbenoid and subsequent transannular cyclization of the electrophilic carbon onto the adjacent keto group to generate a five-membered cyclic carbonyl ylide which undergoes a subsequent 1,3-dipolar cycloaddition reaction. The regiochemical results encountered can be rationalized on the basis of FMO considerations. Treatment of the cycloadduct with *p*-toluenesulfonic acid results in loss of water followed by a subsequent acid-catalyzed cyclopropyl ketone rearrangement to give dihydrobenzofuran **21**. The product distribution derived from the SmI_2-induced reduction of the dipolar cycloadduct was found to depend on the reaction conditions. Under kinetic conditions, the reduction resulted in opening of the cyclopropyl ring adjacent to the carbonyl group. However, under thermodynamic conditions, cleavage of the oxy bridge corresponded to the major pathway. The cycloaddition−reduction protocol provides a rapid assembly of the basic core unit of ptaquilosin having most of the functionality in place. Generation of a carbanion adjacent to the oxy bridge leads to opening of the oxabicyclic ring system in a highly regioselective manner. A short synthesis of (±)-illudin M and the closely related isodehydroilludin M is described in which the key step involves a dipolar cycloaddition using a carbonyl ylide.

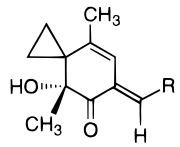
Illudins M (**1**) and S (**2**) are extremely toxic sesquiterpenes produced by *Omphalotus illudens*, the jack-o'-lantern mushroom.[1−4] Recently, two new members of this family (**3** and **4**) have been isolated from a closely related fungus.[5] The illudins and certain derivatives have been evaluated for antitumor activity at the NCI and show selective toxicity for human myelocytic leukemia and other carcinoma cells of various species of origin.[6] Most of the existing illudin analogs in the literature have been derived from the natural products.[7−9] The spirocyclopropane and α,β-unsaturated ketone present in the illudin skeleton constitutes a bis-electrophile that is undoubtedly responsible for the DNA damage.[10] Some simpler illudin analogs such as the dehydroilludins M (**5**) as well as isodehydroilludin M (**6**) have recently been shown to possess high efficacy against a number of adenocarcinomas.[9,10]



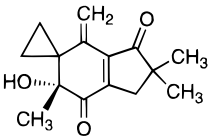
1; Illudin M (R=H)
2; Illudin S (R=OH)



3; Illudin A (R=H, X=OH, Y=CH_3)
4; Illudin B (R=OH, X=CH_3,Y=OH)



5; R=Cl, CH_3, aryl



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A number of compounds related to the illudin family have also been isolated from the bracken fern *Pteridium aquilinium*.[11] This fern is widely distributed throughout the world and its lethal properties toward cattle was first reported in the late 19th century.[12] Cattle which consume bracken fern exhibit the syndrome known as "*cattle bracken poisoning*", the features of which include hemorrhage, anorexia, extensive intestine damage, ulceration, and pyrexia.[11,12] Epidemiological studies provide evidence that esophageal cancer in Japan is correlated with the consumption of bracken.[13] In 1983 the Yamada group

[†] Current address: Wyeth-Ayerst Research Lederle Laboratories, 401 N. Middletown Rd., Pearl River, NY 10965.

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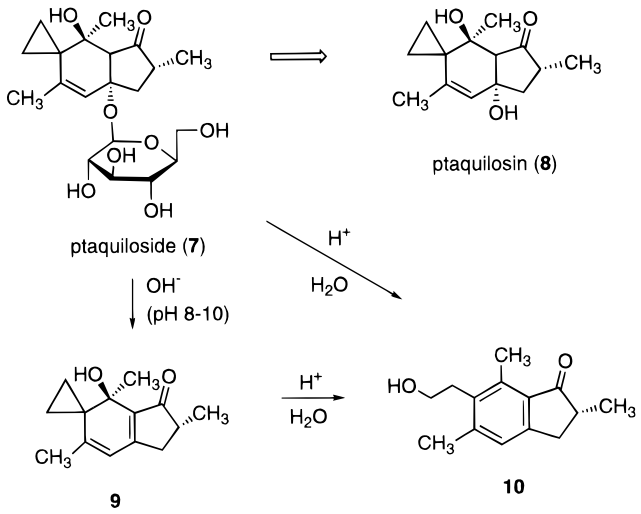
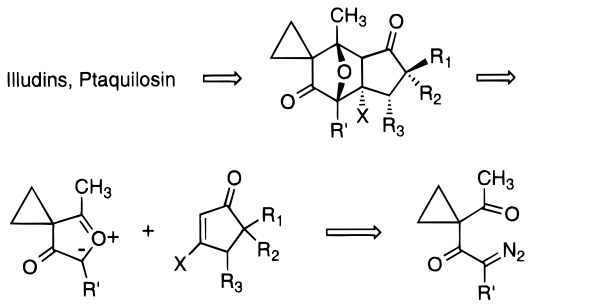
Scheme 1



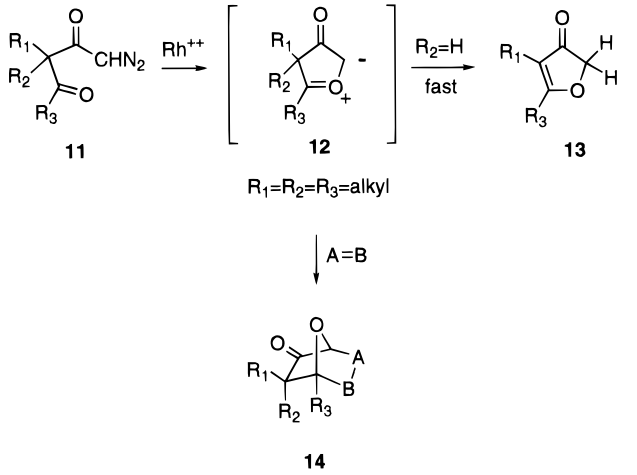
isolated a carcinogen ptaquiloside (**7**) from bracken fern,[14] elucidated its structure,[15] and established its carcinogenicity.[16] The ultimate carcinogen derived from ptaquilosine (**8**), the aglycon of ptaquiloside, is dienone **9** which acts as a powerful alkylating agent toward amino acids and nucleic acid bases, and it causes cleavage of DNA.[17,18] Ptaquiloside (**7**) was found to be unstable in both acidic and basic solution at 25 °C and was converted to pterosin B (**10**).[18] Yamada and co-workers demonstrated that ptaquiloside can be readily transformed into dienone **9** by elimination of D-(+)-glucose under basic conditions.[14,18] Dienone **9** is rapidly converted to **10** under weakly acidic conditions (Scheme 1).[14,18]

As a consequence of their biological activity, it is not surprising that these compounds have received considerable attention as synthetic targets. The total synthesis of (±)-illudin M was first achieved by Matsumoto in 1968.[19,20] Kigoshi and co-workers reported the total synthesis of (−)-ptaquilosin (**8**) in 1993 in 20 steps (2.9% overall yield).[21] In light of the interest in this class of antitumor agents, we undertook a study designed to provide a general means for the synthesis of the core skeleton of these molecules.[22] In addition, because of their extreme toxicity and consequent low therapeutic index, it seemed reasonable to us to modify the basic skeleton so as to reduce cytotoxicity without compromising antitumor activity.[23] Specifically, we envisioned the use of a dipolar cycloaddition reaction of a cyclic carbonyl ylide dipole as the key step for the construction of the illudin/ptaquilosin skeleton.[22] This strategy provides for a rapid assembly of the basic core unit of the target molecules having most of the functionality in place (Scheme 2). As shown in the retrosynthetic scheme, opening of the oxy bridge of the cycloadduct would ultimately lead to the core structure of the target molecules in a highly convergent manner. In this paper, we detail the extension of our tandem cyclization−cycloaddition chemistry of rhodium carbenoids[24] toward a synthesis of (±)-illudin M (**1**) and the closely related isodehydroilludin M (**6**).

Scheme 2



Scheme 3



Results and Discussion

Earlier reports from this laboratory have described the formation of cyclic carbonyl ylides by a process involving a transannular cyclization of an electrophilic rhodium carbenoid onto an adjacent carbonyl group.[24,25] Five-membered-ring carbonyl ylides were generated by treating 1-diazobutanediones with rhodium(II) carboxylates (Scheme 3).[26] However, it was necessary to block the α-position of the 1-diazobutanedione with two substituent groups in order for the cycloaddition to occur. When only a single substituent group was present, the five-membered dipole was found to undergo proton transfer at a faster rate than bimolecular dipolar cycloaddition, leading to furanones of type **13**.[26] The formation of furanone **13** is not surprising as one of the characteristic reactions

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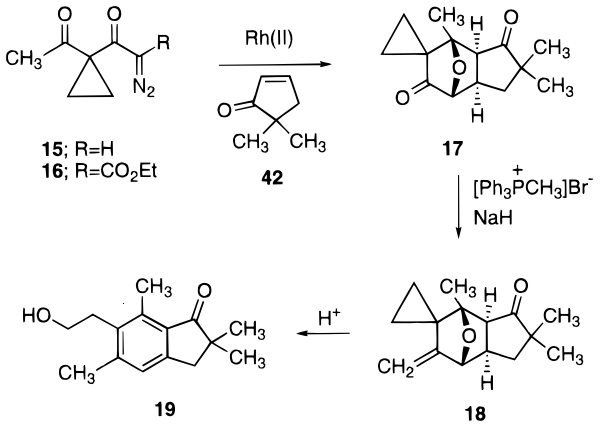
Scheme 4

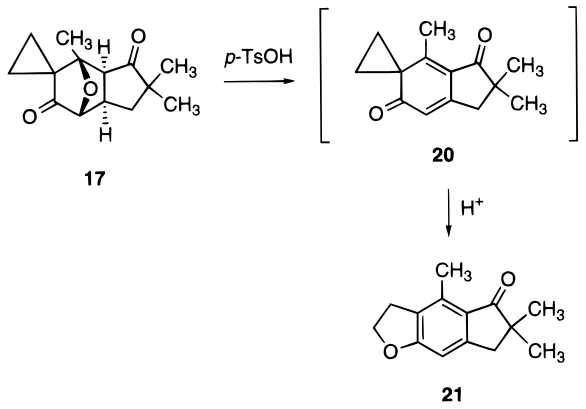


of carbonyl ylides derived from the reaction of α-diazoalkanes with ketones consists of intramolecular proton transfer.[27−29] During the course of these studies we discovered that the Rh(II) catalyzed reaction of cyclopropyl substituted α-diazo ketones **15** and **16** resulted in a smooth cycloaddition to a variety of acyclic and cyclic alkenes.[22] This dipolar cycloaddition strategy was successfully applied toward the synthesis of several members of the pterosin family of sesquiterpenes by converting the initial cycloadduct **17** (R = H) to the corresponding methylene derivative **18**, followed by a subsequent acid-catalyzed cyclopropyl ring opening reaction to give **19** (Scheme 4).[30]

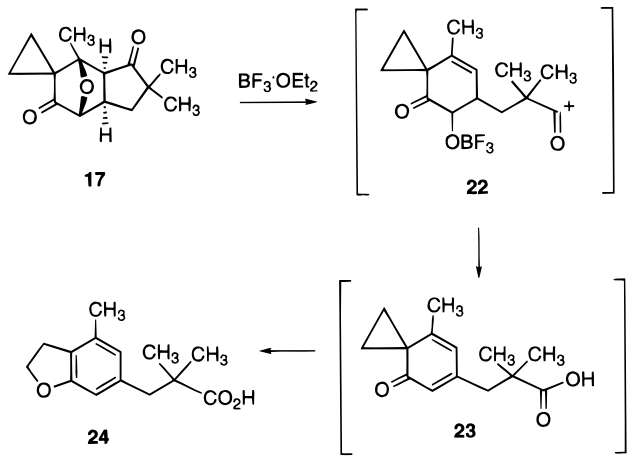
Having established that the tandem cyclization−cycloaddition reaction of α-diazo ketones **15** and **16** occurred with ease, we next turned our attention to the oxy-bridge ring cleavage. Several issues emerged at the outset of these investigations: (1) what type of reagents work best, (2) how to control the regioselectivity of the cleavage reaction and, (3) the possiblity of keeping the labile spiro cyclopropyl ring intact. Translation of the stereochemical features present in the oxybicyclic framework of the dipolar cycloadduct **17** to the stereochemistry of the illudin/ptalquilosin family of sesquiterpenes was a major objective of our studies. We therefore initiated an investigation dealing with the cleavage reaction of several of the dipolar cycloadducts with various reagents, to eventually give products belonging to the illudin/ptalquilosin family.

Our initial studies focused on the acid-catalyzed reaction of spirotricyclodecanone **17**. Treatment of **17** with *p*-toluenesulfonic acid afforded dihydrobenzofuran **21** in 70% yield. The formation of **21** proceeds by an initial oxy-bridge ring opening followed by a subsequent dehydration to give **20** as a nonisolable intermediate which reacts further by an acid-catalyzed cyclopropyl ketone rearrangement (Scheme 5).[31−33] The facility of the process is undoubtedly related to the aromaticity gained in the final step. Interestingly, when **17** was treated with

Scheme 5



Scheme 6



$BF_3{\cdot}OEt_2$, the only product isolated (50%) corresponded to the unexpected carboxylic acid **24** (Scheme 6). More than likely, this compound is derived by a Lewis acid-induced C−C bond cleavage to generate the acylium cation **22** which is converted to dienone **23** and then to the rearranged acid **24**.

Since the acid-induced opening of the dipolar cycloadduct destroyed the cyclopropyl ring, we opted to study other reagents capable of cleaving the oxabicyclic ring system. In recent years, samarium(II) iodide has emerged as a powerful, yet highly selective, reducing agent.[34] Molander has utilized the selective nature of SmI_2 to effect reduction of functionalized vinyloxirane derivatives,[35] and these results prompted us to explore the use of this reagent in the present study. Overwhelming evidence suggests that free radicals are formed during SmI_2 reductions.[34] Consequently, a major concern associated with the planned illudin/ptaquilosin approach was that the cyclopropyl ring present in the dipolar cycloadduct would be cleaved when treated with SmI_2.[36] Indeed, treatment of cycloadduct **25** with SmI_2/THF/MeOH at −78 °C produced the cyclopropyl ring-opened

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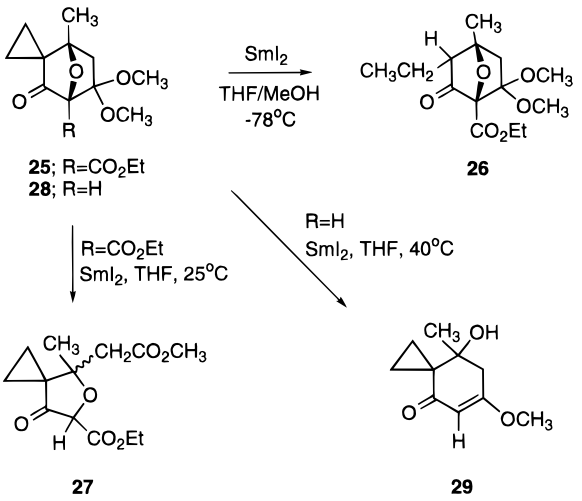
Scheme 7



product **26** in 61% yield (2:1 mixture of diastereomers) (Scheme 7). Apparently, the SmI_2−MeOH combination is a sufficiently powerful reducing agent that rapidly donates an additional electron to the putative ring-opened carbon-centered radical, thereby generating an organosamarium intermediate that is irreversibly protonated.

Cyclopropyl ketyl anions, whose only substituents on the cyclopropyl ring are alkyl or hydrogen, are known to undergo a reversible ring-opening reaction.[37] This observation suggested that if the SmI_2-promoted cyclopropyl carbinyl ketyl ring opening reaction proceeded under kinetic control, then cleavage of the oxy bridge might occur under thermodynamic conditions. Toward this end, we examined the SmI_2-induced reaction of **25** without MeOH (proton source) at 25 °C. However, the only product formed corresponded to furanone **27** (5:1 mixture of diastereomers, 85%). Under these conditions, SmI_2 acts as a Lewis acid[34] and induces a retro-Claisen-type fragmentation *via* a dimethoxy carbenium ion. In support of this suggestion, the reaction of **25** with 1 equiv of $SnCl_2$ gave **27** in 79% yield. Realizing that the presence of the carbethoxy group promotes the retro-Claisen fragmentation, we turned our attention to cycloadduct **28** wherein the ester functionality is replaced by a hydrogen. As indicated in Scheme 7, this substrate underwent efficient oxy bridge ring opening to give **29** (62%) when treated with SmI_2 in THF at 40 °C. No signs of any cyclopropyl ring opened product was detected in the crude reaction mixture. Under thermodynamic conditions, cleavage of the oxy bridge is followed by a subsequent elimination of methoxide from the resulting samarium enolate, producing **29** as the exclusive product. An alternate explanation, which is also consistent with the product crossover, assumes that SmI_2 is less strongly solvated in THF and therefore is a more selective reducing agent with respect to C−O bond cleavage. Indeed, the reducing power of SmI_2 has been shown to be closely related to the coordinating power of the reaction medium.[38]

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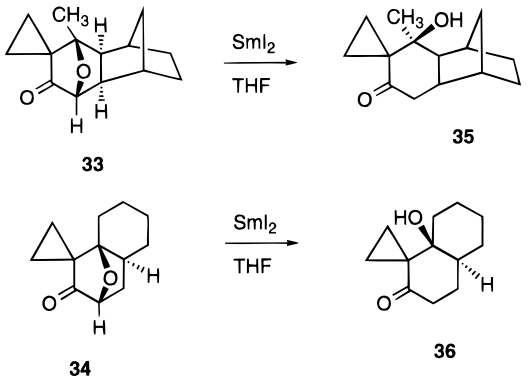
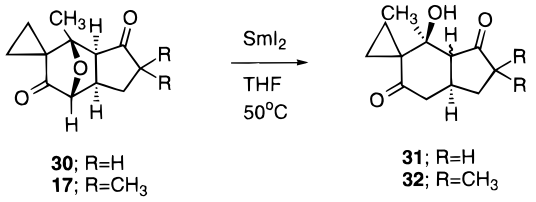
Scheme 8



Several other SmI_2 induced ring-opening reactions were carried out to further demonstrate the scope and generality of the oxy bridge cleavage reaction. Thus, treatment of cycloadducts **30** and **17**[30] with SmI_2 at 50 °C in THF gave the desired ring-opened products **31** and **32** in 62% and 60%, respectively. In both cases, there

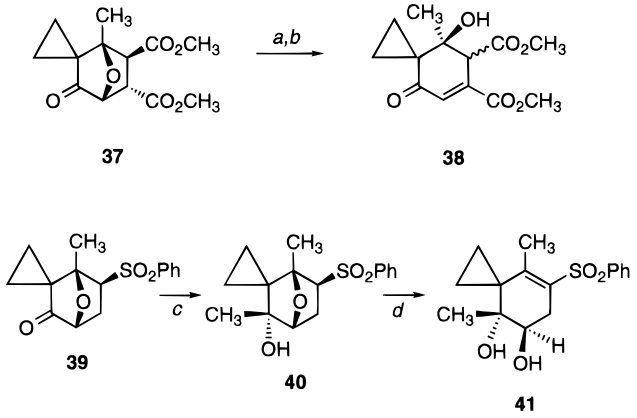


was no indication of any product(s) derived from reduction of the five-membered ring. When the dimethylated cycloadduct **17** was used, a 3:1-mixture of the *cis* and *trans* isomers of **32** was obtained. Assignment of the stereochemistry was based on ^{1}H-NMR spectral data, extensive decoupling experiments, and a 2D-NOESY experiment. Presumably, the Lewis acid character[34] of SmI_2 had resulted in the epimerization of the *cis*-isomer, although it is not evident why this did not occur with **31**.

In an analogous manner, treatment of cycloadducts **33** and **34**[30] with SmI_2 (THF, 50 °C) cleanly afforded compounds **35** and **36** in 75% and 70% yield, respectively (Scheme 8). Isolation of the spiro-cyclopropylcarbinyl alcohol **36** demonstrates the complexity of structures that can be obtained by this method. Thus, the strategy of a rhodium(II)-catalyzed cyclization−cycloaddition reaction followed by reductive cleavage of the resulting cycloadduct represents an effective method for generating multiple contiguous stereocenters on polyfunctional fused ring systems. Further efforts directed toward applying this method to ptaquilosin (**8**) are currently underway in our laboratory.

The generation of a carbanion adjacent to the oxy bridge has also been found to result in a smooth ring opening of the 7-oxabicyclo[2.2.1]heptane ring system. Reaction of cycloadduct **37** with LDA at −78 °C produced hydroxy-enone **38** in 78% yield as a 3:1 mixture of diastereomers. Apparently, the initial ring-opened product epimerizes under the workup conditions. The Rh(II)-catalyzed reaction of diazo ketone **15** with phenyl vinyl sulfone afforded cycloadduct **39** as an 8:3 mixture of *exo*/*endo* diastereomers. The thermodynamically more stable *exo*-cycloadduct was easily obtained as a crystalline solid by silica gel chromatography of the mixture. Treatment of **39** with 1 equiv of methylmagnesium bromide resulted in attack from the less hindered *exo*-(top) face

Scheme 9

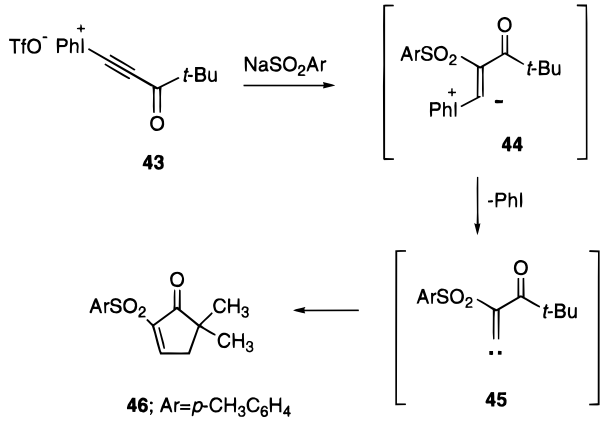


Reagents: (a) LDA, -78°C; (b) H_2O; (c) CH_3MgBr; (d) *n*-BuLi

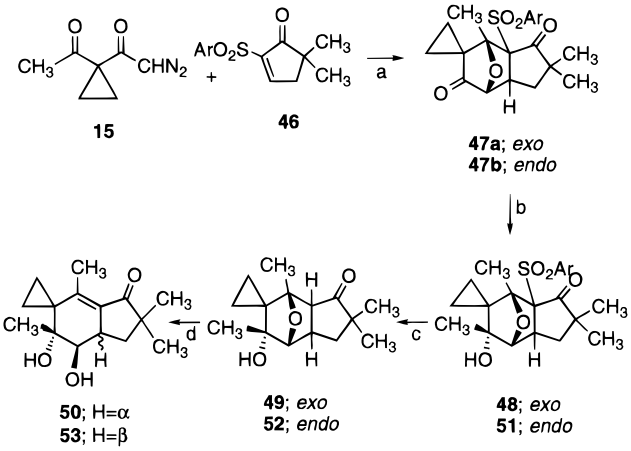
of the oxabicyclic ring leading to a single diastereomer in 80% yield. Further reaction of **40** with *n*-BuLi in THF afforded diol **41** in 70% yield (Scheme 9). This model study demonstrates that it is possible to effect a base-induced ring opening of the oxabicyclic ring with high stereoselectivity. The simplicity of the sequence and the rapid construction of adjacent stereocenters encouraged us to examine this pathway as a route to (±)-illudin M (**1**).

The Rh(II)-catalyzed cycloaddition reaction of α-diazo ketone **15** with 5,5-dimethylcyclopentenone (**42**) proceeded in only 51% yield (Scheme 4), and a significant amount of unreacted cyclopentenone was recovered.[39] We attribute the low yield to the existence of significant steric interactions of the dipole with the methyl groups of the dipolarophile in the transition state for the cycloaddition. Given the limited success of this reaction, we turned our attention to a more highly activated cyclopentenone, one that we expected would undergo the reaction with a significant rate enhancement. Earlier studies in our laboratory demonstrated that the bimolecular cycloaddition of cyclic carbonyl ylides with phenylsulfonyl-substituted alkenes was a remarkably efficient process.[40] MO calculations using the AM1 Hamiltonian reveal a small energy gap between the HOMO of the dipole and the LUMO of the phenylsulfonyl-substituted alkene. This led us to examine 2-(phenylsulfonyl)-5,5-dimethylcyclopentenone (**46**) as a surrogate for **42**, since the sulfonyl group can easily be removed by reductive desulfonylation.[41] The requisite phenylsulfonyl cyclopentenone **46** was prepared in high yield from the reaction of the iodonium salt **43** with anhydrous sodium *p*-toluenesulfinate according to the general procedure of Stang and coworkers.[42] The initially formed alkylidenecarbene **45** undergoes a subsequent intramolecular 1,5-carbon−hydrogen insertion reaction to give **46** in 73% yield (Scheme 10).

Scheme 10



Scheme 11



Reagents: (a) $Rh_2(OAc)_4$; (b) CH_3MgI; (c) Na(Hg); (d) base

The preparation and use of the required cycloadduct **47** is detailed in Scheme 11. Treatment of diazo ketone **15** with **46** in the presence of a catalytic amount of $Rh_2(OAc)_4$ afforded a 2:1-mixture of the *exo*- and *endo* cycloadducts **47** in 98% yield. The two diastereomers could easily be separated by silica gel chromatography. Reaction of the *exo*-cycloadduct **47a** with methylmagnesium iodide regiospecifically gave alcohol **48** in 90% yield where attack occurred from the less hindered *exo*-face of the oxabicyclo[2.2.1]heptane ring system. Sodium amalgam desulfonylation proceeded smoothly to give **49** in 87% yield. We were gratified to find that treatment of **49** with KOH/MeOH led to rapid oxabicyclic ring opening to afford the desired diol **50** in 80% yield. A related set of reactions occurred with the corresponding *endo*-diastereomer **47b** which ultimately gave the epimeric diol **53** in 39% overall yield from **47b**.

At this stage of the synthesis, we felt that it would be prudent to carry out the above sequence of reactions using a mixture of cycloadducts **47**. This would allow quicker assembly of (±)-illudin M (**1**) and its analogs and would also be more amenable to scale-up. The final elaboration of **50**/**53** into illudin M (**1**) consisted of a Swern oxidation to give dione **54** (5:3 mixture of diastereomers) (Scheme 12). Curiously, this compound was resistant to introduction of the double bond in the five-membered ring. The difficulty in the oxidation of **54** is presumably a result of the crowded environment about the ring juncture. Screening of a series of oxidants showed that DDQ was capable of effecting the desired

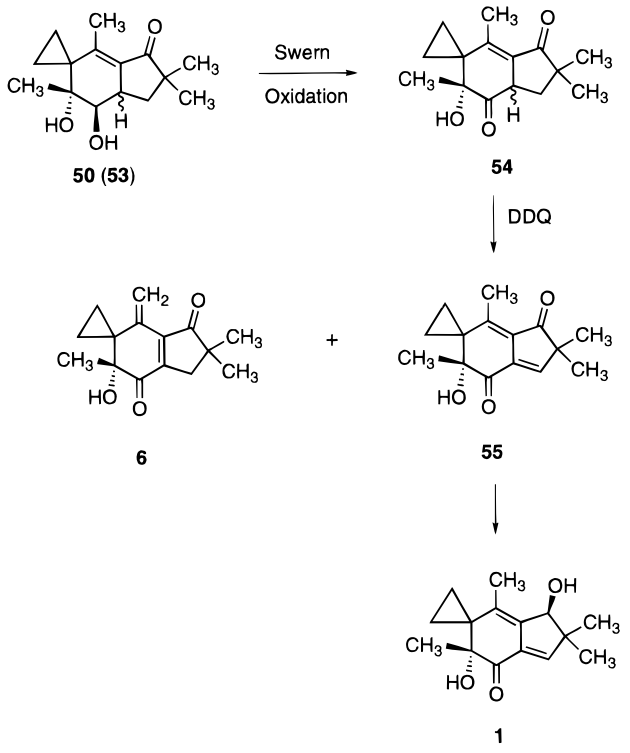
(39) The Rh(II)-catalyzed reaction of **15** with 5,5-dimethylcyclopent-2-en-1-one produced cycloadduct **17** in 80% yield when less than 0.5 g of starting material was employed. However, attempts to scale up the procedure to produce **17** in quantities greater than 1 g always resulted in a lower yield of the cycloadduct (*i.e.* 51%). An alternative method that was also investigated involved the cycloaddition of **15** with cyclopent-2-en-1-one followed by dimethylation of the resulting cycloadduct. However, the overall yield of this two-step sequence was only 54%.

(40) Padwa, A. *Acc. Chem. Res.* **1991**, *24*, 22.

(41) Smith, A. B., III; Hale, K. J.; McCauley, J. P., Jr. *Tetrahedron Lett.* **1989**, *30*, 5579.

(42) Williamson, B. L.; Stang, P. J.; Arif, A. M. *J. Am. Chem. Soc.* **1993**, *115*, 2590.

Scheme 12



transformation to dione **55** but only in 14% yield. Since dehydroilludin (M) **55** had previously been converted to (±)-illudin M,[20] its formation from **54** constitutes a formal synthesis of this unique sesquiterpene. The major product (56%) isolated from the DDQ oxidation of **54** corresponded to the isodehydroilludin M analog **6**.

In summary, the Rh(II)-catalyzed cyclization−cycloaddition methodology is amenable to the synthesis of (±)-illudin M together with the novel antitumor analog isodehydroilludin M. We are currently investigating further application of the method outlined here to related sesquiterpenes.

Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in flame-dried glassware under an atmosphere of dry nitrogen. Solutions were evaporated under reduced pressure with a rotary evaporator, and the residue was chromatographed on a silica gel column using an ethyl acetate−hexane mixture as the eluent unless specified otherwise.

Spiro[1,4,4-trimethyl-10-oxatricyclo[5.2.1.0^{2,6}]decane-3,8-dione-9,1′-cyclopropane] (17). To a solution containing 0.4 g (1.9 mmol) of spiro[1-methyl-10-oxatricyclo[5.2.1.0^{2,6}]deca-3,8-dione-9,1′-cyclopropane] (**30**)[30] in 10 mL of dry THF was added 0.35 mL (5.7 mmol) of potassium hexamethyldisilazide at −78 °C, and the reaction mixture was stirred at this temperature for 30 min. To this mixture was added 0.35 mL (5.7 mmol) of iodomethane in one portion, and the resulting solution was stirred at −78 °C for 1 h. The reaction was allowed to slowly warm to rt, quenched with water, extracted with ether, dried over $MgSO_4$, and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography to give 0.23 g (48%) of **17** as a white solid: mp 120−121 °C; IR (neat) 1754, 1732, 1381, and 980 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.66 (m, 1H), 0.93−1.14 (m, 2H), 0.99 (s, 3H), 1.03 (s, 3H), 1.26 (s, 3H), 1.28 (m, 1H), 1.76 (dd, 1H, J = 13.2 and 7.8 Hz), 2.11 (dd, 1H, J = 13.2 and 9.0 Hz), 2.65 (d, 1H, J = 8.4 Hz), 2.82 (q, 1H, J = 8.4 Hz), and 4.23 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.8, 13.5, 14.4, 22.5, 25.8, 38.6, 39.5, 40.2, 47.6, 56.2, 85.4, 87.8, 212.3, and 219.3. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.75; H, 7.71.

Acid Induced Rearrangement of Spiro[1,4,4-trimethyl-10-oxatricyclo-[5.2.1.0^{2,6}]deca-3,8-dione-9,1′-cyclopropane] (17). A solution containing 0.1 g (0.43 mmol) of α-diazo ketone **17** in 5 mL of CH_2Cl_2 was treated with a 10-fold excess of *p*-toluenesulfonic acid, and the resultant mixture was heated at reflux for 10 h. The reaction was quenched by the addition of water, the mixture was extracted with ether, and the extracts were dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.07 g (70%) of 4,6,6-trimethyl-2,3,6,7-tetrahydro-1-oxaindacen-5-one (**21**) as a white solid: mp 98−99 °C; IR ($CDCl_3$) 3146, 1680, 1595, 1467, 1310, and 1090 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.16 (s, 6H), 2.52 (s, 3H), 2.82 (s, 2H), 3.11 (t, 2H, J = 8.4 Hz), 4.65 (t, 2H, J = 8.4 Hz), and 6.55 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 15.0, 25.6, 27.4, 42.4, 45.9, 72.4, 126.1, 127.2, 136.2, 148.6, 156.0, 165.4, and 210.3. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.69; H, 7.51.

A rearrangement of α-diazo ketone **17** was also carried out using $BF_3{\cdot}OEt_2$. To a solution containing 0.23 g (0.90 mmol) of **17** in 10 mL of dry CH_2Cl_2 was added 0.36 mL (2.9 mmol) of $BF_3{\cdot}OEt_2$, and the resulting mixture was stirred at rt for 1 h. The reaction was quenched by the addition of 10 mL of water, extracted with CH_2Cl_2, and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The product was purified by silica gel chromatography followed by recrystallization to give 0.12 g (50%) of 3-(methyl-2,3-dihydrobenzofuran-6-yl)propionic acid (**24**) as a white solid: mp 101−102 °C; IR (neat) 3452, 1695, 1261, and 990 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.20 (s, 6H), 2.21 (s, 3H), 2.81 (s, 2H), 3.08 (t, 2H, J = 9.0 Hz), 4.55 (t, 2H, J = 9.0 Hz), 6.45 (s, 1H), and 6.47 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 18.9, 24.7, 28.5, 43.3, 45.8, 71.0, 108.6, 123.4, 124.1, 133.9, 137.6, 159.7, and 183.7. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.84; H, 7.79.

General Procedure for Samarium(II) Diiodide Reductions. To a solution containing 25 mL (2.5 mmol) of 0.1 M samarium(II) diiodide in THF was added a solution containing 0.13 g (0.46 mmol) of the appropriate cycloadduct in 2 mL of THF followed by 0.5 mL (12 mmol) of MeOH at −78 °C. The reaction mixture was stirred for 15 min under argon until the blue color disappeared, and then the reaction was quenched with water and extracted with ether. After removal of the solvent, the residue was purified by silica gel chromatography to give the ring opened product.

Reduction of Ethyl 6,6-Dimethyl-5,8-epoxy-8-methyl-4-oxospiro[2.5]octane-5-carboxylate (25). A 0.13 g (0.46 mmol) of cycloadduct **25**[30] was reduced according to the general procedure to give 0.08 g (61%) of an inseparable 2:1 mixture of the diastereoisomers of ethyl 2,2-dimethoxy-5-ethyl-4-methyl-6-oxo-7-oxabicyclo[2.2.1]heptane-1-carboxylate (**26**): IR (neat) 1773, 1730, 1289, and 876 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.06 (t, 3H, J = 7.5 Hz), 1.26−1.39 (m, 1H), 1.29 (t, 3H, J = 7.5 Hz), 1.57 (s, 3H), 1.65−1.77 (m, 1H), 2.00−2.03 (m, 3H), 3.20 (s, 3H), 3.33 (s, 3H), and 4.29 (m, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.6, 13.9, 20.8, 21.8, 43.8, 49.7, 50.8, 57.1, 61.8, 83.7, 93.7, 110.3, 163.1, and 203.6; HRMS Calcd for $C_{14}H_{22}O_6$: 286.1416. Found: 286.1422.

Samarium(II) Diiodide-Induced Ring-Opening of Ethyl 6,6-Dimethyl-5,8-epoxy-8-methyl-4-oxospiro[2.5]octane-5-carboxylate (25). A 0.2 g (0.7 mmol) sample of cycloadduct **25**[30] was reduced according to the general procedure but without added MeOH to give 0.16 g (85%) of an inseparable 4:1 mixture of the diastereomers of ethyl 4-[(methoxycarbonyl)-methyl]-4-methyl-7-oxo-5-oxaspiro[2.4]heptane-6-carboxylate (**27**): IR (neat) 1731, 1323, 1197, 1092, and 835 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) major isomer: δ 0.94 (m, 1H), 1.08−1.26 (m, 6H), 1.35 (s, 3H), 2.47 (d, 1H, J = 16.2 Hz), 2.68 (d, 1H, J = 16.2 Hz), 3.59 (s, 3H), 4.18 (m, 2H), and 4.79 (s, 1H); ^{1}H-NMR (300 MHz, $CDCl_3$) minor isomer: δ 0.94 (m, 1H), 1.08−1.26 (m, 6H), 1.35 (s, 3H), 2.71 (m, 2H), 3.59 (s, 3H), 4.18 (m, 2H), and 4.68 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.1, 14.7, 16.3, 17.4, 18.9, 25.5, 26.4, 35.7, 44.7, 51.6, 61.9, 79.2,

80.4, 81.7, 167.0, 170.4, and 206.9; HRMS Calcd for $C_{13}H_{18}O_6$: 270.1103. Found: 270.1104.

Reduction of 6,6-Dimethoxy-5,8-epoxy-8-methyl-4-oxaspiro[2.5]octane (28). A 0.1 g (0.47 mmol) sample of **28**[30] was reduced according to the general procedure to give 0.05 g (62%) of 8-hydroxy-6-methoxy-8-methylspiro[2.5]oct-5-en-4-one (**29**): IR (neat) 1623, 1445, 1190, and 816 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.81 (m, 1H), 1.00−1.10 (m, 2H), 1.18 (m, 1H), 1.21 (s, 3H), 1.70 (s, 1H), 2.57 (d, 1H, J = 16.8 Hz), 2.66 (d, 1H, J = 16.8 Hz), 3.70 (s, 3H), and 5.45 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.6, 11.8, 25.6, 35.4, 43.0, 55.8, 70.6, 101.4, 174.9 and 197.9; HRMS Calcd for $C_{10}H_{14}O_3$: 182.0943. Found: 182.0948.

Reduction of Spiro[1-methyl-10-oxatricyclo-[5.2.1.0^{2,6}]-deca-3,8-dione-9,1′-cyclopropane] (30). A 0.32 g (1.6 mmol) of cycloadduct **30**[30] was reduced according to the general procedure to give spiro[7-hydroxy-7-methylhexahydro-indene-1,5-dione-6,1′-cyclopropane] (**31**) (62%) as a yellow oil: IR (neat) 1752, 1446, 1382, and 991 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.85−0.95 (m, 2H), 1.05−1.25 (m, 1H), 1.20−1.35 (m, 1H), 1.25 (s, 3H), 1.80−1.95 (m, 1H), 2.10−2.25 (m, 1H), 2.40−2.55 (m, 3H), 2.60−2.75 (m, 2H), 2.90−3.05 (m, 1H), and 4.18 (s, 1H, exchanged with D_2O); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 10.0, 14.7, 26.7, 27.6, 32.6, 36.7, 37.6, 41.6, 56.7, 71.9, 209.0, and 220.8; HRMS Calcd for $C_{12}H_{16}O_3$: 208.1099. Found: 208.1099.

Reduction of Spiro[1,4,4-trimethyl-10-oxa-tricyclo-[5.2.1.0^{2,6}]decane-3,8-dione-9,1′-cyclopropane] (17). A 0.15 g (0.6 mmol) sample of cycloadduct **17** was reduced according to the general procedure and was subsquently purified by silica gel chromatography. The first fraction isolated from the column contained 0.07 g (45%) of *cis*-spiro[7-hydroxy-2,2,7-trimethylhexahydroindene-1,5-dione-6,1′-cyclopropane] (**32a**): mp 110−111 °C; IR ($CDCl_3$) 1718, 1675, 1374, and 1102 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.87−0.98 (m, 2H), 1.03−1.10 (m, 1H), 1.09 (s, 3H), 1.11 (s, 3H), 1.19−1.28 (m, 1H), 1.37 (s, 3H),1.58 (dd, 1H, J = 13.5 and 7.2 Hz), 2.12 (dd, 1H, J = 13.5 and 8.1 Hz), 2.53 (dd, 1H, J = 16.8 and 6.6 Hz), 2.78 (dd, 1H, J = 15.9 and 6.9 Hz), 2.82 (d, 1H, J = 10.5 Hz), 2.94 (m, 1H), and 4.30 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.4, 15.8, 23.9, 26.0, 27.9, 28.5, 37.8, 42.6, 44.3, 46.0, 53.0, 71.9, 209.9, and 225.4. Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.07; H, 8.52.

The second fraction isolated from the column contained 0.02 g (15%) of *trans*-spiro[7-hydroxy-2,2,7-trimethylhexahydroindene-1,5-dione-6,1′-cyclopropane] (**32b**); mp 108−109 °C; IR ($CDCl_3$) 1718, 1675, 1374, and 1102 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.89−0.96 (m, 1H), 0.99−1.15 (m, 2H), 1.08 (s, 3H), 1.10 (s, 3H), 1.26 (s, 3H), 1.34−1.40 (m, 1H), 1.53 (dd, 1H, J = 13.2 and 10.5 Hz), 2.22 (dd, 1H, J = 13.8 and 6.6 Hz), 2.32 (dd, 1H, J = 19.8 and 11.4 Hz), 2.80 (d, 1H, J = 10.5), 2.85−2.95 (m, 2H), and 3.29 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 13.6, 16.8, 22.5, 24.8, 25.7, 26.9, 38.8, 42.6, 46.5, 46.9, 53.8, 70.9, 209.8 and 225.4. Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.07; H, 8.52.

Reduction of Spiro[5,8-epoxy-1,4-methano-8-methyl-6-oxooctahydronaphthalene-7,1′-cyclopropane] (33). A 0.01 g (0.5 mmol) of cycloadduct **33**[30] was reduced according to the general procedure to give 0.07 g (75%) of spiro[8-hydroxy-1,4-methano-8-methyl-6-oxooctahydronaphthalene-7,1′-cyclopropane] (**35**): mp 106−107 °C; IR ($CDCl_3$) 1682, 1367 and 1310 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.72−0.79 (m, 1H), 0.92−0.96 (m, 3H), 1.02 (s, 3H), 1.08 (m, 1H), 1.15−1.23 (m, 2H), 1.28−1.35 (m, 1H), 1.53−1.58 (m, 3H), 1.90−1.98 (m, 3H), 2.30−2.37 (m, 2H), and 2.72 (dd, 1H, J = 14.7 and 13.5 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.2, 17.6, 25.1, 29.0, 30.9, 34.2, 37.1, 38.4, 41.2, 41.3, 42.2, 51.4, 73.5, and 212.8. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.25; H, 9.14.

Reduction of Spiro[6,8a-epoxy-7-oxo-octahydronaphthalene-8,1′-cyclopropane] (34). A 0.10 g (0.52 mmol) sample of cycloadduct **34**[30] was reduced according to the general procedure to give 0.07 g (70%) of spiro[8a-hydroxy-7-oxooctahydronaphthalene-8,1′-cyclopropane] (**36**) as a thick oil: IR ($CDCl_3$) 3467, 1687, and 1449 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.58−0.64 (m, 1H), 0.76−0.82 (m, 1H), 0.92−0.98 (m, 1H), 1.04−1.11 (m, 1H), 1.20 (m, 2H), 1.33−1.80 (m, 9H), 1.92−2.06 (m, 1H), 2.29−2.41 (m, 1H), and 2.47−2.54 (m, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 6.8, 17.2, 20.5, 25.4, 26.6, 28.8, 32.7, 39.3, 39.4, 42.1, 72.8, and 210.6; HRMS Calcd for $C_{12}H_{18}O_2$: 194.1307. Found: 194.1316.

Dimethyl 4-Hydroxy-4-methyl-8-oxospiro[2.5]oct-6-ene-5,6-dicarboxylate (38). To a solution containing 0.34 mL (2.4 mmol) of diisopropylamine in 5 mL of THF was added 0.9 mL (2.2 mmol) of n-BuLi at −78 °C, and the mixture was stirred at this temperature for 15 min under argon. A solution containing 0.5 g (1.9 mmol) of dimethyl 4,7-epoxy-4-methyl-8-oxospiro[2.5]octane-5,6-dicarboxylate (**37**)[30] in 5 mL of THF was slowly added, and the mixture was allowed to stir for 10 min. The solution was quenched with a saturated aqueous NH_4Cl solution and extracted with ether. The organic layer was dried over $MgSO_4$, the solvent was removed under reduced pressure, and the crude residue was purified by silica gel chromatography to give 0.38 g (78%) of a 8:3 mixture of the diastereomers of **38**: major isomer: IR (neat) 1726, 1663, 1158, and 779 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.90−0.97 (m, 1H), 1.08−1.22 (m, 2H), 1.19 (s, 3H), 1.26−1.34 (m, 1H), 2.29 (brs, 1H), 3.71 (s, 3H), 3.81 (s, 3H), 3.92 (s, 1H), and 6.87 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.4, 15.2, 23.3, 36.2, 52.5, 52.7, 53.6, 72.5, 133.3, 141.8, 166.3, 169.8, and 197.8; HRMS Calcd for $C_{13}H_{16}O_6$: 268.0947. Found: 268.0960.

Minor isomer: IR (neat) 1723, 1666, 1012, and 777 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.81−0.88 (m, 1H), 0.96−1.03 (m, 1H), 1.12−1.18 (m, 1H), 1.35 (s, 3H), 1.40−1.46 (m, 1H), 3.70 (s, 3H), 3.85 (s, 3H), 3.91 (s, 1H), 4.12 (s, 1H), and 5.03 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 9.1, 17.9, 27.8, 36.1, 50.8, 52.9, 53.0, 71.0, 133.6, 141.9, 166.0, 171.1, and 198.9; HRMS Calcd for $C_{13}H_{16}O_6$: 268.0947. Found: 268.0941.

5,8-Epoxy-4-hydroxy-4,8-dimethyl-7-(phenylsulfonyl)-spiro[2.5]octane (40). To a solution containing 0.35 g (2.1 mmol) of phenyl vinyl sulfone in 5 mL of benzene was added a solution containing 0.32 g (2.1 mmol) of 1-acetyl-1-(diazoacetyl)cyclopropane (**15**),[30] and the mixture was stirred in the presence of 2 mg of rhodium(II) acetate. After stirring for 6 h at rt, the solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.48 g (79%) of a 8:3-mixture of the diastereomers of 5,8-epoxy-8-methyl-4-oxo-7-(phenylsulfonyl)spiro[2.5]octane (**39**): major isomer: mp 170−171 °C; IR ($CDCl_3$) 1749, 1436, 1372, and 1145 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.81(m, 1H), 1.04 (m, 1H), 1.12 (m, 1H), 1.38 (m, 1H), 1.65 (s, 3H), 1.83 (dd, 1H, J = 13.8 and 8.7 Hz), 2.34 (m, 1H), 3.50 (dd, 1H, J = 8.7 and 6.0 Hz), 4.53 (d, 1H, J = 6.3 Hz), 7.51−7.65 (m, 3H), and 7.85 (m, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.2, 14.9, 31.3, 40.3, 66.8, 79.4, 87.1, 128.3, 129.4, 133.9, 139.0, and 210.6. Anal. Calcd for $C_{15}H_{16}O_4S$: C, 61.63; H, 5.52. Found: C, 61.55; H, 5.51.

To a solution containing 0.2 g (0.7 mmol) of **39** in 8 mL of THF was added 0.2 mL (0.7 mmol) of a solution of methylmagnesium iodide (3 M in hexane) at 0 °C. The mixture was stirred for 4 h, quenched with a saturated NH_4Cl solution and extracted with ether. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.17 g (80%) of **40**: mp 183−184 °C; IR ($CDCl_3$) 3502, 1296, 1139, and 1075 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.25 (m, 1H), 0.54 (m, 1H), 0.65 (m, 1H), 0.85 (m, 1H), 1.15 (s, 3H), 1.20 (s, 1H), 1.43 (s, 3H), 1.98 (m, 1H), 2.36 (dd, 1H, J = 12.9 and 9.0 Hz), 3.51 (dd, 1H, J = 9.0 and 6.3 Hz), 4.18 (d, 1H, J = 5.4 Hz), 7.49−7.62 (m, 3H), and 7.83 (d, 2H, J = 6.9 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 6.1, 8.3, 15.2, 26.2, 30.2, 40.5, 67.4, 76.9, 83.3, 88.6, 128.3, 129.2, 133.5, and 139.3. Anal. Calcd for $C_{16}H_{20}O_4S$: C, 62.32; H, 6.54. Found: C, 62.29; H, 6.50.

4,8-Dimethyl-7-(phenylsulfonyl)spiro[2.5]oct-7-ene-4,5-diol (41). To a solution of containing 0.1 g (0.3 mmol) of **40** in 4 mL of THF was added 0.5 mL of a solution of n-butyllithium (2.5 M in hexane) and the resultant mixture was stirred for 3 h at rt. The reaction mixture was quenched by the addition of a saturated aqueous NH_4Cl solution and was then extracted with ether. After removal of the solvent, the residue was purified by silica gel chromatography to give 0.07 g (70%) of **41**: mp 178−179 °C; IR ($CDCl_3$) 1727, 1372, 1294, and 1131 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.58 (m, 1H), 0.86 (m, 1H), 0.98 (m, 1H), 1.03 (s, 3H), 1.15 (m, 1H), 1.76 (s,

3H), 2.23−2.24 (m, 2H), 3.00 (dd, 1H, J = 17.4 and 6.3 Hz), 3.77 (dd, 1H, J = 9.9 and 6.3 Hz), 7.50−7.61 (m, 3H), and 7.83 (d, 2H, J = 7.5 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 7.1, 10.4, 14.4, 18.9, 32.1, 33.7, 71.2, 71.8, 126.9, 129.1, 130.3, 133.0, 141.7, and 150.2. Anal. Calcd for $C_{16}H_{20}O_4S$: C, 62.32; H, 6.54. Found: C, 62.06; H, 6.70.

2-(*p*-Tolylsulfonyl)-5,5-dimethylcyclopentenone (46). A mixture containing 0.91 g (2.0 mmol) of (trimethylacetyl)-[phenyl[[(trifluoromethyl)sulfonyl]oxy]iodo]acetylene (**43**)[42] and 0.36 g (2.02 mmol) of anhydrous sodium *p*-toluenesulfinate in 30 mL of CH_2Cl_2 was allowed to stir for 30 min at rt. At the end of this time, 20 mL of H_2O was added and the two phases were separated. The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure to give 0.39 g (73%) of **46** as a white solid: mp 125−126 °C; IR (KBr) 2930, 2870, 1722, 1706, and 1085 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.04 (s, 6H), 2.38 (s, 3H), 2.60 (d, 2H), 7.28 (d, 2H), 7.89 (d, 2H) and 8.33 (t, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 21.6, 24.6, 43.1, 45.8, 128.5, 129.7, 136.0, 144.6, 145.0, 167.3 and 203.7. Anal. Calcd for $C_{14}H_{16}O_3S$: C, 63.61; H, 6.10. Found: C, 63.54; H, 5.98.

Spiro[1,4,4-trimethyl-2-(*p*-tolylsulfonyl)-10-oxatricyclo-[5.2.1.0^{2,6}]deca-3,8-dione-9,1′-cyclopropane] (47). To a solution containing 0.83 g (6.5 mmol) of 1-acetyl-1-(diazoacetyl)cyclopropane (**15**)[30] and 1.7 g (6.5 mmol) of **46** in 50 mL dry CH_2Cl_2 was added 2 mg of rhodium(II) acetate, and the reaction mixture was stirred at rt for 1 h. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 2.5 g (100%) of **47** as a 2:1 mixture of *exo*- and *endo*-isomers. The *exo* isomer exhibited the following spectral properties: mp 222−223 °C; IR (neat) 1751, 1723, 1310, and 1147 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.00 (m, 2H), 1.06 (s, 6H), 1.38 (m, 1H), 1.49 (s, 3H), 1.70 (m, 1H), 1.86 (m, 2H), 2.41 (s, 3H), 3.38 (m, 1H), 4.44 (s, 1H), 7.31 (d, 2H, J = 8.1 Hz), and 7.65 (d, 2H, J = 8.1 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.3, 15.8, 16.7, 21.6, 26.2, 38, 40.4, 44.7, 47.5, 86.4, 88.4, 92.7, 129.3, 129.8, 130.5, 136.1, 145.7, 210.0, and 214.3. Anal. Calcd for $C_{21}H_{24}O_5S$: C, 64.93; H, 6.23; S, 8.25. Found: C, 65.03; H, 6.27; S, 8.30.

The *endo* isomer exhibited the following spectral properties: mp 168−169 °C; IR (neat) 1744, 1730, 1310, and 1139 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.72 (m, 2H), 0.95 (s, 3H), 1.15 (s, 3H), 1.23 (d, 2H, J = 7.0 Hz), 1.44 (s, 3H), 1.70 (m, 1H), 2.15 (m, 1H), 2.37 (s, 3H), 4.09 (m, 1H), 4.50 (d, 1H, J = 6.0 Hz), 7.27 (d, 2H, J = 8.1 Hz), and 7.62 (d, 2H, J = 8.1 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.1, 15.6, 15.7, 21.7, 27.1, 29.5, 33.5, 39.4, 45.9, 51.0, 83.4, 86.4, 88.9, 129.3, 131.1, 134.1, 145.5, 210.5, and 213.3. Anal. Calcd for $C_{21}H_{24}O_5S$: C, 64.93; H, 6.23; S, 8.25. Found: C, 65.04; H, 6.25; S, 8.33.

Spiro[8-hydroxy-1,4,4,8-tetramethyl-2α-(*p*-tolylsulfonyl)-10-oxatricyclo[5.2.1.0^{2,6}]deca-3,8-dione-9,1′-cyclopropane] (48). To a solution containing 0.5 g (1.3 mmol) of **47** in 15 mL of THF at 0 °C was added 0.56 mL (1.7 mmol) of a solution containing 3 M methylmagnesium iodide, and the resulting mixture was stirred at rt for 4 h. The solution was quenched by the addition of a saturated NH_4Cl solution and was extracted with ether. The combined organic layers were washed with a 5% aqueous $Na_2S_2O_3$ solution and dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The crude residue was purified by silica gel chromatography to give 0.47 g (90%) of **48** as a white solid: mp 119−120 °C: IR (neat) 3480, 1730, 1452, 1296, and 1139 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.65 (m, 1H), 0.57 (m, 1H), 0.99 (s, 3H), 1.01 (m, 1H), 1.15 (s, 3H), 1.25 (s, 3H), 1.32 (m, 1H), 1.66 (m, 1H), 1.79 (m, 1H), 2.38 (s, 3H), 3.82 (m, 1H), 4.13 (s, 1H), 4.18 (s, 1H), 7.28 (d, 2H, J = 8.1 Hz), and 7.66 (d, 2H, J = 8.1 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 8.6, 9.4, 15.3, 21.6, 25.7, 26.3, 26.4, 37.1, 41.2, 41.7, 47.1, 76.8, 86.9, 94.1, 94.5, 129.8, 130.6, 136.1, 145.6, and 215.6; HRMS Calcd for $C_{22}H_{28}O_5S$: 404.1657. Found: 404.1656.

Spiro[8-hydroxy-1,4,4,8-tetramethyl-10-oxatricyclo-[5.2.1.0^{2,6}]deca-3,8-dione-9,1′-cyclopropane] (49). To a solution containing 0.63 g (1.56 mmol) of **48** in 10 mL of a 5:1 THF:MeOH mixture was added 0.82 g of 6% Na(Hg), and the resulting mixture was stirred for 12 h at rt. The mixture was quenched with water, washed with a 1 N HCl solution, extracted with ether, and dried over anhydrous $MgSO_4$. After removal of the solvent, the residue was purified by silica gel chromatography to give 0.34 g (87%) of **49** as a white solid: mp 91−92 °C; IR (neat) 3487, 1730, 1452, and 1374 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.03 (m, 1H), 0.40 (m, 1H), 0.54 (m, 1H), 0.71 (m, 1H), 0.87 (s, 3H), 0.91 (s, 3H), 0.98 (s, 3H), 1.07 (s, 3H), 1.44 (m, 1H), 1.90 (m, 1H), 2.37 (m, 1H), 2.45 (d, 1H, J = 7.0 Hz), 3.22 (dd, 1H, J = 7.0 and 6.0 Hz), and 3.80 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 5.9, 7.7, 14.0, 22.6, 26.1, 26.3, 36.5, 39.8, 40.9, 46.8, 56.3, 76.5, 89.3, 89.4, and 222.4. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.68; H, 8.69.

Spiro[4,5-dihydroxy-2,2,5,7-tetramethyl-2,3,3aα,4,5,6-hexahydroinden-1-one-6,1′-cyclopropane] (50). A solution containing 0.25 g (1.0 mmol) of **49** and 10 mL of 10% KOH in MeOH was heated at reflux for 5 h. The reaction mixture was cooled, neutralized with 1 N HCl, and extracted with ether. The organic layer was dried over anhydrous $MgSO_4$, and the crude residue obtained after removal of the solvent was purified by silica gel chromatography to give 0.2 g (80%) of **50** as a white solid: mp 134−135 °C; IR (neat) 3459, 1687, 1609, 1450, and 1367 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.98 (m, 4H), 1.04 (s, 3H), 1.07 (s, 6H), 1.69−1.73 (m, 3H), 1.84 (d, 3H, J = 2.1 Hz), 3.33 (m, 2H), and 3.63 (d, 1H, J = 3.6 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 6.6, 11.8, 13.8, 22.9, 24.5, 24.7, 29.1, 36.0, 36.2, 45.9, 73.3, 73.8, 128.2, 149.5, and 209.9. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.95; H, 8.85 .

Spiro[8-hydroxy-1,4,4,8-tetramethyl-2β-(*p*-tolylsulfonyl)-10-oxatricyclo[5.2.1.0^{2,6}]deca-3,8-dione-9,1′-cyclopropane] (51). To a solution containing 1.0 g (2.6 mmol) of **47b** in 45 mL of THF at 0 °C was added 3 mL (3.1 mmol) of 3 M methylmagnesium bromide solution, and the resulting mixture was stirred at 0 °C for 5 h. The reaction mixture was quenched by the addition of a saturated NH_4Cl solution, extracted with ether, and dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.84 g (80%) of **51** as a white solid: mp 93−94 °C: IR (KBr) 3470, 1725, 1460, 1290, and 1140 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.30−0.35 (m, 2H), 0.60−1.00 (m, 3H), 1.20 (s, 3H), 1.30 (s, 3H), 1.35 (s, 3H), 1.36 (s, 3H), 2.05 (m, 1H), 2.41 (s, 3H), 3.00 (dd, 1H, J = 14.1 and 3.6 Hz), 4.03 (m, 1H), 4.17 (d, 1H, J = 6.3 Hz), 7.26 (d, 2H, J = 8.4 Hz), and 7.62 (d, 2H, J = 8.4 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 6.5, 9.8, 16.9, 21.6, 26.9, 30.1, 31.0, 32.8, 37.4, 47.3, 52.0, 79.3, 83.4, 89.9, 91.5, 128.9, 131.2, 134.8, 144.8, and 215.9. Anal. Calcd for $C_{22}H_{28}O_5S$: C, 65.32; H, 6.98. Found: C, 65.23; H, 6.99.

Spiro[8-hydroxy-1,4,4,8-tetramethyl-10-oxatricyclo-[5.2.1.0^{2,6}]deca-3,8-dione-9,1′-cyclopropane] (52). To a solution containing 0.42 g (1.04 mmol) of **51** in 10 mL of a 5:1 THF:MeOH mixture was added 0.6 g of 6% Na(Hg), and the resulting mixture was stirred for 12 h at rt. The reaction was quenched by the addition of water, washed with a 1 N HCl solution, extracted with ether, and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.18 g (70%) of **52** as a white solid: mp 119−120 °C; IR (neat) 3459, 1716, 1460, 1374, and 1146 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.29 (m, 1H), 0.45−0.53 (m, 1H), 0.57 (m, 2H), 1.01 (s, 3H), 1.06 (s, 3H), 1.22 (s, 3H), 1.26 (s, 3H), 1.68 (dd, 2H, J = 13.2 and 9.6 Hz), 2.93 (d, 1H, J = 12.0 Hz), 3.11 (dd, 1H, J = 13.2 and 8.7 Hz), 3.24 (m, 1H), and 4.05 (d, 1H, J = 5.4 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 5.2, 6.0, 19.3, 23.0, 27.1, 29.9, 35.1, 35.3, 42.6, 52.5, 62.1, 79.8, 84.8, 87.3, and 220.4. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.77; H, 8.91.

Spiro[4,5-dihydroxy-2,2,5,7-tetramethyl-2,3,3aβ,4,5,6-hexahydroindene-1-one-6,1′-cyclopropane] (53). A solution containing 0.1 g (0.4 mmol) of **52** and 0.5 mL of 1.7 M *t*-BuLi in 4 mL (0.8 mmol) of isopropyl ether was heated at reflux for 2 h. The reaction mixture was cooled, quenched with water and extracted with ether. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.07 g (70%) of **53** as a white

solid: mp 104−105 °C; IR ($CDCl_3$) 3445, 1687, 1595, 1374, and 1075 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.67 (m, 1H), 0.90−1.10 (m, 3H), 1.04 (s, 3H), 1.06 (s, 3H), 1.17 (s, 3H), 1.36 (t, 1H, J = 11.7 Hz), 1.80 (d, 3H, J = 2.1 Hz), 2.15 (dd, 1H, J = 12.0 and 6.6 Hz), 2.68 (m, 3H), and 3.43 (d, 1H, J = 9.0 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 7.8, 11.2, 12.2, 20.4, 24.5, 24.7, 32.9, 40.9, 41.3, 46.2, 72.4, 77.9, 129.5, 151.2, and 209.9. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.70; H, 8.82.

Spiro[5-hydroxy-2,2,5,7-tetramethyl-3,3a,5,6-tetrahydro-2*H*-indene-1,4-dione-6,1′-cyclopropane] (54). To a solution containing 0.1 mL (1.1 mmol) of oxalyl chloride in 2 mL of CH_2Cl_2 was added a solution containing 0.15 mL (2.2 mmol) of dimethyl sulfoxide in 2 mL of CH_2Cl_2 at −78 °C. The resulting mixture was stirred for 15 min at −78 °C, and a solution containing 0.2 g (0.80 mmol) of a 5:3 mixture of compounds **50**/**53** derived from cycloadduct **47** in 4 mL of CH_2Cl_2 was added. After stirring for 1 h, 0.4 mL of triethylamine was added, and the mixture was allowed to warm to rt during a period of 15 min. The reaction mixture was quenched with water and extracted with ether. The combined organic layers were washed with small amount of 1 N HCl solution and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.15 g (75%) of **54** as a 5:3 mixture of diasteromers; IR ($CDCl_3$) 3473, 1694, 1609, 1452, and 1104 cm^{-1}; major isomer: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.62 (m, 1H), 1.00 (m, 1H), 1.08−1.20 (m, 2H), 1.10 (s, 3H), 1.11 (s, 3H), 1.51 (s, 3H), 1.80 (m, 1H), 1.89 (d, 3H, J = 2.7 Hz), 2.01 (m, 1H), 3.68 (s, 1H), and 3.86 (m, 1H); minor isomer: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.50 (m, 1H), 0.94 (m, 1H), 1.01−1.20 (m, 2H), 1.06 (s, 3H), 1.12 (s, 3H), 1.21 (s, 3H), 1.63 (t, 1H, J = 12.0 Hz), 2.08 (d, 3H, J = 3.0 Hz), 2.28 (m, 1H), 3.23 (s, 1H), and 3.47 (m, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 5.6, 8.4, 9.8, 11.1, 12.5, 14.6, 24.1, 24.2, 24.4, 24.5, 25.4, 32.4, 35.6, 37.1, 38.6, 43.9, 45.1, 45.8, 46.9, 73.7, 75.0, 128.1, 129.4, 151.1, 152.6, 207.3, 207.8, 210.1, and 214.8; HRMS Calcd for $C_{15}H_{20}O_3$: 248.1412. Found: 248.1416.

Oxidation of Spiro[5-hydroxy-2,2,5,7-tetramethyl-3,3a,5,6-tetrahydro-2*H*-indene-1,4-dione-6,1′-cyclopropane] (54) with DDQ. A solution containing 0.1 g (0.4 mmol) of **54**, 0.11 g (0.5 mmol) of DDQ, and 10 mg (0.05 mmol) of *p*-TsOH·H_2O in 20 mL of benzene was heated at reflux for 12 h. The reaction mixture was filtered, the solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give a 1:4 mixture of spiro[5-hydroxy-2,2,5,7-tetramethyl-5,6-dihydro-2*H*-indene-1,4-dione-6,1′-cyclopropane] (**55**)[20] and spiro[5-hydroxy-2,2,5-trimethyl-7-methylene-3,5,6,7-tetrahydro-2*H*-indene-1,4-dione-6,1′-cyclopropane] (**6**) in 70% yield. The minor product **55** was a white solid: mp 66−67 °C; IR ($CDCl_3$) 3488, 1703, 1618, and 1165 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.59 (m, 1H), 1.05−1.17 (m, 2H), 1.19 (s, 3H), 1.24 (s, 3H), 1.33 (m, 1H), 1.34 (s, 3H), 2.04 (s, 3H), 3.61 (s, 1H), and 6.83 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 11.7,12.8, 22.9, 23.0, 25.1, 33.8, 51.5, 75.6, 129.5, 134.8, 141.7, 151.2, 199.0, and 206.8. Anal. Calcd for $C_{15}H_{18}O_3$:C, 73.15; H, 7.37. Found: C, 73.19 ; H, 7.22.

The major product **6** was a yellow solid: mp 63−64 °C; IR ($CDCl_3$) 3491, 1700, 1672, and 1232 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.21 (m, 1H), 0.93−1.06 (m, 3H), 1.19 (s, 3H), 1.20 (s, 3H), 1.34 (s, 3H), 2.52 (d, 1H, J = 19.5 Hz), 2.73 (d, 1H, J = 19.5 Hz), 3.30 (s, 1H), 5.29 (s, 1H), and 6.38 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 4.2, 12.6, 24.8, 25.1, 25.4, 31.8, 38.8, 45.8, 75.5, 115.8, 138.6, 144.6, 151.8, 202.5 and 212.0. Anal. Calcd for $C_{15}H_{18}O_3$:C, 73.15; H, 7.37. Found: C, 73.24 ; H, 7.44.

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Supporting Information Available: ^{1}H-NMR and ^{13}C-NMR spectra for new compounds lacking analyses (9 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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