synthetic route for triazole preparation.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and were not corrected. NMR spectra were run on a Varian XL-300 300 MHz spectrometer in $CDCl_3$ solutions with TMS as internal standard. C, H, and N elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

Nickel Peroxide (NiO_2) Oxidation of 1,2,3-Triazolines: Synthesis of 1*H*-1,2,3-Triazoles. To a solution of the 1,2,3-triazoline[3-4,23,28-30] (0.005 mol) in reagent-grade benzene (100 mL) was added dried, finely powdered NiO_2[18] (0.060 mol), and the mixtire was refluxed with vigorous magnetic stirring for 3-4 h. The reaction mixture was then allowed to cool to room temperature and filtered under gravity to remove the spent NiO_2. The residual NiO_2 was washed with hot $CHCl_3$, and the combined filtrates were subjected to rotary evaporation. The resulting oily residue was cooled and triturated with petroleum ether or an ether-petroleum ether mixture, when it solidified to a clean crystalline mass, and the colored impurities remained in solution. Many of the triazoles at this point were quite pure, giving reasonably sharp melting points and little, if any, N_2 gas evolution, which is indicative of the presence of appreciable amounts of unreacted triazoline.[28] Recrystallization from acetone-petroleum ether gave analytically pure samples, with only slight changes in the previously determined melting points.

Triazoles **1**, **2**, and **26**, however, showed wide melting point ranges with significant gas evolution; NMR analysis indicated 28% unreacted triazoline **26** and 12-13% **1** and **2**. Two crystallizations from acetone-petroleum ether mixture were required before the characteristic ABC multiplet of the $4CH_2$-5CH triazoline protons[23] in the δ 4-6 region disappeared from the NMR spectrum. Triazole **26**, prepared by permanganate oxidation, resulted in 34% yield, of which almost 30% was unchanged triazoline, as revealed by NMR.

Synthesis of 1,2,3-Triazolines. The 1,2,3-triazolines were synthesized according to the Kadaba procedure by the cycloaddition of diazomethane to Schiff bases in a dioxane-water mixture, utilizing the catalytic effect of water on the addition (eq 1).[3,4,23,28-30] Triazolines **4**, **14**, **20**, **22**, **25**, **28**, **29**, **31**, and **33** were newly synthesized and gave satisfactory elemental analysis for C, H and N; compound numbers, melting points, and percent yields of pure compounds were as follows: **4**, 151-152 dec, 69; **14**, 139-140 dec, 78; **20**, 127-128 dec, 65; **22**, 67-70, 45; **25**, 150-153 dec, 83; **28** 133-136 dec, 48; **29**, 130-132 dec, 80; **31**, 146-148 dec, 70; **33**, 84-88, 73.

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Registry No. **1**, 68090-19-7; **2**, 68090-21-1; **3**, 68090-20-0; **4**, 129239-50-5; **5**, 68090-18-6; **6**, 129239-51-6; **7**, 110684-22-5; **8**, 129239-52-7; **9**, 31802-50-3; **10**, 18250-08-3; **11**, 110684-40-7; **12**, 110684-41-8; **13**, 110684-21-4; **14**, 129239-53-8; **15**, 128229-10-7; **16**, 84817-40-3; **17**, 128229-11-8; **18**, 128229-12-9; **19**, 128229-13-0; **20**, 128252-72-2; **21**, 129239-54-9; **22**, 128229-14-1; **23**, 128229-15-2; **24**, 128229-16-3; **25**, 128229-17-4; **26**, 128229-18-5; **27**, 84817-41-4; **28**, 129239-55-0; **29**, 129239-56-1; **30**, 129239-57-2; **31**, 129239-58-3; **32**, 129239-59-4; **33**, 129239-60-7; NiO_2, 12035-36-8; 1-(4-methylphenyl)-5-(4-pyridyl)-1,2,3-triazoline, 55643-89-5; 1-(4-methoxyphenyl)-5-(4-pyridyl)-1,2,3-triazoline, 55643-90-8; 1-(4-chlorophenyl)-5-(4-pyridyl)-1,2,3-triazoline, 55643-87-3; 1-(4-nitrophenyl)-5-(4-pyridyl)-1,2,3-triazoline, 129239-61-8; 1-phenyl-5-(4-pyridyl)-1,2,3-triazoline, 55643-88-4; 1-(4-fluorophenyl)-5-(4-pyridyl)-1,2,3-triazoline, 97230-32-5; 1-(4-nitrophenyl)-5-(2-pyridyl)-1,2,3-triazoline, 110684-20-3; 1-phenyl-5-(4-nitrophenyl)-1,2,3-triazoline, 10445-18-8; 1-(4-bromophenyl)-5-phenyl-1,2,3-triazoline, 10480-35-0; 1-(4-bromophenyl)-5-(2-pyridyl)-1,2,3-triazoline, 17843-17-3; 1-(3,4-difluorophenyl)-5-(2-pyridyl)-1,2,3-triazoline, 110684-19-0; 1-(3,4-dichlorophenyl)-5-(4-pyridyl)-1,2,3-triazoline, 106878-43-7; 1-(4-methoxyphenyl)-5-(2-quinolyl)-1,2,3-triazoline, 129239-62-9; 1-(4-methoxyphenyl)-5-(2-chlorophenyl)-1,2,3-triazoline, 91283-09-9; 1-(3,4-dichlorophenyl)-5-(2-chlorophenyl)-1,2,3-triazoline, 14717-17-0; 1-phenyl-5-(2,4-dichlorophenyl)-1,2,3-triazoline, 14632-41-8; 1-(4-chlorophenyl)-5-(2,4-dichlorophenyl)-1,2,3-triazoline, 91283-12-4; 1-(3-chlorophenyl)-5-(2,4-dichlorophenyl)-1,2,3-triazoline, 14632-43-0; 1-(4-fluorophenyl)-5-(2,4-dichlorophenyl)-1,2,3-triazoline, 128229-07-2; 1-(4-bromophenyl)-5-(2,4-dichlorophenyl)-1,2,3-triazoline, 14632-44-1; 1-(4-(trifluoromethyl)phenyl)-5-(2,4-dichlorophenyl)-1,2,3-triazoline, 128229-08-3; 1-(3-(trifluoromethyl)phenyl)-5-(2,4-dichlorophenyl)-1,2,3-triazoline, 91283-11-3; 1-phenyl-5-(2,6-dichlorophenyl)-1,2,3-triazoline, 91283-13-5; 1-(4-chlorophenyl)-5-(2,6-dichlorophenyl)-1,2,3-triazoline, 128229-09-4; 1-(3-chlorophenyl)-5-(2,6-dichlorophenyl)-1,2,3-triazoline, 91283-14-6; 1-(4-bromophenyl)-5-(2,6-dichlorophenyl)-1,2,3-triazoline, 84817-34-5; 1-(4-(trifluoromethyl)phenyl)-5-(2,6-dichlorophenyl)-1,2,3-triazoline, 129239-63-0; 1-(3-(trifluoromethyl)phenyl)-5-(2,6-dichlorophenyl)-1,2,3-triazoline, 129239-64-1; 1-(3,4-dichlorophenyl)-5-(2,4-dichlorophenyl)-1,2,3-triazoline, 14632-48-5; 1-(4-chlorophenyl)-5-(2-nitrophenyl)-1,2,3-triazoline, 129239-65-2; 1-(3,4-dichlorophenyl)-5-(2-nitrophenyl)-1,2,3-triazoline, 14717-16-9; 1-(3-(trifluoromethyl)phenyl)-5-(2-nitrophenyl)-1,2,3-triazoline, 129239-66-3.

Synthesis of Spiroketals: A General Approach

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A general procedure for the synthesis of functionalized spiroketals from lactones is described. Addition of the lithium acetylide of cis-1-methoxy-1-buten-3-yne to lactones followed by a hydration of the acetylene, hydrolysis of the enol ether and cyclization gives excellent yields of spiroketals containing a useful enone functionality.

The presence of highly substituted and functionalized spiroketals in many biologically significant natural products has stimulated a great deal of synthetic work directed toward the synthesis of these systems.[2] These include complex molecules such as calcimycin (A-23187),[3] okadaic acid,[4] monensin,[5] aplysiatoxin,[6] phyllanthocin,[7] and the

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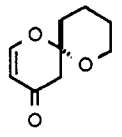
milbemycins[8] and avermectins.[9] While the majority of synthetic approaches rely heavily on acyclic stereocontrol to establish relative and absolute stereochemistry about the periphery of the spirocyclic system, some approaches have utilized the spiroketal as a template for stereochemical control.[2,10] The former approach can be a very useful and successful one, but usually requires that a different basic strategy be invoked for each individual molecule. The latter approach can in principal be more general if the initial spiroketal contains a sufficient useful functionality for further elaboration of the spirocyclic template. We report here our studies directed toward the construction of spiroketal systems which contain a versatile enone functionality.

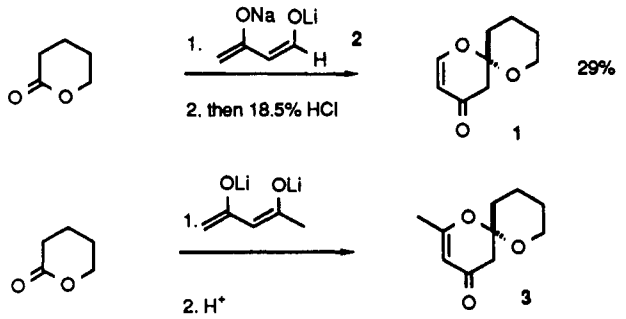
If one examines many of the known spiroketal containing natural products, two features are immediately obvious. Many contain hydroxyl substituents on the carbon β to the spiroketal center as well as a substituent on the carbon bearing the spiroketal oxygen in that same ring. A potentially useful approach to construction of these types of systems would be to utilize an α,β-unsaturated system such as 1 which contains an oxygen at a suitable position and presents the opportunity for introduction of substituents β to that oxygen as well. Additionally, the multitude of reactions which can be carried out on α,β-unsaturated enone systems could allow the incorporation of a wide variety of substituents and functionality into these systems.



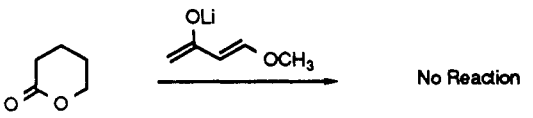
1

Results and Discussion

The simplest approach to systems of this type might be to utilize the addition of the dianion[11] of formyl acetone 2 to lactones followed by acid-catalyzed cyclization to the spiroketals. Barrett has used an analogous procedure involving the dianions of β-diketones to prepare substituted systems such as 3.[10d] In an attempt to execute this plan, addition of 2 equiv of *n*-butyllithium to a suspension of sodioformyl acetone in tetrahydrofuran followed by addition of δ-valerolactone gave, after acidification and purification, a modest yield (29%) of the desired spiroketal 1.



While this procedure is very direct and works with a variety of substituted lactones (Table I), the low yields (due primarily to the difficulties encountered with the preparation, storage and metallation of sodioformylacetone) led us to search for a more suitable equivalent to formylacetone dianion. The obvious first alternative, 4-methoxy-3-buten-2-one, underwent smooth metalation but failed to react with δ-valerolactone to any appreciable extent. Another alternative was the lithium acetylide 8 of 1-methoxy-1-buten-3-yne wherein the enol ether serves as the formylacetone aldehyde and the acetylene is a latent



carbonyl. This acetylide proved to be an extraordinary nucleophile for the addition to lactone carbonyls. Addition of δ-valerolactone to a solution of acetylide 8 in THF at −78 °C produced the acetylenic ketone 9 in >95% yield after workup. A variety of acids and solvent systems were investigated in an attempt to effect direct hydrolysis and cyclization of the acetylenic ketone 9 to the desired spiroketal 1 (Scheme I). The best combination of acid and solvent was found to be 30% perchloric acid–dichloromethane. This biphase system gave yields of up to 50–60% for spiroketals derived from simple lactones (Table II),[12] although the results were not always reproducible and the conditions failed when substitution on the lactones was increased. If the acetylenic ketone 9 was subjected to potassium carbonate in methanol, the enol ether–acetal 15 was produced in near quantitative yield. Acid hydrolysis of this acetal as before gave fairly consistent good yields of the spiroketals if the rate of stirring of the biphase system was rapid (Table III). Insufficient mixing of the two phases results in production of significant amounts (up to 50%) of the β-methoxy derivatives such as 16. While elimination of methanol from 16 to produce 1 could be accomplished with BF_3–Et_2O in dichloromethane at −78 °C or with wet Amberlyst 15 in dichloromethane at 40 °C, the consistent presence of even small amounts of this contaminant was troublesome.

The main problem with this procedure for the preparation of spiroketals such as 1 was again the reduced yields which resulted from the use of more highly substituted lactones. For example 5,6-dimethylvalerolactone 18 underwent smooth addition with acetylide 8 and the resultant acetylenic ketone gave a nearly quantitative yield of the acetal 19, but only trace amounts of the spiroketal 4 were produced under the biphase conditions (Scheme II). This problem was attributed to the decreased hydrophilicity of

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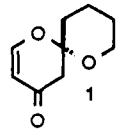
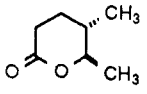
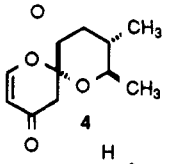
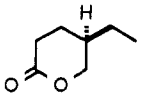
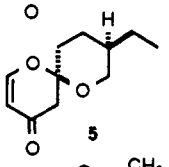
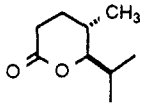
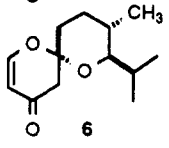
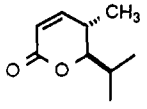
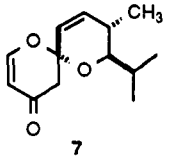
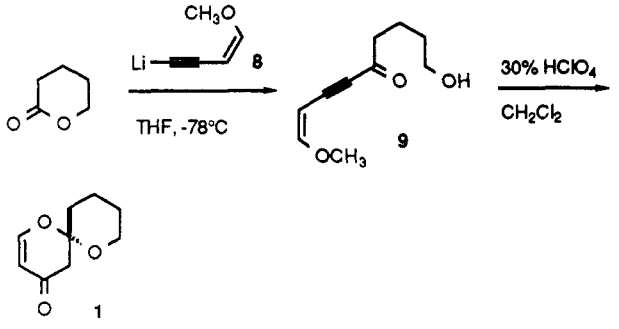
Table I. Addition of Sodiolithioformylacetone to Lactones

lactone	spiroketal (yield)
	 29% **1**
	 34% **4**
	 20% **5**
	 36% **6**
	 27% **7**

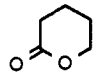
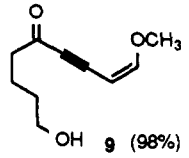
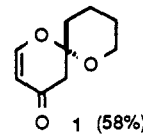
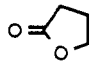
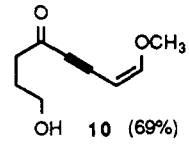
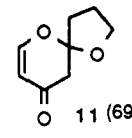
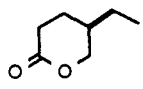
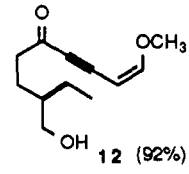
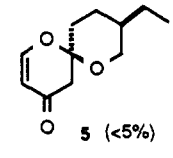
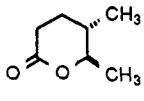
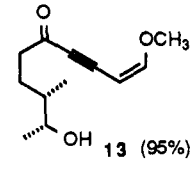
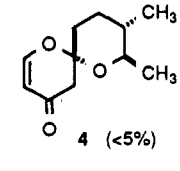
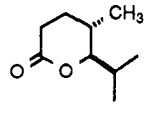
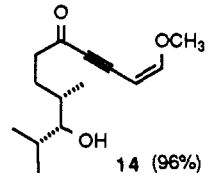
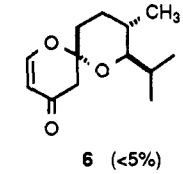
Scheme I



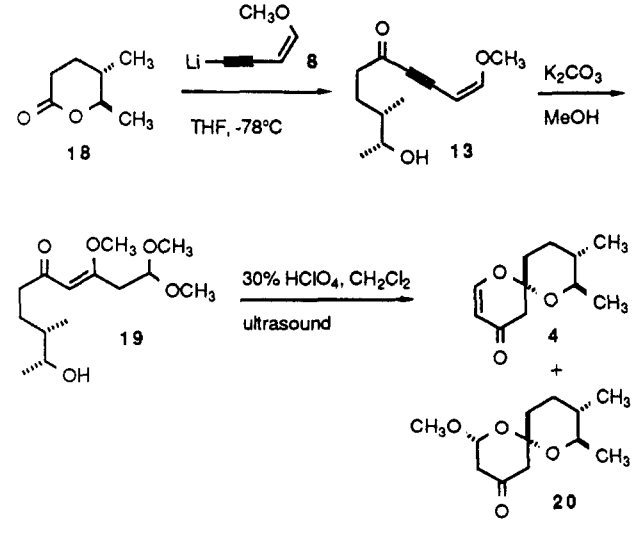
the more highly substituted system. To effect better contact of the aqueous and organic phases in the hydrolysis, the mixture was irradiated with ultrasonic waves. This procedure produced a significant increase in the yield of the spiroketal, and **4** was isolated in 35% yield along with 20% of the corresponding β-methoxy derivative **20**. This ultrasonic irradiation of the hydrolysis mixture proved reasonably effective in other systems as well (Table III), but the overall yield of spiroketal from lactone was still less than we had hoped in the highly substituted systems since these lactones often required several steps to prepare.

Ultimately, the best solution was found while attempting to construct a system which contained an α-substituent on the δ-lactone which could eventually be eliminated to form a double bond in the spiroketal. When the lactone **25** was treated with the acetylide **8** a 95% yield of the acetylenic ketone **26** was obtained (Scheme III). This acetylenic ketone could be readily converted to the acetal **27** with potassium carbonate in methanol, but the acetal **27** failed to produce the spiroketal **28** under the usual conditions described above. A survey of several other acids and solvent systems did not yield a significant amount of the spiroketal **28**, but treatment of **27** with *p*-toluenesulfonic acid in 4:1 tetrahydrofuran–water at reflux for 12 h cleanly produced a near quantitative yield of the pyrone

Table II. Direct Hydrolysis of Hydroxyacetylenic Ketones to Spiroketals

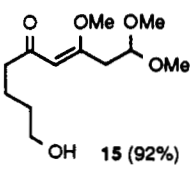
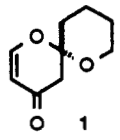
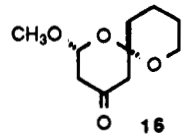
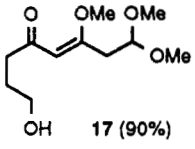
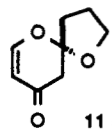
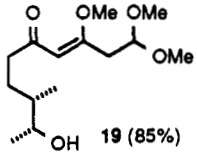
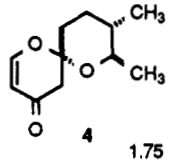
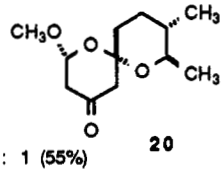
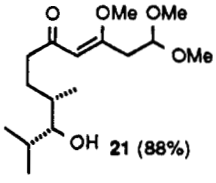
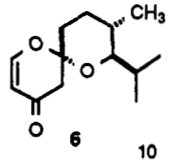
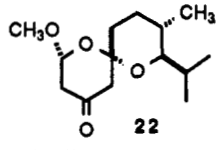
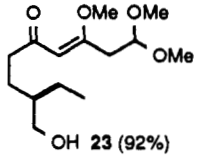
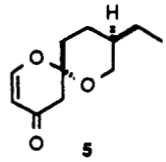
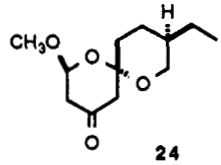
lactone	acetylenic ketone (yield)	spiroketal (yield)
	 **9** (98%)	 **1** (58%)
	 **10** (69%)	 **11** (69%)
	 **12** (92%)	 **5** (<5%)
	 **13** (95%)	 **4** (<5%)
	 **14** (96%)	 **6** (<5%)

Scheme II

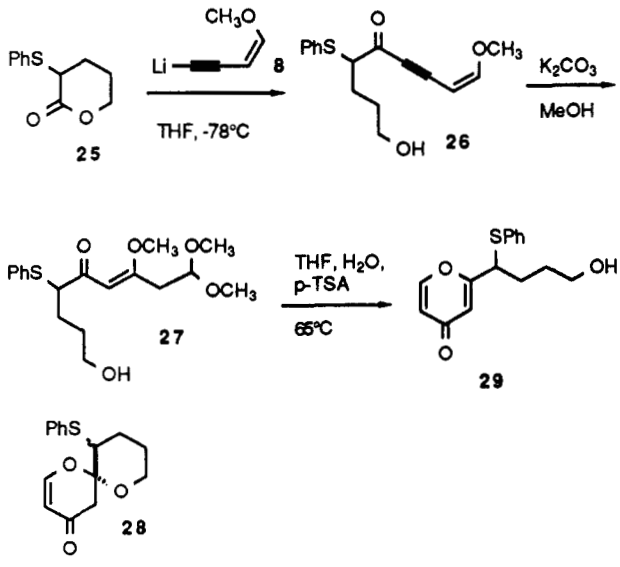


29 as the sole product. At this point it was clear that hydroxy pyrones of this type might be cyclized to the desired spiroketals under acidic conditions. We reasoned that since the spiroketals had been the major product in previous reactions in nonaqueous solvents, it might be possible to close the pyrones to the spiroketals if the proper organic solvent and acid were found. The acetal **15** also gave high yields of the corresponding pyrone **30** when exposed to *p*-toluenesulfonic acid in aqueous THF. After investigation of several solvents and acids the best system

Table III. Hydrolysis of the Enol Ether Acetals with 30% $HClO_4$–CH_2Cl_2 Biphase

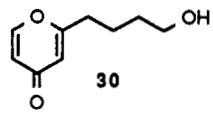
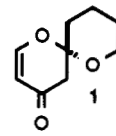
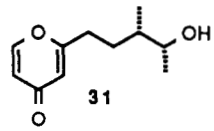
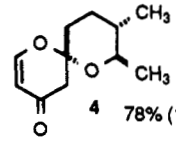
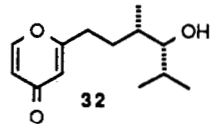
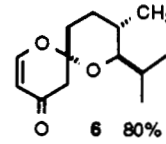
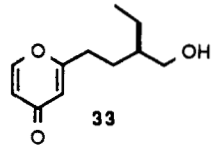
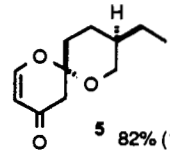
acetal (yield)	spiroketal(s) (yield)
 15 (92%)	 1  16 1 : 1 (85%)
 17 (90%)	 11 (69%)
 19 (85%)	 4  20 1.75 : 1 (55%)
 21 (88%)	 6  22 10 : 1 (60%)
 23 (92%)	 5  24 1.1 : 1 (42%)

Scheme III



was found to be trifluoroacetic acid in benzene or toluene. These conditions converted the pyrone **30** into a 1:2 mixture of the spiroketal **1** and the starting pyrone **30**. This method, in contrast to the earlier procedures improved significantly as the substitution on the lactone ring increased as shown in Table IV. It is noteworthy that as

Table IV. Cyclization of Hydroxypyrones-*d*

pyrone	spiroketal (overall yield from lactone; pyrone:spiroketal)
 30	 1 65% (2:1)
 31	 4 78% (1:4)
 32	 6 80% (0:100)
 33	 5 82% (1:3.5)

the substitution on the lactone is increased, an increasing amount of the spiroketal is produced in the initial hydrolysis step to form the pyrone. Additionally, the position of the equilibrium in the TFA–benzene cyclization is shifted further toward the spiroketal as the substitution is increased.

The initial production of the pyrone in aqueous THF is probably due to a hydrogen bonding stabilizaton of the open chain hydroxyl by the aqueous media. This effect is not available in the nonpolar benzene media. The increase in the amount of spiroketal as the substitution on the lactone increases is possibly due to increased van der Waals interactions between the substituents in the open chain which minimize available degrees of freedom and therefore increasingly favor the cyclic side of the equilibrium.

Regardless of the reason the four operations from lactone to spiroketal can now be performed in yields of 70–80% for most highly substituted lactones in a single sequence. For lesser substituted systems, the product pyrones can be trivially separated from the desired spiroketals and resubjected to the TFA–benzene step to produce additional spiroketal. While this recycle procedure is not ideal, it is only necessary for the cases which work well with 30% perchloric acid–dichloromethane.

Application of this methodology to the synthesis of various spiroketal containing natural products is currently in progress.[13-15]

Experimental Section

General Experimental Procedures. Preparative column chromatography was performed with "silica gel for flash chromatography" manufactured by J.T. Baker Chemical Co. "Dry" solvents were distilled immediately prior to use from an appropriate drying agent. Diethyl ether, benzene, and tetrahydrofuran (THF) were distilled from sodium benzophenone. *cis*-1-methoxy-1-buten-3-yne was purchased from Aldrich Chemical Company as a 50% solution in methanol–water. This mixture

(13) Crimmins, M. T.; Hollis, W. G., Jr.; Bankaitis-Davis, D. M. *Tetrahedron Lett.* **1987**, *28*, 3651.
(14) Crimmins, M. T.; Bankaitis-Davis, D. M.; Hollis, W. G., Jr. *J. Org. Chem.* **1988**, *53*, 652.
(15) Crimmins, M. T.; O'Mahony, R. *J. Org. Chem.* **1989**, *54*, 1157.

was carefully distilled to obtain the pure acetylene which was redistilled immediately prior to metalation. The purity of all title compounds was shown to be ≥95% by elemental analysis or homogeneous by TLC and ^{1}H NMR.

General Procedure for the Addition of Sodiolithioacetoacetaldehyde to Substituted Lactones. A 100-mL three-necked round bottom flask equipped with a stir bar and nitrogen bubbler was charged with 0.22 mL (1.6 mmol) of diisopropylamine and 50 mL of THF and was then cooled to −5 °C (ice/acetone). To this solution was added dropwise 0.63 mL (1.6 mmol) of 2.5 M *n*-butyllithium. After 15 min, 0.253 g (2.30 mmol) of sodioacetoacetaldehyde was added, and the bath was removed. When most of the solid had dissolved (30 min), the solution was cooled to −5 °C, and 0.78 mmol of the lactone was added. After 20 min the reaction was quenched with 10 mL of 18.5% HCl and stirred for an additional 5 min. The reaction was then diluted with ether, washed with brine and saturated $NaHCO_3$, dried over $MgSO_4$, concentrated, and chromatographed to yield the spiroketal.

Dioxaspiro[5.5]undec-2-en-4-one (1). According to the general procedure above 0.18 mL (2.0 mmol) of δ-valerolactone provided 0.096 g (29%) of spiroketal **1**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.49–2.08 (6 H, band, $CH_2CH_2CH_2$), 2.65 (2 H, AB, $\Delta\nu$ = 24, J = 16, J_w = 1 Hz), 3.64–3.80 (2 H, m, OCH_2), 5.46 (1 H, dd, J = 6, 1 Hz, OCH=C*H*), 7.22 (1 H, d, J = 6 Hz, OC*H*=); ^{13}C NMR ($CDCl_3$) δ 17.98, 24.29, 33.67, 48.04, 62.53, 103.17, 107.30, 158.69, 191.57; IR (film) 1680, 1610, 1405, 1235 cm^{-1}. Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.27. Found: C, 64.14; H, 7.27.

8(*R*),9(*S*)-Dimethyldioxaspiro[5.5]undec-2-en-4-one (4). According to the general procedure above 0.10 g (0.78 mmol) of dimethylvalerolactone provided 0.052 g (34%) of spiroketal **4**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.83 (3 H, d, J = 6 Hz, CH(CH_3)), 1.13 (3 H, d, J = 6 Hz, CH(CH_3)), 1.25–2.06 (5 H, band, CH_2CH_2CH-(Me)), 2.64 (2 H, AB, J = 16, J_w = 1, $\Delta\nu$ = 28 Hz, $COCH_2$), 3.41–3.53 (1 H, m, OC*H*(Me)), 5.45 (1 H, dd, J = 6, 1 Hz, OCH=C*H*), 7.20 (1 H, d, J = 6 Hz, OC*H*=); ^{13}C NMR ($CDCl_3$) δ 17.70, 19.22, 26.91, 33.87, 35.93, 47.83, 73.83, 103.44, 106.99, 159.05, 192.10; IR (film) 1675, 1610, 1410, 1380, 1240 cm^{-1}; $[\alpha]^{21}_D$ = +201.8° ($CHCl_3$, c = 4.87). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.27; H, 8.07.

8(*R*)-Ethyldioxaspiro[5.5]undec-2-en-4-one (5). According to the general procedure above 0.10 g (0.78 mmol) of 4-ethylvalerolactone provided 0.031 g (20%) of spiroketal **5**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90 (3 H, t, J = 7.5 Hz, CH_2CH_3), 1.20 (2 H, m, CH_2CH_3), 1.65 (4 H, m, CH_2's), 2.05 (1 H, m, $CHCH_2CH_3$), 2.63 (2 H, AB, J = 16.5 Hz, $\Delta\nu$ = 37.6 Hz, J_w = 1 Hz, CH_2CO), 3.35 (1 H, dd, J = 10.5, 10.5 Hz, $OCH_{axial}H_{eq}$), 3.66 (1 H, ddd, J = 10.5, 2, 4.5 Hz, $OCH_{axial}H_{eq}$), 5.45 (1 H, dd, J = 6 Hz, J_w = 1 Hz, OCH=CHCO), 7.21 (1 H, d, J = 6 Hz, OC*H*=CHCO); ^{13}C NMR ($CDCl_3$) δ 10.97, 24.16, 24.93, 33.68, 35.88, 47.54, 67.11, 103.45, 107.68, 158.78, 192.01; IR (film) 1690, 1610 cm^{-1}; $[\alpha]^{22}_D$ = −223.3° ($CHCl_3$, c = 4.235). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.35; H, 8.16. Found: C, 67.36; H, 8.26.

8(*R*)-Isopropyl-9(*S*)-methyldioxaspiro[5.5]undec-2-en-4-one (6). According to the general procedure above, 0.10 g (0.64 mmol) of methylisopropylvalerolactone provided 0.039 g (36%) of spiroketal **6**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.79 (3 H, d, J = 7 Hz, CH(CH_3)), 0.84 (3 H, d, J = 7 Hz, CH(CH_3)), 0.87 (3 H, d, J = 7 Hz, CH(CH_3)), 1.45–2.04 (6 H, band), 2.63 (2 H, AB, $\Delta\nu$ = 32 Hz, J = 16, 1 Hz, $COCH_2$), 3.21 (1 H, dd, J = 2.9 Hz, OC*H*(iPr)), 5.45 (1 H, dd, J = 6, 1 Hz, C*H*=), 7.18 (1 H, d, J = 6 Hz, CH=C*H*OMe); ^{13}C NMR ($CDCl_3$) δ 13.87, 17.05, 20.02, 27.41, 27.89, 30.99, 33.95, 47.70, 80.75, 103.46, 107.19, 158.57, 191.97; IR (film) 1680, 1610 cm^{-1}; $[\alpha]^{22}_D$ = +326° ($CHCl_3$, c = 1.0 g/100 mL). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.54; H, 8.83.

8(*R*)-Isopropyl-9(*S*)-methyldioxaspiro[5.5]undeca-2,10-dien-4-one (7). According to the general procedure above, 0.10 g (0.65 mmol) of unsaturated methylisopropylvalerolactone provided 0.052 g (27%) of the very unstable spiroketal **7**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.84 (3 H, d, J = 6 Hz, CH(CH_3)), 0.95 (3 H, d, J = 7.5 Hz, CH(CH_3)), 0.96 (3 H, d, J = 7.5 Hz, CH(CH_3)), 1.78–1.99 (1 H, m, CH(CH_3)$_2$), 2.18–2.38 (1 H, m, CH=CHC*H*-(Me)), 2.69 (2 H, AB, $\Delta\nu$ = 26 Hz, J = 16 Hz, J_w = 1 Hz, $COCH_2$), 3.41 (1 H, dd, J = 3, 10 Hz, OC*H*(iPr)), 5.47 (1 H, dd, J = 6, 1 Hz, OCH=C*H*), 5.74 (1 H, dd, J = 12, 3 Hz, C*H*=), 5.93 (1 H, dd, J = 2, 12 Hz, C*H*=), 7.18 (1 H, d, J = 6 Hz, OC*H*=CH).

General Procedure for the Addition of the Lithium Acetylide of *cis*-1-Methoxy-1-buten-3-yne to Lactones. A 50-mL three-necked round bottom flask equipped with a stir bar and nitrogen bubbler was charged with 10 mL of THF and 0.05 mL (0.53 mmol) of freshly distilled *cis*-1-methoxy-1-buten-3-yne and was cooled to −78 °C. A solution of 0.21 mL (0.53 mmol) of 2.5M *n*-butyllithium was then added dropwise. After 50 min, 0.48 mmol of lactone in 5 mL of THF was added. After 0.5 h the reaction was quenched with saturated NH_4Cl, diluted with ether, and washed with brine. The organic phase was dried over $MgSO_4$ and concentrated to yield the acetylenic ketone.

9-Hydroxy-1-methoxynon-1-en-3-yn-5-one (9). According to the general procedure described above 2.01 g (20.0 mmol) of δ-valerolactone produced 3.48 g (95%) of the acetylenic ketone **9**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.53–1.80 (4 H, band, $CH_2CH_2CH_2OH$), 2.62 (2 H, t, J = 7 Hz, CH_2CO), 2.87 (1 H, br s, O*H*), 3.62 (2 H, t, J = 5.5 Hz, CH_2OH), 3.86 (3 H, s, OCH_3), 4.67 (d, J = 6 Hz, C*H*=CHOMe), 6.62 (1 H, d, J = 6 Hz, CH=C*H*OMe); exact mass calcd for $C_{10}H_{14}O_3$ 182.0943, found 182.0942; ^{13}C NMR ($CDCl_3$) δ 20.36, 31.92, 44.82, 61.38, 62.22, 82.83, 87.75, 92.36, 162.13, 188.00; IR (film) 3630, 3470, 2170, 1725, 1660, 1620 cm^{-1}; HRMS calcd for $C_{10}H_{14}O_3$ 182.0942, found 182.0940.

8-Hydroxy-1-methoxyoct-1-en-3-yn-5-one (10). According to the general procedure described above, 1.257 g (14.6 mmol) of γ-butyrolactone produced 1.624 g (69%) of the acetylenic ketone **10**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.87 (2 H, m, CH_2CH_2OH), 2.34–2.96 (4 H, band, $COCH_2CH_2CH_2OH$), 3.72 (2 H, t, J = 7, CH_2OH), 3.76 (3 H, s, CH=CHO*Me*), 4.48 (1 H, d, J = 6 Hz, C*H*=CHOMe), 5.06 (1 H, s, O*H*), 6.29 (1 H, d, J = 6 Hz, CH=C*H*OMe); IR (film) 3640, 3460, 2170, 1735, 1665, 1620 cm^{-1}. Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.16; H, 6.98.

2(*R*)-Ethyl-1-hydroxy-9-methoxynon-8-en-6-yn-5-one (12). According to the general procedure described above, 1.63 g (12.7 mmol) of 4-ethylvalerolactone gave 2.52 g (95%) of the crude ketone: IR (film) 3430, 2120, 1665, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90 (3 H, t, J = 7.5 Hz, CH_2CH_3), 1.14–1.79 (5 H, band), 2.63 (2 H, dd, J = 7.5, 7.0 Hz, CH_2CO), 2.74 (1 H, br s, O*H*), 3.52 (2 H, dd, J = 5, 3 Hz, CH_2OH), 3.86 (3 H, s, OCH_3), 4.67 (1 H, d, J = 6.0 Hz, C*H*=CHOMe), 6.61 (1 H, d, J = 6.0 Hz, CH=C*H*OMe); exact mass calcd for $C_{12}H_{18}O_3$ 210.1256, found 210.1246; ^{13}C NMR ($CDCl_3$) δ 11.14, 23.38, 24.62, 41.52, 42.74, 61.36, 64.52, 82.89, 87.78, 92.41, 162.09, 188.33; IR (film) 3430, 2170, 1735, 1665, 1620 cm^{-1}; HRMS calcd for $C_{12}H_{18}O_3$ 210.1255, found 220.1258.

9(*R*)-Hydroxy-1-methoxy-8(*S*)-methyldec-1-en-3-yn-5-one (13). According to the general procedure described above, 1.10 g (8.61 mmol) of dimethylvalerolactone produced 1.72 g (95%) of the acetylenic ketone **13**: ^{1}H NMR (100 MHz, $CDCl_3$) δ 0.90 (d, J = 7.2 Hz, 3 H, CH_3), 1.16 (d, J = 7.2 Hz, 3 H, CH_3), 1.40–2.15 (band, 3 H, C*H*Me, CH_2), 2.63 (m, 2 H, CH_2CO), 3.51–3.80 (m, 2 H, C*H*OH), 3.90 (s, 3 H, OCH_3), 5.71 (d, J = 6.8 Hz, 1 H, C*H*=CHOMe), 6.63 (d, J = 6.8 Hz, 1 H, CH=C*H*OMe); exact mass calcd for $C_{12}H_{18}O_3$ 210.1256, found 210.1253; ^{13}C NMR ($CDCl_3$) δ 14.70, 19.68, 26.83, 39.58, 42.98, 61.36, 71.40, 82.93, 87.63, 92.41, 162.01, 188.17; IR (film) 3620, 2970, 2940, 2880, 2170, 1735, 1665, 1625 cm^{-1}; HRMS calcd for $C_{12}H_{18}O_3$ 210.1255, found 220.1256.

9(*R*)-Hydroxy-1-methoxy-8(*S*),10-dimethylundec-1-en-3-yn-5-one (14). According to the general procedure described above, 2.53 g (16.2 mmol) of methylisopropylvalerolactone produced 3.83 g (99%) of the acetylenic ketone **14**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.90 (d, J = 7.2 Hz, 3 H, CH_3), 0.93 (d, J = 7.2 Hz, 3 H, CH_3), 0.96 (d, J = 6.8 Hz, 3 H, CH_3), 1.45–2.17 (band, 4 H, CH_2 and C*H*'s), 2.66 (m, 2 H, CH_2CO), 3.09 (dd, J = 5.7 Hz, J = 5.7 Hz, 1 H, C*H*OH), 3.79 (s, 1 H, O*H*), 3.88 (s, 3 H, OCH_3), 5.69 (d, J = 6.8, Hz, 1 H, C*H*=CHOMe), 6.58 (d, J = 6.8 Hz, 1 H, CH=C*H*OMe); exact mass calcd for $C_{14}H_{22}O_3$ 238.1569, found 238.1571; ^{13}C NMR ($CDCl_3$) δ 16.18, 16.31, 20.03, 25.83, 30.09, 35.27, 42.91, 61.33, 80.70, 82.95, 87.49, 92.46, 161.92, 188.39; IR (film) 3630, 3460, 2170, 1735, 1665, 1625 cm^{-1}; HRMS calcd for $C_{14}H_{22}O_3$ 238.1568, found 238.1559.

9-Hydroxy-1-methoxy-6-(phenylthio)non-1-en-3-yn-5-one (26). According to the general procedure described above, 0.10 g (0.48 mmol) of phenylthiolactone produced 0.13 g (90%) of the acetylenic ketone **26**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.58–2.10 (4 H, band, $CH_2CH_2CH_2OH$), 2.28 (1 H, br s, O*H*), 3.62 (2 H, t, J

= 6 Hz, CH_2OH), 3.74 (1 H, dd, J = 7, 8 Hz, CHSPh), 3.83 (3 H, s, OCH_3), 4.65 (1 H, d, J = 7 Hz, CH=CHOMe), 6.58 (1 H, d, J = 7 Hz, CH=CHOMe), 7.22–7.54 (5 H, m, C_6H_5).

General Procedure for the Methanolysis of the Acetylenic Ketones. A 100-mL round-bottom flask equipped with a stir bar and stopper was charged with 0.43 mmol of ketone, 30 mL of methanol, and 0.06 g (0.04 mmol) of K_2CO_3. After stirring for 2 h, the reaction was partially concentrated, diluted with ether, and dried over $MgSO_4$. Concentration provided the enone.

1-Hydroxy-7,9,9-trimethoxynon-6-en-5-one (15). According to the general procedure described above, 3.48 g (19.1 mmol) of acetylenic ketone **9** produced 4.56 g (92%) of the trimethoxy ketone **15**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.32–1.78 (4 H, band, CH_2CH_2), 2.49 (2 H, t, J = 6 Hz, CH_2CO), 3.12 (2 H, d, J = 6 Hz, $CH_2CH(OCH_3)$), 3.34 (6 H, s, $CH(OCH_3)_2$), 3.62 (2 H, t, J = 5 Hz, CH_2OH), 3.68 (3 H, s, OCH_3), 4.73 (1 H, t, J = 6 Hz, $CH(OMe)_2$), 5.53 (1 H, s, CH=); exact mass calcd for $C_{12}H_{22}O_5$ 246.1467, found 246.1459; ^{13}C NMR ($CDCl_3$) δ 20.48, 32.20, 36.44, 44.10, 52.96, 55.62, 62.05, 99.77, 102.26, 171.10, 199.26; IR (film) 3450, 1680, 1585, 1120, 1070, 1050 cm^{-1}; HRMS calcd for $C_{12}H_{22}O_5$ 246.1466; found 246.1476.

1-Hydroxy-6,8,8-trimethoxyoct-5-en-4-one (17). According to the general procedure described above, 173 mg (1.03 mmol) of acetylenic ketone **10** produced 215 mg (90%) of the trimethoxy ketone **17**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.52–1.78 (2 H, band, CH_2), 2.50 (2 H, t, J = 6 Hz, CH_2CO), 3.12 (2 H, d, J = 6 Hz, $CH_2CH(OCH_3)$), 3.34 (6 H, s, $CH(OCH_3)_2$), 3.62 (2 H, t, J = 5 Hz, CH_2OH), 3.71 (3 H, s, OCH_3), 4.72 (1 H, t, J = 6 Hz, $CH(OMe)_2$), 5.51 (1 H, s, CH=); IR (film) 3450, 1680, 1585, 1120, 1070, 1050 cm^{-1}. Anal. Calcd for $C_{11}H_{20}O_5$: C, 56.88; H, 8.68. Found: C, 56.57; H, 8.31.

1,7-Dioxaspiro[5.4]dec-2-en-4-one (11). The crude trimethoxy ketone **17** above (215 mg) was dissolved in 30 mL of dichloromethane, the solution was cooled to 0 °C, and 30 mL of 30% perchloric acid was added with vigorous stirring. After 10 min the organic layer was washed with $NaHCO_3$, dried, and concentrated to afford 77 mg (53%) of spiroketal **11**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.50–2.50 (band, 4 H, $(CH_2)_2$), 2.73 (d, 1 H, J = 16.2 Hz, CH_2CO, axial), 2.92 (d, 1 H, J = 16.5 Hz, CH_2CO, equatorial), 4.00–4.20 (m, 2 H, CH_2O), 5.47 (d, 1 H, J = 5.9 Hz, =CHCO), 7.22 (d, 1 H, J = 6.1 Hz, OCH=CHCO); IR ($CDCl_3$) 1680, 1605, 1405 cm^{-1}. Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.14; H, 6.64.

9(*R*)-Hydroxy-1,1,3-trimethoxy-8(*S*)-methyldec-3-en-5-one (19). According to the general procedure described above, 0.889 g (4.23 mmol) of acetylenic ketone **13** produced 0.987 g (85%) of trimethoxy ketone **19**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.88 (d, J = 6.5 Hz, 3 H, CH_3), 1.15 (d, J = 6.5 Hz, 3 H, CH_3), 1.40–1.60 (band, 2 H, CH_2), 1.79 (m, 1 H, CHMe), 2.05 (broad s, 1 H, OH), 2.30–2.70 (band, 2 H, CH_2CO), 3.12 (d, J = 6 Hz, 2 H, CH_2), 3.34 (s, 6 H, OCH_3's), 3.58 (m, 1 H, CHOH), 3.68 (s, 3 H, OCH_3), 4.72 (t, J = 6 Hz, 1 H, $CH(OMe)_2$), 5.52 (s, 1 H, CH=C); exact mass calcd for $C_{14}H_{26}O_5$ 274.1780, found 274.1784; ^{13}C NMR ($CDCl_3$) δ 14.89, 1973, 27.13, 36.46, 39.87, 41.96, 52.98 (2), 55.64, 71.18, 99.81, 102.23, 171.10, 199.54; IR ($CDCl_3$) 3630, 3640, 1680, 1585, 1455 cm^{-1}; HRMS calcd for $C_{14}H_{26}O_5$ 274.1779, found 274.1789.

9(*R*)-Hydroxy-1,1,3-trimethoxy-8(*S*),10-dimethylundec-3-en-5-one (21). According to the general procedure described above, 3.83 g (16.1 mmol) of acetylenic ketone **14** produced 4.31 g (88%) of trimethoxy ketone **21**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.88 (d, J = 6.7 Hz, 3 H, CH_3), 0.91 (d, J = 6.0 Hz, 3 H, CH_3), 0.96 (d, J = 6.3 Hz, 3 H, CH_3), 1.43–1.67 (band, 2 H, CH_2), 1.76–2.05 (band, 3 H, CH_2, $CH(Me)_2$), 2.38–2.67 (band, 2 H, CH_2CO), 3.08 (m, 1 H, CHOH), 3.13 (d, J = 5.6 Hz, 2 H, OCH_3), 3.35 (s, 6 H, OCH_3), 3.69 (s, 3 H, OCH_3), 4.72 (dd, J = 5.6 Hz, J = 5.6 Hz, 1 H, $CH(OMe)_2$), 5.54 (s, 1 H, CH=C); exact mass calcd for $C_{16}H_{30}O_5$ 302.2093, found 302.2095; ^{13}C NMR ($CDCl_3$) δ 15.82, 16.43, 20.21, 26.39, 30.00, 35.62, 36.50, 41.96, 53.04 (2), 55.67, 80.36, 99.76, 102.30, 171.07, 199.78; IR (neat) 2965, 2935, 2875, 2170, 1730, 1660, 1620, 1465 cm^{-1}; HRMS calcd for $C_{16}H_{30}O_5$ 302.2093, found 302.2093.

2(*R*)-Ethyl-1-hydroxy-7,9,9-trimethoxynon-6-en-5-one (23). According to the general methanolysis procedure, 3.46 g (19.1 mmol) of 2(*R*)-ethyl-1-hydroxy-9-methoxynon-8-en-6-yn-5-one yielded 4.56 g (92%) of 2(*R*)-ethyl-1-hydroxy-7,9,9-trimethoxynon-6-en-5-one (**23**) as a pale yellow oil: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90 (3 H, t, J = 7.5 Hz, CH_2CH_3), 1.48–1.76 (7 H, band), 2.50 (2 H, t, J = 7.5 Hz, CH_2CO), 2.93 (1 H, br s, OH), 3.10 (2 H, d, J = 6 Hz, $CH_2CH(OMe)_2$), 3.33 (6 H, s, $CH(OCH_3)_2$), 3.48 (2 H, t, J = 7 Hz, CH_2OH), 3.69 (3 H, s, OCH_3), 4.70 (1 H, t, J = 6.0 Hz, $CH(OMe)_2$), 5.54 (1 H, s, J = 6.0 Hz, CH=COMe); exact mass calcd for $C_{14}H_{26}O_5$ 274.1780, found 274.1777; ^{13}C NMR ($CDCl_3$) δ 11.35, 23.66, 24.51, 36.54, 41.80, 42.01, 53.05 (2), 55.69, 64.25, 99.79, 102.27, 171.28, 199.78; IR (film) 3450, 1685, 1590 cm^{-1}; HRMS calcd for $C_{14}H_{26}O_5$ 274.1779, found 274.1772.

9-Hydroxy-6-(phenylthio)-1,1,3-trimethoxynon-3-en-5-one (27). According to the general procedure described above, 0.126 g (0.430 mmol) of phenylthioacetylenic ketone **26** produced 0.143 g (93%) of the trimethoxy ketone **27**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.56–2.08 (4 H, band, $CH_2CH_2CH_2OH$), 3.06 (2 H, d, J = 6 Hz, $CH_2CH(OMe)_2$), 3.14 (1 H, dd, J = 6, 7.5 Hz, PhSCH), 3.30 (6 H, s, $CH(OCH_3)_2$), 3.62 (3 H, s, CH=CHOCH_3), 3.66 (2 H, m, CH_2OH), 4.61 (1 H, t, J = 6 Hz, $CH(OMe)_2$), 5.69 (1 H, s, CH=), 7.21–7.44 (5 H, m, C_6H_5).

General Procedure for the Conversion of Trimethoxyenones to Pyrones. A 250-mL round-bottom flask equipped with a stir bar, heating mantle, and condenser was charged with 3.4 mmol of the appropriate enone, 100 mL of THF, 20 mL of water, and 0.1 g of (catalytic) *p*-toluenesulfonic acid. After being heating at reflux for 15 h, the reaction mixture was neutralized with solid $NaHCO_3$, diluted with ether, dried over $MgSO_4$, and concentrated to yield the pyrone.

(*Z*)-2-(1-(Phenylthio)-4-hydroxybutyl)-4-pyrone (29). According to the general procedure, 1.20 g (3.40 mmol) of trimethoxyenone **27** produced 0.889 g (100%) of pyrone **29**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.56–2.09 (5 H, band), 2.67 (1 H, br s, OH), 3.67 (2 H, t, J = 6 Hz, CH_2OH), 3.83 (1 H, t, J = 8 Hz, PhSCH), 5.94 (1 H, d, J = 3 Hz, COCH=), 6.25 (1 H, dd, J = 3, 6 Hz, OCH=CH), 7.70 (1 H, d, J = 6 Hz, OCH=); IR (film) 3380, 1650, 1600, 1420 cm^{-1}.

2-(4-Hydroxybutyl)-4-pyrone (30). According to the general procedure, 4.56 g (17.7 mmol) of enone **15** produced 2.54 g (85%) of pyrone **30**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.48–1.80 (4 H, band), 2.50 (2 H, t, J = 7.5 Hz, =CCH_2), 2.95 (1 H, br s, OH), 3.61 (2 H, t, J = 6 Hz, CH_2OH), 6.12 (1 H, d, J = 2 Hz, COCH=), 6.22 (1 H, dd, J = 2, 6 Hz, OCH=CH), 7.68 (1 H, d, J = 6 Hz, OCH=); exact mass calcd for $C_9H_{12}O_3$ 168.0786, found 168.0782; ^{13}C NMR ($CDCl_3$) δ 23.08, 31.71, 33.31, 61.75, 114.63, 116.45, 155.40, 169.92, 179.56; IR (film) 3400, 1660, 1610, 1420, 1380, 940 cm^{-1}; HRMS calcd for $C_9H_{12}O_3$ 168.0786, found 168.0780.

2-(4-Hydroxy-3,4-dimethylbutyl)-4-pyrone (31). According to the general procedure, 0.641 g (2.30 mmol) of trimethoxy enone **19** produced 0.363 g (84%) of pyrone **31**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.93 (3 H, d, J = 6.5 Hz, $CH(CH_3)$), 1.17 (3 H, d, J = 6.3 Hz, $CH(CH_3)$), 1.39–1.60 (2 H, m, CH_2), 1.84–1.98 (1 H, m, CH(Me)), 2.42–2.70 (2 H, m, =CCH_2), 3.20 (1 H, br s, OH), 3.64 (1 H, m, CH(Me)OH), 6.20 (1 H, d, J = 2.5 Hz, COCH=), 6.28 (1 H, dd, J = 2.5, 6 Hz, OCH=CH), 7.75 (1 H, d, J = 6 Hz, OCH=); HRMS calcd for $C_{11}H_{16}O_3$ 196.1099, found 196.1112; ^{13}C NMR ($CDCl_3$) δ 14.90, 20.17, 29.58, 31.43, 39.51, 71.23, 114.59, 116.53, 155.20, 170.11, 179.40; IR (film) 3430, 1680, 1630, 1430, 1390, 1270, 940, 910, 70, 740 cm^{-1}; $[\alpha]^{21}_D$ −15.82° ($CHCl_3$, c = 2.560); HRMS calcd for $C_{11}H_{16}O_3$ 196.1099, found 196.1105.

2-(4-Hydroxy-4-isopropyl-3-methylbutyl)-4-pyrone (32). According to the general procedure, 0.987 g (0.330 mmol) of trimethoxy enone **21** produced 0.0672 g (92%) of a 3:2 mixture of pyrone **32**:spiroketal **6**: ^{1}H NMR (250 MHz, $CDCl_3$) pyrone **32** δ 0.78–0.96 (9 H, band), 1.42–2.73 (4 H, band), 3.11 (2 H, t, J = 5.5 Hz, =CCH_2), 3.46 (1 H, dd, J = 4, 8 Hz, OCH(iPr)), 6.21 (1 H, d, J = 2 Hz, C(=O)CH=), 6.30 (1 H, dd, J = 2, 6 Hz, OCH=CH), 7.71 (1 H, d, J = 6 Hz, OCH=); exact mass calcd for $C_{13}H_{20}O_3$ 224.1412, found 224.1412; ^{13}C NMR ($CDCl_3$) δ 16.31, 19.33, 19.95, 30.14, 31.23, 31.37, 35.19, 80.56, 114.61, 116.56, 155.12, 170.25, 179.39; IR (film) 3470, 1680, 1590, 1470 cm^{-1}; HRMS calcd for $C_{13}H_{20}O_3$ 224.1412, found 224.1411.

Pyrone 33. According to the general procedure, 4.162 g (14.55 mmol) of 2(*R*)-ethyl-1-hydroxy-7,9,9-trimethoxynon-6-en-5-one gave 2.809 g (98%) a mixture of pyrone **33** and enone **5**. Chromatography (90% EtOAc–10% methanol, silica gel) yielded 2.111 g (74%) of pyrone **33** [^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.92 (3 H, t, J = 7.5 Hz, CH_2CH_3), 1.28–1.87 (5 H, band), 2.58 (2 H, t, J = 8.0 Hz, CH=CHCH_2), 3.39 (1 H, br s, OH), 3.58 (2 H, AB of ABX,

J = 5.5, 10.9, 20.8 Hz), 6.19 (1 H, d, J = 2.5 Hz, OC(CH_2)=C*H*), 6.28 (1 H, dd, J = 2.5, 5.8 Hz, OCH=C*H*), 7.75 (1 H, d, J = 5.8 Hz, OC*H*=CHCO); exact mass calcd for $C_9H_{12}O_3$ 196.1099, found 196.1098; ^{13}C NMR ($CDCl_3$) δ 11.14, 23.33, 27.74, 31.15, 41.29, 64.23, 114.48, 116.43, 155.37, 170.44, 179.60; IR (film) 3450, 1685, 1590 cm^{-1}; $[\alpha]^{20}_D$ = -0.567 ($CHCl_3$, c = 4.06)] and 698 mg (24%) of enone **5** (HRMS calcd for $C_{11}H_{16}O_3$ 196.1099, found 196.1096).

General Procedure for the Conversion of Pyrones to Spiroketals. A 25-mL round-bottom flask equipped with a stir bar and stopper was charged with 20 mL of benzene, 1.0 mmol of pyrone, and 4 drops of trifluoroacetic acid. After stirring for 72 h, the reaction mixture was concentrated to provide the spiroketal-pyrone mixture. Chromatography (silica gel, 10% ethyl acetate in hexanes followed by 10% methanol in ethyl acetate) provided the pure spiroketal and recovered pyrone.

Dioxaspiro[5.5]undec-2-en-4-one (1). According to the general procedure above, 0.100 g (0.595 mmol) of valerolactone pyrone **30** provided 0.847 g (85%) of a 2.3:1 mixture of pyrone **30**-spiroketal **1**.

8(*R*),9(*S*)-Dimethyl-1,7-dioxaspiro[5.5]undec-2-en-4-one (4). According to the general procedure above, 0.053 g (0.29 mmol) of pyrone **31** provided 0.051 g (95%) of a 4:1 mixture of pyrone **31**-spiroketal **4**.

8(*R*)-Ethyl-1,7-dioxaspiro[5.5]undec-2-en-4-one (5). According to the general procedure above, 1.37 g (6.97 mmol) of pyrone **33** produced 0.788 g (58%) of enone **5** and 0.497 (36%) of recovered pyrone **33**.

8(*R*)-Isopropyl-9(*S*)-methyl-1,7-dioxaspiro[5.5]undec-2-en-4-one (6). According to the general procedure above, 1.00 g (4.46 mmol) of pyrone **32** provided 0.988 g (99%) of spiroketal **6**.

Enone 5 from Methoxyspiroketal 24 (BF_3·Et_2O). A 25-mL two-necked round-bottom flask equipped with a stir bar and nitrogen bubbler was charged with 0.083 g (0.36 mmol) of methoxyspiroketal **24** and 2 mL of CH_2Cl_2 and was cooled to 0 °C. To this solution was added 0.06 mL (0.4 mmol) of BF_3·Et_2O, and the reaction mixture was stirred for 5 min. The reaction was quenched with saturated NH_4Cl; the organic phase was dried over $MgSO_4$, concentrated, and chromatographed (25% ethyl acetate/75% hexanes) to yield 30 mg (44%) of enone **5** identical with that prepared above.

Enone 5 from Methoxyspiroketal 24 (Amberlyst). A suspension of 2 g of Amberlyst 15 in a solution of 966 mg (4.24 mmol) of spiroketal **24** and 50 mL of dichloromethane was heated to reflux for 16 h, then cooled, filtered, and concentrated. The residue was flash chromatographed (25% ethyl acetate in hexanes) to provide 484 mg (58%) of spiroketal **5** identical with that prepared above.

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Registry No. **1**, 128777-42-4; **4**, 112320-64-6; **5**, 118418-86-3; **6**, 114066-16-9; **7**, 128683-62-5; **9**, 112320-60-2; **10**, 128683-63-6; **11**, 88400-10-6; **12**, 128777-43-5; **13**, 112320-62-4; **14**, 114066-14-7; **15**, 128683-64-7; **16**, 128777-44-6; **17**, 128683-65-8; **18**, 82467-25-2; **19**, 128777-45-7; **20**, 128777-46-8; **21**, 114066-15-8; **22**, 128777-47-9; **23**, 128777-48-0; **24**, 128777-49-1; **25**, 89036-08-8; **26**, 128683-66-9; **27**, 128683-67-0; **29**, 128683-68-1; **30**, 128683-69-2; **31**, 128683-70-5; **32**, 128683-71-6; **33**, 118418-87-4; MeOCH=CHCOCH$_3$, 4652-27-1; (*Z*)-MeOCH=CHC≡CH, 3685-19-6; δ-valerolactone, 542-28-9; (5*R*)-5-ethyltetrahydropyran-2-one, 118490-63-4; (5*S*,6*R*)-6-ethyl-5-methyltetrahydropyran-2-one, 114179-37-2; (5S,6*R*)-5,6-dihydro-6-ethyl-5-methyl-2*H*-pyran-2-one, 128683-72-7; sodioacetoacetaldehyde, 926-59-0; γ-butyrolactone, 96-48-0.

Supplementary Material Available: ^{13}C NMR and ^1H NMR spectra for key compounds (36 pages). Ordering information is given on any current masthead page.

Theoretical and Experimental Study on the Stereoselectivity of Michael Addition of Alkoxide Anion to Nitro Olefin

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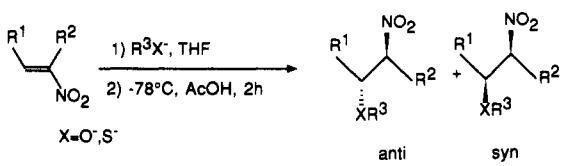
The Michael addition of alkoxide anions to nitro olefins is studied in terms of ab initio and MNDO molecular orbital calculations. We have also done experiments using nitro olefins with the same substituents calculated here. It is proposed that the stereoselectivity of the reaction is due to the endo alkoxy effect, which is structural, and the electronic effect in nitronate anion intermediates. The effect does not exist in intermediates of conjugate addition of simple alkyl group to nitro olefines. The difference depends on whether the atom in the γ-position possesses lone pair orbitals or not. High stereoselectivity was observed in the Michael addition to nitro olefins with the bulky substituents of the α-carbon. This is due to the difficulty in rotating the alkoxy fragment about the C_α-C_β axis.

Introduction

Michael addition is one of the most useful reactions in organic synthesis. Nitro olefins have been used as Michael acceptors because of their high electron deficiency.[1] For example, the reaction of thiols with nitro olefins proceeds smoothly in the presence of catalytic amounts of base to give corresponding β-nitro sulfides in quantitative yields. However, products of the method are usually mixtures of diastereoisomers, whose ratio is nearly 1:1. In order to control stereoselectivity of the Michael reaction with nitro olefin, several procedures have been developed and improved.[2,3] Recently, Ono and his co-workers also devel-

Scheme I



	1	2	3	4	5	6	7
R^1	H	H	Me	Me	Me	H	Me
R^2	H	Me	Me	Et	i-Pr	H	Me
R^3X	MeO	MeO	MeO	MeO	MeO	Et	$PhCH_2O$

(1) (a) *Houben-Weyl: Methoden der Organische Chemie*, 4th ed.; Muller, E., Ed.; George Thieme Verlag: Stuttgart, 1955; Part I, Vol. X. (b) Barrett, A. C. M.: Graboski, G. G. *Chem. Rev.* **1986**, *86*, 751.

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