and isolation of (3*E*,5*E*)-2,4,5,7-tetramethyl-3,5-octadiene[22] serves as a representative example. A suspension of methylcopper in ether was prepared by the dropwise addition of 54.5 mL (81 mmol) of CH_3Li to a 0 °C suspension of 15.45 g (81 mmol) of CuI in 15 mL of ether. The resultant yellow slurry was stirred for 15 min at 0 °C to ensure complete conversion to CH_3Cu. A solution of 4-methyl-2-penten-2-yldibromoborane–dimethyl sulfide (8.25 g, 26.1 mmol) dissolved in 10 mL of ether was added to the CH_3Cu slurry. The reaction mixture was stirred at 0 °C for 45 min, followed by warming to room temperature and then stirring for an additional 30 min. After the mixture was again cooled to 0 °C, excess saturated NH_4Cl solution was added and the reaction warmed to 25 °C. The organic layer was separated and the copper residue washed with ether (3 × 20 mL). The combined organic layer was dried over anhydrous $MgSO_4$ followed by removal of the volatiles under aspirator vacuum. Kugelrohr distillation at reduced pressure afforded 1.72 g (10.4 mmol, 80%) of a clear liquid. The product was >95% pure by GC: oven distillation temperature 55–60 °C (3.0 mmHg); n^{20}_D 1.4662; ^{1}H NMR ($CDCl_3$) δ 5.30 (d, 2 H, *J* = 8 Hz), 2.55 (m, 2 H), 1.75 (d, 6 H, *J* = 1 Hz), 0.93 (d, 12 H, *J* = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 134.01, 133.38, 27.62, 23.08, 13.85; IR 3.43, 3.48, 6.85, 7.30, 10.2, 12.0 μm.

(22) Zweifel, G.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 2753.

Registry No. 3-Hexyne, 928-49-4; 1-hexyne, 693-02-7; 1-octene, 111-66-0; 1-phenyl-1-propyne, 673-32-5; phenylacetylene, 536-74-3; *cis*-4-octene, 7642-15-1; styrene, 100-42-5; *cis*-propenylbenzene, 766-90-5; *cis*-3-hexene, 7642-09-3; 2-hexyne, 764-35-2; 4-methyl-2-pentyne, 21020-27-9; 4,4-dimethyl-2-pentyne, 999-78-0; 1-propynylcyclohexane, 18736-95-3; 3,3-dimethyl-1-butyne, 917-92-0; 5-chloro-1-pentyne, 14267-92-6; (*E*)-1-hexen-1-yldibromoborane–dimethyl sulfide, 72228-56-9; (*Z*)-3-hexen-3-yldibromoborane–dimethyl sulfide, 72228-58-1; (*E*)-3,3-dimethyl-1-buten-1-yldibromoborane–dimethyl sulfide, 72228-60-5; (*Z*)-4-methyl-2-penten-2-yldibromoborane–dimethyl sulfide, 72228-62-7; (*E*)-5-chloro-1-penten-1-yldibromoborane–dimethyl sulfide, 72228-64-9; $HBBr_2{\cdot}SMe_2$, 55671-55-1; phenylacetone, 103-79-7; propiophenone, 93-55-0; 1-phenyl-1-propanol, 93-54-9; 1-phenyl-2-propanol, 698-87-3; 3-hexanone, 589-38-8; hexanal, 66-25-1; 3,3-dimethylbutanal, 2987-16-8; 4-methyl-2-pentanone, 108-10-1; 4-octyne, 1942-45-6; (*E*)-1-hexenylboronic acid, 42599-18-8; (*E*)-1-hexenyldibromoborane, 72228-55-8; (*E*)-1-iodo-1-hexene, 16644-98-7; (*E*,*E*)-2,4,5,7-tetramethyl-3,5-octadiene, 63787-85-9; methylcopper, 1184-53-8; (*E*,*E*)-4,5-diethyl-3,5-octadiene, 72228-65-0.

Three-Carbon Annelations. Regiocontrolled Reactivity of Trimethylsilyl- and Ethoxyethyl-Protected Cyanohydrins. Versatile Homoenolate and Acyl Anion Equivalents

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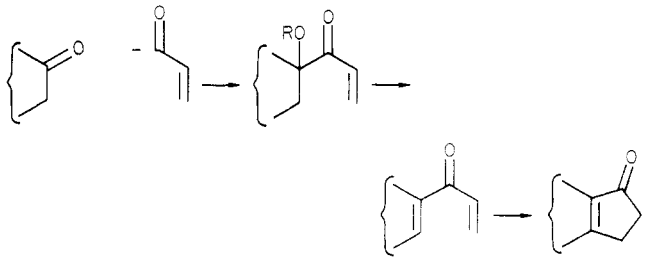
Received July 19, 1979

The trimethylsilyl- (**2**) and ethoxyethyl- (**4**) protected cyanohydrins of α,β-unsaturated aldehydes are utilized as three-carbon annelation reagents. Metalated reagent **2** displays exclusive α reactivity with aldehydes and ketones at −78 °C. Metalated reagent **4** displays exclusive α reactivity at −78 °C and exclusive γ reactivity at 0 °C. Reagent **4** thus allows for complete regiocontrol in its addition to aldehydes and ketones which permits selective addition of either a homoenolate or an acyl anion equivalent. Metalation of the α product **11** at −78 °C with subsequent warming to 0 °C produces exclusively the γ product, confirming the reversible nature of the addition to the carbonyl. The derived α′-trimethylsiloxy enones **17** (R_3 = Me_3Si), α′-hydroxy enones **17** (R_3 = H), α′-acetoxy enones **17** (R_3 = Ac), and γ-lactones **10** are useful cyclopentenone precursors. Treatment of **17** with *p*-TsOH in toluene at reflux produces cyclopentenones. The reaction proceeds via the postulated intermediacy of a pentadienyl cation **15** which undergoes in situ electrocyclic ring closure.

As cyclopentyl ring systems are found in a wide variety of natural products, methods which allow for their construction have been a topic of current discussion.[1] We have been especially interested in annelative techniques for cyclopentane construction. The widely used Robinson annelation has no such general counterpart in the synthesis of cyclopentane ring systems. Although a variety of useful three-carbon annelation techniques exist there is a continuing need for the development of new methodology.

We felt that the electrocyclic ring closure of 1,4-pentadien-3-ones (Nazarov cyclization)[2] would prove useful if a facile method for their preparation were available.[3] Retrosynthetic analysis prompted us to consider the addition of acyl anion equivalents of α,β-unsaturated aldehydes to carbonyl compounds. Dehydration of the addition product would generate the pentadienone system we desired.



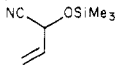
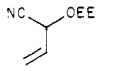
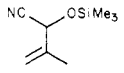
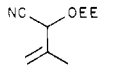
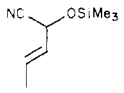
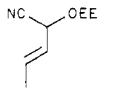
(1) (a) R. M. Jacobson and G. P. Lahm, *J. Org. Chem.*, **44**, 462 (1979), and references cited therein; (b) R. M. Jacobson, A. A. Abbaspour, and G. P. Lahm, *J. Org. Chem.*, **43**, 4650 (1978); (c) B. M. Trost and W. C. Vladuchick, *J. Org. Chem.*, **44**, 148 (1979); (d) N. E. Schore, *Synth. Commun.*, 41 (1979); (e) M. Bertrand, J. P. Dulcere, G. Gil, and M. L. Roumestant, *Tetrahedron Lett.*, 1845 (1979).

(2) (a) I. N. Nazarov and M. S. Burmistrova, *J. Gen. Chem. USSR (Engl. Transl.)*, **20**, 2091 (1950); (b) I. N. Nazarov and L. N. Pinkina, *ibid.*, **20**, 2079 (1950).

(3) (a) T. Hiyama, M. Tsukanaka, and H. Nozaki, *J. Am. Chem. Soc.*, **96**, 3713 (1974); (b) T. Hiyama, M. Shinoda, and H. Nozaki, *Tetrahedron Lett.*, 771 (1978); (c) T. Hiyama, M. Shinoda, and H. Nozaki, *J. Am. Chem. Soc.*, **101**, 1599 (1979); (d) F. Cooke, J. Schwindemann, and P. Magnus, *Tetrahedron Lett.*, 1995 (1979); (e) W. E. Fustad, D. S. Dime, T. R. Bailey, and L. A. Paquette, *Tetrahedron Lett.*, 1999 (1979).

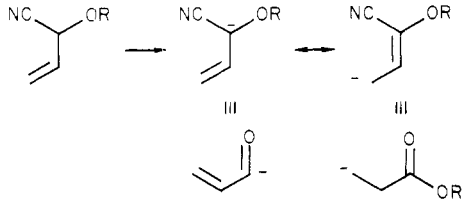
0022-3263/80/1945-0395$01.00/0

Table I. Protected Cyanohydrin Reagents

reagent	yield,[a] %	reagent	yield,[a] %
 2a	89	 4a	64 (A)[b] 71 (B)[c]
 2b	77	 4b	76 (A)
 2c	96	 4c	44 (A) 79 (B)

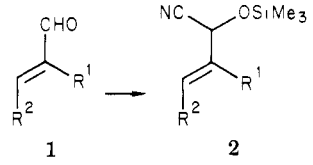
[a] Yield based on material isolated after fractional distillation. [b] Method A: prepared via HCN method, yield based on starting α,β-unsaturated aldehyde. [c] Method B: prepared via Me_3SiCN method, yield based on starting α,β-unsaturated aldehyde.

The use of protected cyanohydrins as acyl anion equivalents has been studied by Stork[4] and Hünig[5] and has found wide applicability in chemical synthesis. We were intrigued by the possibility that the protected cyanohydrins might serve as either acyl anion equivalents[6] or homoenolate equivalents.[7] An investigation into the chemistry of these reagents and their application to three-carbon annelation is presented here.



Reagents

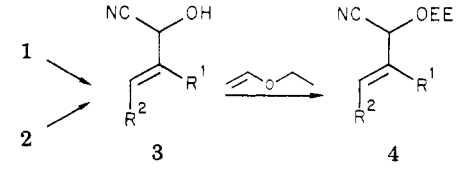
Throughout the course of this work six reagents were studied. The trimethylsilyl reagents **2a–c** are conveniently prepared by the addition of (trimethylsilyl)carbonitrile to α,β-unsaturated aldehydes using ZnI_2 catalysis.[8]



1 2

a, $R^1 = R^2 = H$; b, $R^1 = Me$, $R^2 = H$; c, $R^1 = H$, $R^2 = Me$

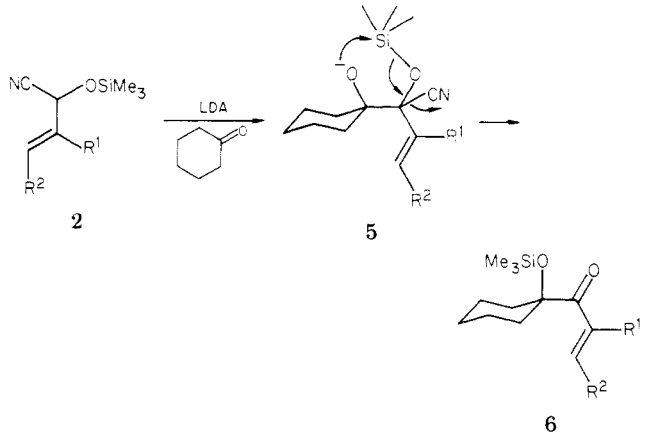
The ethoxyethyl (EE) protected cyanohydrins **4a–c** are prepared from cyanohydrins **3a–c** by treatment with ethyl



3 4

vinyl ether under acid (CF_3CO_2H) catalysis. Cyanohydrins **3a–c** can be prepared by two methods: method A, the triethylamine-catalyzed addition of anhydrous HCN to the α,β-unsaturated aldehyde or, more reproducibly, method B, reaction of the trimethylsilyl-protected cyanohydrins **2a–c** with dilute aqueous HCl in THF (see Table I).

Reactivity of the Trimethylsilyl Reagents with Aldehydes and Ketones. Reaction of the lithium anion of the trimethylsilyl-protected cyanohydrin of α,β-unsaturated aldehydes **2a–c** with alkyl halides is known to give exclusive α-alkylation.[5d] We were interested in the reactivity of the reagents **2a–c** with aldehydes and ketones. Since the effects producing α vs. γ reactivity are known to be highly dependent on reaction conditions[9] such as reagent, solvent, temperature, and substrate, we felt the metalated reagent might display α and/or γ reactivity. Thus, metalation of **2a–c** in the range of −70 to −100 °C in tetrahydrofuran with lithium diisopropylamide (LDA) produces yellow solutions of the allylic carbanions. Addition of 0.9 equiv of the aldehyde or ketone results in immediate loss of color. NMR analysis of the crude product indicated exclusive α addition. The addition products obtained were the α'-trimethylsiloxy enones **6**



2 5 6

formed via an intramolecular silyl transfer (i.e., **5**) with

(4) (a) G. Stork and L. Maldonado, *J. Am. Chem. Soc.*, **93**, 5286 (1971); (b) *ibid.*, **96**, 5272 (1974).

(5) (a) K. Deuchert, U. Hertenstein, and S. Hünig, *Synthesis*, 777 (1973); (b) S. Hünig and G. Wehner, *ibid.*, 180 (1975); (c) *ibid.*, 391 (1975); (d) U. Hertenstein, S. Hünig, and M. Öller, *ibid.*, 416 (1976).

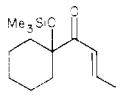
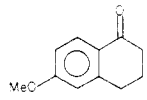
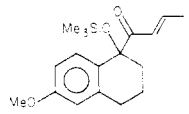
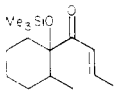
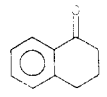
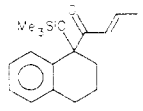
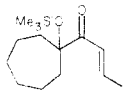
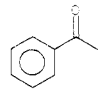
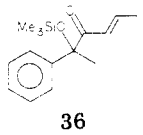
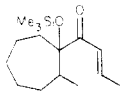
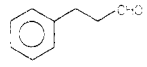
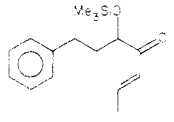
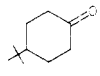
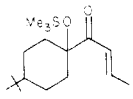
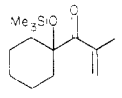
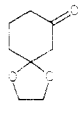
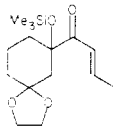
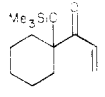
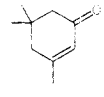
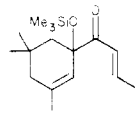
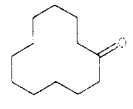
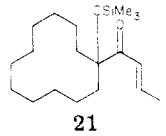
(6) For a review of acyl anion equivalents, see: (a) O. W. Lever, *Tetrahedron*, **32**, 1943 (1976); (b) B. T. Gröbel and D. Seebach, *Synthesis*, 357 (1977).

(7) (a) D. A. Evans, J. M. Takacs, and K. M. Hurst, *J. Am. Chem. Soc.*, **101**, 371 (1979); (b) W. C. Still and T. L. MacDonald, *ibid.*, **96**, 5561 (1974); (c) D. A. Evans, G. C. Andrews, and B. Buckwalter, *ibid.*, **96**, 5560 (1974); (d) D. Ayalon-Chass, E. Ehlinger, and P. Magnus, *J. Chem. Soc., Chem. Commun.*, 772 (1977); (e) H. Ahlbrecht and G. Vonderheid, *Synthesis*, 512 (1975); (f) S. Strutz, B. Corbel, and J. P. Paugam, *Tetrahedron Lett.*, 47 (1976); (g) D. Caine and A. S. Frobese, *ibid.*, 883 (1978); (h) G. Büchi and H. Wüest, *J. Org. Chem.*, **34**, 1122 (1969); (i) J. Haslouin and F. Rouessac, *Tetrahedron Lett.*, 4651 (1976); (j) E. Nakamura and I. Kuwajima, *J. Am. Chem. Soc.*, **99**, 7360 (1977); (k) J. C. Stowell, *J. Org. Chem.*, **41**, 560 (1976); (l) A. A. Ponaras, *Tetrahedron Lett.*, 3105 (1976); (m) K. Kondo and D. Tunemoto, *ibid.*, 1397 (1975); (n) D. Seebach, M. S. Hoekstra and G. Protschuk, *Angew. Chem., Int. Ed. Engl.*, **16**, 321 (1977); (o) M. Wada, H. Nakamura, T. Taguchi, and H. Takei, *Chem. Lett.*, 345 (1977); (p) H. J. Reich and S. K. Shah, *J. Am. Chem. Soc.*, **99**, 263 (1977); (q) R. M. Carlson, A. R. Oyler, and J. R. Peterson, *J. Org. Chem.*, **40**, 1610 (1975); (r) J. Fayos and J. Clardy, *J. Org. Chem.*, **42**, 1349 (1977); (s) S. F. Martin and P. J. Garrison, *Tetrahedron Lett.*, 3875 (1977); (t) A. Debal, T. Cuvigny, and M. Larcheveque, *ibid.*, 3187 (1977); (u) K. Iwai, H. Kosugi, A. Miyazaki, and H. Uda, *Synth. Commun.*, **6**, 357 (1976); (v) R. R. Schmidt and J. Talbiersky, *Angew. Chem., Int. Ed. Engl.*, **15**, 171 (1976); (w) M. Schlosser and E. Hammer, *Helv. Chim. Acta*, **57**, 2547 (1974); (x) S. Nishida and F. Kataoka, *Chem. Lett.*, 1297 (1976); (y) Also see ref 9i,k.

(8) D. A. Evans, L. K. Truesdale, and G. L. Carroll, *J. Chem. Soc., Chem. Commun.*, 55 (1973).

(9) (a) H. J. Reich, *J. Org. Chem.*, **40**, 2570 (1975); (b) J. Hartman, R. Muthukrishnan, and M. Schlosser, *Helv. Chim. Acta*, **57**, 2261 (1974); (c) W. C. Still, *J. Org. Chem.*, **41**, 3620 (1976); (d) P. M. Atlanti, J. F. Biellmann, S. Dube, and J. J. Vicens, *Tetrahedron Lett.*, 2265 (1974); (e) K. Geiss, B. Seuring, R. Pieter, and D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **13**, 479 (1974); (f) D. A. Evans and G. C. Andrews, *Acc. Chem. Res.*, **7**, 147 (1974); (g) W. S. Murphy and S. Wattanasin, *Tetrahedron Lett.*, 1827 (1979); (h) B. Renger and D. Seebach, *Chem. Ber.*, **110**, 2334 (1977); (i) S. F. Martin and M. T. Dupriest, *Tetrahedron Lett.*, 3925 (1977); (j) H. Ahlbrecht and J. Eichler, *Synthesis*, 672 (1974); (k) W. Oppolzer and R. L. Snowden, *Tetrahedron Lett.*, 4187 (1976); (l) Also see ref 7a–f and 5d.

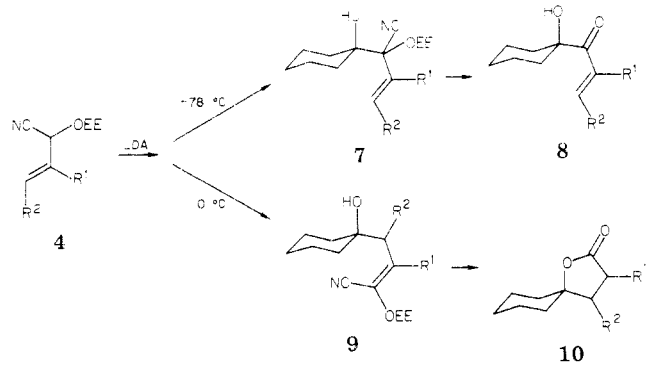
Table II. α′-Trimethylsilyloxy Enones Derived from 2a-c

SM	α-Me_3Si enone	yield,[a] %	SM	α-Me_3Si enone	yield,[a] %
	 **27**	68		 **34**	89
	 **28**	71		 **35**	78
	 **29**	64		 **36**	69
	 **30**	44 (63)[b]		 **37**	47 (58)[b]
	 **31**	70		 **38**	46
	 **32**	54 (88)[b]		 **39**	30
	 **33**	53		 **21**	30 (57)[b]

[a] Yields based on isolated compound chromatographed and distilled. [b] Yields based on unrecovered starting material.

concomitant loss of lithium cyanide. The crude products were chromatographed, distilled, and fully characterized. They are summarized with the yields obtained in Table II.

Reactivity of the Ethoxyethyl Reagents with Aldehydes and Ketones. The ethoxyethyl reagents **4a,b** upon metalation with lithium diisopropylamide form bright yellow solutions of the allylic carbanions at −78 °C in tetrahydrofuran. The addition of ketones or aldehydes at −78 °C results in rapid disappearance of color. Quenching with water after a period of 5 min produces exclusively the α product **7**. The crude products were

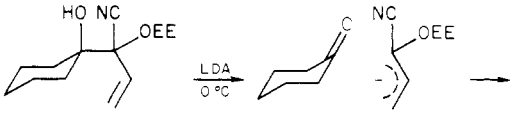


generally hydrolyzed to the α′-hydroxy enones **8** by treatment with dilute aqueous H_2SO_4 in THF and subsequent treatment with aqueous NaOH in THF. In no instance was there any detectable amount of products derived from the γ mode of addition.

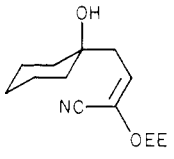
Although the metalated trimethylsilyl reagents **2a–c** underwent decomposition upon warming to temperatures of 0 °C, the ethoxyethyl reagents were stable. Reagents **4a,b** produced orange solutions at 0 °C upon metalation with lithium diisopropylamide in tetrahydrofuran. Addition of aldehydes and ketones at 0 °C followed by quenching with water after a period of 5–10 min produced the γ products, e.g., **9**. NMR analysis of the crude product mixture revealed exclusively γ addition, producing a single geometrical isomer of undetermined stereochemistry, and complete absence of any of the isomeric α product. The crude γ products were routinely hydrolyzed with aqueous acid and the γ-lactones **10** obtained were fully characterized. NMR analysis of the crude hydrolyzed product revealed complete absence of absorption in the olefinic region and confirmed the exclusive γ reactivity.

Addition of aldehydes and ketones to the metalated reagents **4a,b** at −78 °C with subsequent warming to 0 °C also produced the γ products in good to excellent yields, and we found this to be the method of choice for the preparation of these compounds. This suggested a reversible addition of the allylic carbanion to the carbonyl. Thus at −78 °C the α products obtained were derived from

a kinetic process, and warming to 0 °C produced the thermodynamic γ products. The fact that such a process indeed took place was shown by treatment of the α product **11** (which had been isolated and purified) with lithium



11 **12**



13

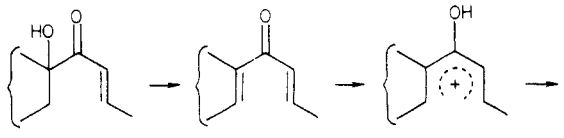
diisopropylamide at −78 °C with subsequent warming to 0 °C. The only product obtained was the γ product **13**.

Thus the ethoxyethyl reagents ***4a,b*** *may function as either acyl anion equivalents or homoenolate equivalents, their mode of reactivity being dependent on the reaction conditions employed.*

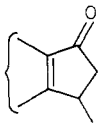
The reactivity of reagent **4c** was in sharp contrast to that observed for reagents **4a,b**. In addition to the absence of reactivity at −78 °C, the reagent was also found to undergo exclusive α addition at 0 °C.[10] Higher temperatures resulted in decomposition of the metalated reagent. The decreased reactivity of reagent **4c** is unexpected, and we have yet to ascertain the reason for this. The reactions of reagents **4a–c** with ketones and aldehydes are summarized in Table III.

Cyclopentenone Annelation

In a preliminary paper we reported that the α′-trimethylsiloxy enones **6c** and the α′-hydroxy enones **8c** served as useful cyclopentenone precursors.[1a] The reaction conditions found most effective were treatment of **8c** with 0.1 equiv of *p*-TsOH·H_2O in refluxing toluene or treatment of **6c** with 1.1 equiv of *p*-TsOH·H_2O in refluxing toluene. The reaction is believed to proceed via dehydration of the alcohol **8c** to produce the unobserved pentadienone **14**.



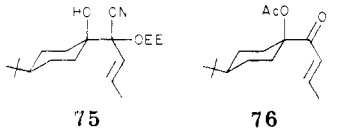
8c **14** **15**



16

Protonation of **14** yields the pentadienyl cation **15** which undergoes in situ electrocyclic ring closure to produce the cyclopentenone **16**.

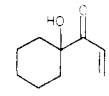
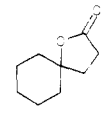
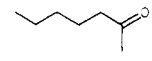
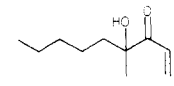
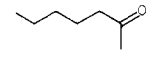
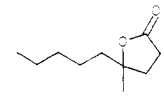
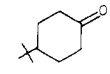
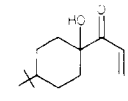
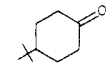
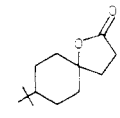
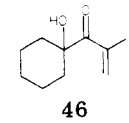
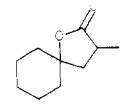
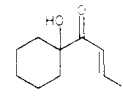
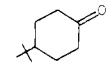
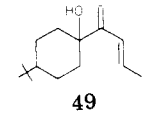
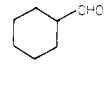
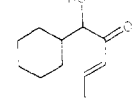
(10) The addition of reagent **4c** to 4-*tert*-butylcyclohexanone produced exclusively isomer **75**. An X-ray structural analysis[11] on the crystalline α′-acetoxy enone **76** proved the stereochemistry.



75 **76**

(11) We thank John Huffman of the Indiana University Molecular Structure Center for the X-ray structure determination (Report No. 7907).

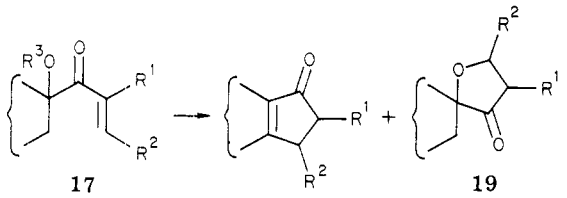
Table III. α′-Hydroxy Enones and Spiro-γ-lactones Derived from 4a-c

starting ketone	reagent	conditions[a]	product[b]	yield,[c] %
	4a	A	 **40**	72
	4a	B	 **41**	60
	4a	A	 **42**	76
	4a	B	 **43**	43
	4a	A	 **44**	80
	4a	B	 **45**	60
	4b	B	 **46**	83
	4b	B	 **47**	65
	4c	C	 **48**	68
	4c	C	 **49**	56
	4c	C	 **50**	69

[a] A, reaction run at −78 °C; B, reaction run at −78 °C with warming to 0 °C; C, reaction run at 0 °C. [b] Yield based on product obtained after removal of ethoxyethyl and cyanohydrin protecting groups. [c] Yield based on material obtained after chromatography and distillation. In all cases the remainder of the starting ketone could be recovered.

The α'-hydroxy enones which produce allylic- or benzylic-stabilized carbonium ions upon dehydration (such as the α'-trimethylsiloxy enone derived from α-tetralone **35**, Table IV) afford the cyclopentenones in reaction times of less than 1 min, whereas **48** requires about 8 h for complete conversion to the cyclopentenones.

A difficulty associated with the α'-hydroxy enones which offer no π conjugate stabilization is cyclization via intramolecular Michael addition to produce 3-tetrahydrofuranones **19**. For example, α'-hydroxy enone **17c** (R^1 = R^3 = H, R^2 = Me) typically produces a 4:1 mixture of **18c** and **19c** in a combined yield of 60%.



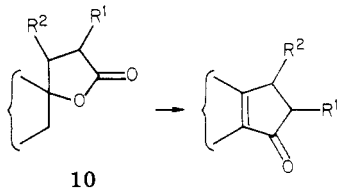
17 18 19

This problem is further amplified when the α'-hydroxy enones derived from **4a** or **4b** are employed. Treatment of **17a** (R^1 = R^2 = R^3 = H) with p-TsOH·H_2O in toluene results in formation of some of the 3-tetrahydrofuranone **19a** (R^1 = R^2 = H), large amounts of polymeric product, and no detectable amounts of the cyclopentenone.

We have found conversion of the α'-hydroxy enone to the α'-acetoxy enone **17** (R^3 = Ac) followed by treatment with p-TsOH in refluxing toluene results in higher yields of the cyclopentenone without formation of the 3-tetrahydrofurans. Even the unsubstituted α'-acetoxy enones **17a** (R^1 = R^2 = H, R^3 = Ac) produced the cyclopentenones in moderate to good yield. The elimination–cyclization of the acetoxy compounds is considerably faster than the corresponding α'-hydroxy enones. The acetates do require the use of greater than 1 equiv of p-TsOH. It is also necessary that the toluene and p-TsOH·H_2O be carefully dried before addition of the acetate. Drying is readily accomplished by refluxing of the p-TsOH·H_2O in toluene through 4A molecular sieves for about 4 h prior to addition of the acetate. If this is not done, hydrolysis of the acetate becomes a serious side reaction. In some cases benzene may be a more effective solvent for the elimination–cyclization of the acetates **17** (R^3 = Ac). For example, it was found that **17** (R^1 = R^2 = H, R^3 = Ac) produced a 36% yield (GC) of the cyclopentenone upon treatment with dry p-TsOH in toluene and a 46% yield (GC) with dry p-TsOH in benzene. The reaction in benzene, however, took 72 h for completion whereas only 5 h was required in toluene.

The acetates can be obtained in excellent yield by reacting the α'-hydroxy enones with acetic anhydride, triethylamine, and 4-(dimethylamino)pyridine.[12] The α'-hydroxy enones are readily obtained as discussed above or from the α'-trimethylsiloxy enones by treatment with 3% aqueous HCl in THF. Table IV summarizes the cyclopentenone annelations carried out by the methodology discussed.

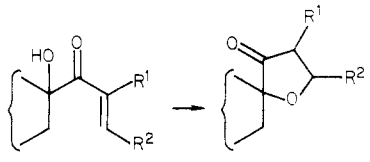
Access to cyclopentenones is also available through the spirolactones **10**. A variety of methods exist which may accomplish the transformation of **10** to the cyclopentenone **20**.[13] We have utilized Eaton's reagent[13a] (P_2O_5/CH_3SO_3H, 1:10) to exemplify the reaction which is summarized in Table V.



10 20

Furanone Synthesis

The α'-hydroxy enones also serve as useful 3-tetrahydrofuranone[14] precursors. If the reaction is carried out under the same conditions that produce cyclopentenones (i.e., p-TsOH, toluene, reflux) with 2 equiv of methanol, the 3-furanone **19** is obtained as the exclusive product in



8 19

high yield. The exact function which the methanol serves in preventing dehydration is unknown, but the reaction times for tetrahydrofuranone formation in the presence of 2 equiv of methanol are comparable with the reaction times necessary for cyclopentenone formation in the absence of methanol. These results are summarized in Table VI.

Conclusion

We believe these reagents will find varied application as useful synthons in organic chemistry. We are pursuing the study of these reagents with an eye toward the further expansion of their synthetic utility. Additionally, we are investigating the total synthesis of naturally occurring guianolides and pseudoguianolides, utilizing the methodology we have discussed.

Experimental Section

All melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. All boiling points are uncorrected. Kugelrohr boiling points were recorded at the temperature at which condensation was observed. ^{1}H NMR spectra were obtained on Varian T-60A and Varian HR 220 spectrometers, using either tetramethylsilane, methylene chloride, or chloroform as an internal standard. Infrared spectra were obtained on a Perkin-Elmer 467 grating infrared spectrometer. Mass spectra were taken on Varian Associates MAT CH-7 and Hewlett-Packard 5992A GC mass spectrometers. Exact mass spectra were obtained on an Associated Electrical Industries MS-9 mass spectrometer. UV spectra were obtained on a Cary 14 recording spectrophotometer.

Analytical thin-layer chromatography was performed on Polygram silica gel plates (0.25 mm) with fluorescent indicator UV_{254}. Preparative thin-layer chromatography was performed on Analtech 1000 μm silica gel GF chromatography plates. Column chromatography was performed by using 63–200 μm (70–230 mesh) silica gel 60 (E. Merck, Germany). Columns were packed and developed with the use of an air flow pressure regulator.[16] Tetrahydrofuran was dried by potassium benzophenone

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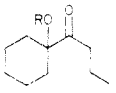
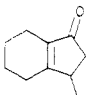
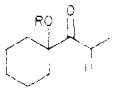
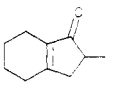
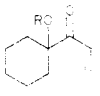
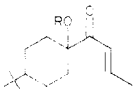
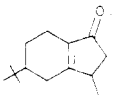
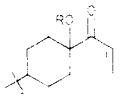
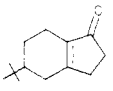
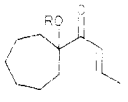
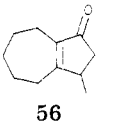
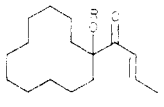
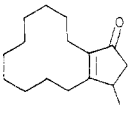
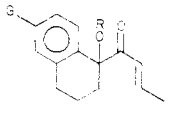
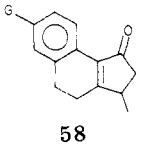
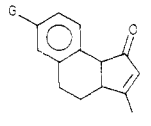
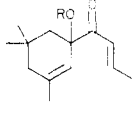
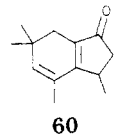
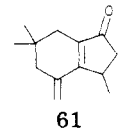
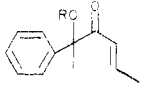
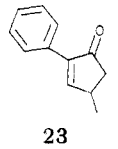
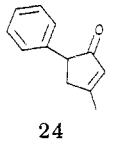
(15) (a) M. A. Baumann, W. Hoffmann, and N. Müller, *Tetrahedron Lett.*, 3585 (1976); (b) D. Felix, J. Schreiber, G. Ohloff, and A. Eschenmoser, *Helv. Chim. Acta*, **54**, 2896 (1971).

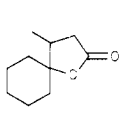
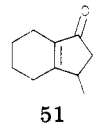
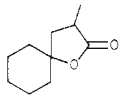
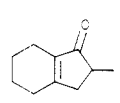
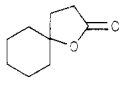
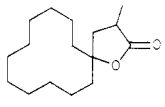
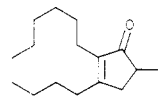
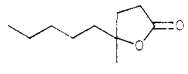
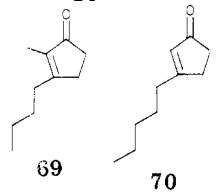
(16) W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, **43**, 2923 (1978).

Table IV. Cyclopentenones Derived from α′-Hydroxy, α′-Trimethylsilyloxy, and α′-Acetoxy Enones

enone structure	cyclopentenone	R (starting enone)	yield, %
	 51	H (48) Me_3Si (27) Ac (62)	48 48 53 (75)[d]
	 52	Me_3Si (38) Ac (63)	19 65
	 53	H (40) Me_3Si (39) Ac (64)	0 0 41 (46)[a,b]
	 54	Me_3Si (31) Ac (65)	81 85
	 55	H (44) Me_3Si (77) Ac (66)	0 0 66 (67)[a]
	 56	H (78) Ac (67)	41 60
	 57	H (22) Ac (68)	47 91
	 58	(a) Me_2Si (35) G = H	99 (50:50, 58a/59a)
	 59	(b) Me_3Si (34) G = OCH_3	99 (23:77, 58b/59b)
	 60	Me_3Si (33)	80 (70:30, 60/61)
	 61		
	 23	Me_3Si (36)	78 (48:52, 23/24)
	 24		

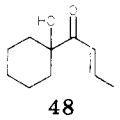
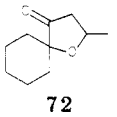
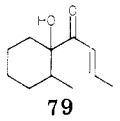
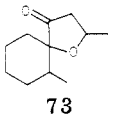
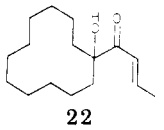
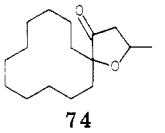
[a] GC yield in parentheses. [b] The solvent used in this case was benzene; when toluene was used as solvent, yields of 30 (36)[a] were obtained.

Table V. Cyclopentenones Derived from Spirolactones

spirolactone	cyclopentenone	yield,[a] %
 71	 51	94
 47	 52	76
 41	 53	89
 25	 26	85
 43	 69 70	89 (93:7, 69/70)

[a] Yield based on product isolated after Kugelrohr distillation. All products show greater than 95% purity (GC).

Table VI. 3-Furanones Derived from α'-Hydroxy Enones

α'-hydroxy enone	3-furanone	yield, %
 48	 72	90
 79	 73	78
 22	 74	80

dianion and was freshly distilled under nitrogen prior to use. Unless otherwise indicated, compounds are homogeneous by TLC and are >96% pure by GLC.

Preparation of (Trimethylsilyl)cyanohydrins. General Procedure. To a 50-mL round-bottom flask containing 200 mmol of the aldehyde is added 20 mg of zinc iodide. (Trimethylsilyl)carbonitrile (150 mmol) is added in 2-mL aliquots (5 min intervals) at ambient temperature, and the reaction is followed by GC. Vacuum distillation through a 6-in. fractionating column affords the (trimethylsilyl)cyanohydrins.

2-[(Trimethylsilyl)oxy]-3-butenenitrile (2a):[8] 89% yield; bp 84 °C (35 torr); ^{1}H NMR (CCl_4) δ 0.20 (s, 9 H), 4.90 (m, 1 H), 5.20–6.13 (m, 3 H); IR (neat) 2243, 1647, 1254 cm^{-1}; mass spectrum (70 eV) *m/e* (relative intensity) 155 (M^+, absent), 140 (100), 113 (20), 84 (77), 73 (25).

2-[(Trimethylsilyl)oxy]-3-methyl-3-butenenitrile (2b):[5d] 77% yield; bp 45 °C (0.05 torr); ^{1}H NMR (CCl_4) δ 0.25 (s, 9 H), 1.88 (d, 3 H, *J* = 1 Hz), 4.78 (s, 1 H), 5.03 (br s, 1 H), 5.27 (br s, 1 H); IR (neat) 2240, 1658, 1252 cm^{-1}; mass spectrum (70 eV) *m/e* (relative intensity) 169 (M^+, 5), 154 (100), 127 (27), 126 (28), 84 (87), 75 (43), 73 (56), 45 (44), 43 (33), 41 (22).

2-[(Trimethylsilyl)oxy]-3-pentenenitrile (2c):[8] 96% yield; bp 104 °C (35 torr); ^{1}H NMR (CCl_4) δ 0.20 (s, 9 H), 1.76 (dd, 3 H), 4.80 (dd, 1 H), 5.27–6.20 (m, 2 H); IR (neat) 2240, 1670, 1265 cm^{-1}; mass spectrum (70 eV) *m/e* (relative intensity) 169 (M^+, 1), 154 (24), 127 (100), 75 (89), 73 (39), 45 (28).

Preparation of Cyanohydrins. General Procedure. Method A. A mixture of 200 mmol of the aldehyde and 10 drops of triethylamine in 50 mL of methylene chloride is cooled to −10 °C (NaCl/ice). To the flask is added 9.5 mL of HCN[17] (266 mmol, cooled to 0 °C) in 1-mL aliquots at 3–5 min intervals. The mildly exothermic reaction is maintained at less than 5 °C (internal temperature). After the addition of HCN is complete, the reaction is stirred at 0 °C for 1 h and then at room temperature for 30 min. The reaction is acidified with several drops of concentrated HCl, and the methylene chloride is then distilled off through a 6-in. Vigreux column. Vacuum distillation affords the cyanohydrin.

Method B. In a round bottom flask are combined 100 mmol of the trimethylsilylcyanohydrin, 50 mL of THF and 50 mL of 1 N aqueous HCl. The mixture is refluxed and followed by NMR. After 3 to 4 hours the reaction is complete. The mixture is saturated with NaCl and the aqueous layer is washed 3 times with ether. The combined extracts are dried over $MgSO_4$ and the solvent is removed in vacuo. Vacuum distillation affords the cyanohydrin.

2-Hydroxy-3-butenenitrile (3a):[18] 72% yield (method A), 90% yield (method B); bp 46–48 °C (0.1 torr); ^{1}H NMR ($CDCl_3$) δ 3.97 (s, 1 H), 5.03 (dd, 1 H), 5.36–6.25 (m, 3 H); IR (neat) 3400, 2270 cm^{-1}.

2-Hydroxy-3-methyl-3-butenenitrile (3b):[19] 90% yield (method A); bp 46–63 °C (0.05 torr); ^{1}H NMR δ 1.87 (br s, 3 H), 4.0 (br s, 1 H), 4.78 (br s, 1 H), 5.05 (br s, 1 H), 5.25 (br s, 1 H); IR (neat) 3400, 2245, 1658 cm^{-1}.

2-Hydroxy-3-pentenenitrile (3c):[18] 47% yield (method A), 87% yield (method B); bp 59–60 °C (0.05 torr); ^{1}H NMR ($CDCl_3$) δ 1.83 (dd, 3 H), 4.23 (br s, 1 H), 4.83 (dd, 1 H), 5.36–6.30 (m, 2 H); IR (neat) 3400, 2280 cm^{-1}.

Preparation of Ethoxyethyl Protected Cyanohydrins. General Procedure. In a 100-mL round-bottom flask are combined 100 mmol of the cyanohydrin and 125 mmol of ethyl vinyl ether. The flask is equipped with a condenser and is acidified with 4–6 drops of trifluoroacetic acid. The exothermic reaction self-refluxes for about 5 min and is then allowed to cool to room temperature. The mixture is basified with 40% aqueous NaOH. Vacuum distillation affords the ethoxyethyl-protected cyanohydrin.

2-(1-Ethoxyethoxy)-3-butenenitrile (4a):[4a] 89% yield; bp 62–66 °C (0.1 torr); ^{1}H NMR ($CDCl_3$) δ 1.20 (t, 3 H), 1.37 (dd, 3 H), 3.53 (m, 2 H), 4.85 (m, 2 H), 5.3–6.0 (m, 3 H); IR (neat) 2950, 2184, 1635 cm^{-1}; mass spectrum (70 eV) *m/e* (relative intensity) 155 (M^+, absent), 154 (1), 73 (59), 66 (66), 45 (100), 43 (44).

2-(1-Ethoxyethoxy)-3-methyl-3-butenenitrile (4b): 84% yield; bp 56–61 °C (0.05 torr); ^{1}H NMR (CCl_4) δ 1.20 (t, 3 H), 1.35 (dd, 3 H), 3.55 (m, 2 H), 4.7–4.9 (m, 2 H), 5.07 (br s, 1 H), 5.27 (m, 1 H); IR (neat) 2990, 2230, 1655 cm^{-1}; mass spectrum (70 eV) *m/e* (relative intensity) 169 (M^+, absent), 123 (11), 98 (15), 80 (55), 73 (71), 53 (50), 52 (11), 45 (100), 43 (55), 41 (14).

2-(1-Ethoxyethoxy)-3-pentenenitrile (4c):[4b] 94% yield; bp 71–73 °C (0.1 torr); ^{1}H NMR (CCl_4) δ 1.13 (t, 3 H), 1.33 (dd, 3 H), 1.75 (dd, 3 H), 3.53 (m, 2 H), 4.87 (m, 2 H), 5.3–6.3 (m, 2 H); IR (CCl_4) 3000, 2210, 1680 cm^{-1}; mass spectrum (70 eV) *m/e* (relative intensity) 169 (M^+, absent), 80 (100), 73 (78), 53 (24), 45 (93).

Preparation of α'-Trimethylsiloxy Enones. General Procedure. To a solution of 2.0 mmol of lithium diisopropylamide in 10 mL of dry THF/hexane (9:1), under N_2 and cooled to −78 °C (−98 °C for reagent **2a**), is added 2.1 mmol of the trimethylsilyl-protected cyanohydrin. After a period of 10 min, 1.5 mmol of the ketone or aldehyde is added followed by additional stirring for 10 min and then quenching of the reaction with water. The mixture is partitioned between ether and water, extracted three times with ether, dried over $MgSO_4$, and concentrated in vacuo. Chromatography on silica gel followed by Kugelrohr

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distillation affords the α′-trimethylsiloxy enone.

1-[1′-[(Trimethylsilyl)oxy]cyclohexyl]-2-buten-1-one (27): chromatography on silica gel (10% ether/hexane); Kugelrohr distillation, bp 110 °C (bath temperature) (0.05 torr); 68% yield; ^{1}H NMR (CCl_4) δ 0.15 (s, 9 H), 1.3–1.7 (m, 10 H), 1.98 (d, 3 H, J = 6 Hz), 6.53 (d, 1 H, J = 15 Hz), 6.97 (dq, 1 H, J = 15, 6 Hz); IR (neat) 1696, 1632, 1250, 850 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 240 (M^+, absent), 225 (6), 172 (13), 171 (100), 75 (15), 73 (77), 69 (4), 45 (6), 41 (4).

1-[1′-[(Trimethylsilyl)oxy]-2′-methylcyclohexyl]-2-buten-1-one (28):[34] chromatography on silica gel (5% ether/hexane); Kugelrohr distillation, bp 80–100 °C (bath temperature) (0.05 torr); 71% yield; ^{1}H NMR (CCl_4) δ 0.16 (s, 9 H), 0.66 (d, 3 H), 1.1–1.9 (m, 9 H), 1.98 (dd, 3 H, J = 1, 6 Hz), 6.41 (dq, 1 H, J = 1, 15 Hz), 7.04 (dq, 1 H, J = 6, 15 Hz); IR (neat) 1680, 1615, 1230, 860 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 254 (M^+, absent), 239 (11), 186 (15), 185 (100), 117 (6), 95 (18), 75 (13), 73 (47), 69 (4), 41 (4).

1-[1′-[(Trimethylsilyl)oxy]cycloheptyl]-2-buten-1-one (29): chromatography on silica gel (1% ether/hexane); Kugelrohr distillation, bp 125 °C (bath temperature) (0.05 torr); 64% yield; ^{1}H NMR (CCl_4) δ 0.15 (s, 9 H), 1.5–2.0 (m, 12 H), 2.00 (d, 3 H, J = 6 Hz), 6.33 (d, 1 H, J = 14 Hz), 7.07 (dq, 1 H, J = 6, 14 Hz); IR (neat) 1695, 1630, 1255, 845 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 254 (M^+, absent), 239 (5), 186 (15), 185 (100), 75 (16), 73 (82), 69 (7), 45 (8), 41 (8).

1-[1′-[(Trimethylsilyl)oxy]-2′-methylcycloheptyl]-2-butene-1-one (30): Reaction at −98 °C; chromatography on silica gel (10% ether/hexane); Kugelrohr distillation, bp 100–115 °C (bath temperature) (0.05 torr); 44% yield (recovered 30% starting material); ^{1}H NMR (220 MHz, CCl_4) δ 0.05 (s, 9 H), 0.47 (d, 3 H), 1.0–1.8 (m, 11 H), 1.74 (dd, 3 H, J = 2, 7 Hz), 6.08 (dq, 1 H, J = 2, 15 Hz), 6.72 (dq, 1 H, J = 7, 15 Hz); IR (CCl_4) 1702, 1632, 1250, 840 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 268 (M^+, absent), 253 (12), 200 (13), 199 (78), 117 (30), 109 (23), 75 (39), 73 (100), 69 (34), 45 (24), 41 (49).

1-[1′-[(Trimethylsilyl)oxy]-4′-*tert*-butylcyclohexyl]-2-buten-1-one (31): chromatography on silica gel (5% ether/hexane); Kugelrohr distillation, bp 110–120 °C (bath temperature) (0.05 torr); 70% yield; ^{1}H NMR (CCl_4) δ 0.13 (s, 9 H), 0.91 (s, 9 H), 1.61 (m, 9 H), 1.98 (dd, 3 H, J = 1, 6 Hz), 6.55 (dq, 1 H, J = 1, 15 Hz), 7.00 (dq, 1 H, J = 6, 15 Hz); IR (neat) 1690, 1625, 1245 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 296 (M^+, absent), 228 (58), 227 (100), 119 (44), 117 (53), 113 (22), 95 (20), 81 (38), 75 (33), 73 (92), 69 (28), 57 (55), 45 (29), 41 (27).

1-[1′-[(Trimethylsilyl)oxy]-3′,3′-(ethylenedioxy)cyclohexyl]-2-buten-1-one (32): chromatography on silica gel (30% ether/hexane); Kugelrohr distillation, bp 125–130 °C (bath temperature) (0.05 torr); 54% yield (recovered 39% starting material); ^{1}H NMR (220 MHz, CCl_4) δ 1.3–1.6 (m, 3 H), 1.7–1.8 (m, 3 H), 1.89 (dd, 3 H, J = 2, 7 Hz), 3.7–3.9 (m, 4 H), 6.55 (dq, 1 H, J = 2, 15 Hz), 6.92 (dq, 1 H, J = 7, 15 Hz); IR (neat) 1696, 1628, 1250, 845 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 298 (M^+, absent), 283 (1), 229 (40), 100 (20), 99 (100), 75 (31), 73 (46), 69 (39), 55 (68), 45 (30), 41 (54).

1-[1′-[(Trimethylsilyl)oxy]-3′,5′,5′-trimethyl-2′-cyclohexenyl]-2-buten-1-one (33): chromatography on silica gel (5% ether/hexane); Kugelrohr distillation, bp 115 °C (bath temperature) (0.05 torr); 53% yield; ^{1}H NMR (CCl_4) δ 0.05 (s, 9 H), 0.92 (s, 3 H), 1.03 (s, 3 H), 1.53 (s, 2 H), 1.75 (m, 2 H), 1.90 (dd, 3 H, J = 1, 6 Hz), 5.37 (m, 3 H), 6.33 (dq, 1 H, J = 1, 15 Hz), 6.75 (dq, J = 6, 15 Hz); IR (neat) 1701, 1632, 1253, 850 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 280 (M^+, absent), 265 (3), 212 (15), 211 (100), 75 (8), 73 (39), 69 (6).

1-[1′-[(Trimethylsilyl)oxy]-6′-methoxy-1′,2′,3′,4′-tetrahydronaphthalenyl]-2-buten-1-one (34): chromatography on silica gel (20% ether/hexane); Kugelrohr distillation, bp 150–160 °C (bath temperature) (0.05 torr); 89% yield; ^{1}H NMR (220 MHz, CCl_4) δ 0.11 (s, 9 H), 1.91 (dd, 3 H, J = 1, 6 Hz), 1.97 (m, 4 H), 2.82 (m, 2 H), 3.79 (s, 3 H), 6.1–7.1 (m, 5 H); IR (neat) 1695, 1626, 1608, 1250, 850 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 318 (M^+, absent), 250 (16), 249 (100), 75 (7), 74 (6), 73 (74), 69 (7), 45 (11), 41 (6).

1-[1′-[(Trimethylsilyl)oxy]-1′,2′,3′,4′-tetrahydronaphthalenyl]-2-buten-1-one (35): chromatography on silica gel (10% ether/hexane); Kugelrohr distillation, bp 140 °C (bath temperature) (0.05 torr); 78% yield; ^{1}H NMR (CCl_4) δ 0.23 (s, 9 H), 1.96 (dd, 3 H, J = 1, 6 Hz), 2.03 (m, 4 H), 2.94 (m, 2 H), 6.36 (dq, 1 H, J = 1, 15 Hz), 6.80 (dq, 1 H, J = 6, 15 Hz), 6.96 (br s, 4 H); IR (neat) 1699, 1628, 1247, 840 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 288 (M^+, absent), 273 (2), 219 (52), 75 (16), 73 (100), 69 (14), 45 (13), 41 (12).

2-Phenyl-2-[(trimethylsilyl)oxy]-4-hexen-3-one (36): chromatography on silica gel (10% ether/hexane); Kugelrohr distillation, bp 120 °C (bath temperature) (0.05 torr); 69% yield; ^{1}H NMR (CCl_4) δ 0.21 (s, 9 H), 1.70 (s, 3 H), 1.88 (dd, J = 1, 6 Hz), 6.33 (dq, 1 H, J = 1, 15 Hz), 6.83 (dq, 1 H, J = 6, 15 Hz), 7.41 (br s, 5 H); IR (neat) 1706, 1639, 1265, 855 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 262 (M^+, absent), 247 (4), 205 (5), 195 (5), 194 (14), 193 (100), 143 (10), 75 (7), 74 (4), 73 (50).

1-Phenyl-3-[(trimethylsilyl)oxy]-5-hepten-4-one (37): addition of 1.1 equiv of $ZnCl_2$ in THF prior to addition of aldehyde; chromatography on silica gel (10% ether/hexane); bp 130 °C (bath temperature) (0.05 torr); 47% yield (19% recovered starting material); ^{1}H NMR (CCl_4) δ 0.12 (s, 9 H), 1.6–2.1 (m, 2 H), 1.95 (d, 3 H, J = 6 Hz), 2.5–2.9 (m, 2 H), 4.11 (t, 1 H), 6.50 (d, 1 H, J = 15 Hz), 6.88 (dq, 1 H, J = 6, 15 Hz), 7.18 (br s, 5 H); IR (CCl_4) 1690, 1630, 1255 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) **276** (M^+, absent), 261 (4), 208 (24), 207 (68), 117 (48), 91 (100), 75 (13), 73 (54), 59 (10).

1-[1′-[(Trimethylsilyl)oxy]cyclohexyl]-2-methyl-2-propen-1-one (38): chromatography on silica gel (10% ether/hexane); Kugelrohr distillation, bp 100 °C (bath temperature) (0.05 torr); 46% yield; ^{1}H NMR (CCl_4) δ 0.05 (s, 9 H), 1.3–1.8 (m, 10 H), 1.83 (d, 3 H, J = 1 Hz), 5.72 (m, 1 H), 6.27 (m, 1 H); IR (CCl_4) 1670, 1620, 1250, 840 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 240 (M^+, absent), 225 (5), 172 (15), 171 (100), 81 (13), 75 (38), 74 (18), 73 (100), 69 (19), 59 (10), 45 (38), 43 (12), 41 (76).

1-[1′-[(Trimethylsilyl)oxy]cyclohexyl]-2-propen-1-one (39): reaction at −98 °C; chromatography on silica gel (5% ether/hexane); Kugelrohr distillation, bp 50–60 °C (bath temperature) (0.05 torr); 30% GC yield (recovered 67% starting material); ^{1}H NMR (CCl_4) δ 0.10 (s, 9 H), 1.61 (m, 10 H), 5.35 (dd, 1 H, J = 3, 10 Hz), 6.18 (dd, 1 H, J = 3, 18 Hz), 6.95 (dd, 1 H, J = 10, 18 Hz); IR (CCl_4) 1700, 1610, 1254, 844 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 226 (M^+, absent), 211 (13), 172 (22), 171 (100), 81 (15), 75 (42), 74 (15), 73 (100), 59 (11), 55 (45), 45 (37), 43 (12), 41 (12).

1-(1′-Hydroxycyclododecyl)-2-buten-1-one (22).[34] The trimethylsiloxy derivative **21** was routinely hydrolyzed in 1 N aqueous HCl/THF to the α′-hydroxy enone **22** to aid in isolation and purification: chromatography on silica gel (5% ether/hexane); Kugelrohr distillation, bp 190 °C (bath temperature) (0.05 torr); recrystallization from hexane/ether, mp 124–125 °C; 30% yield; ^{1}H NMR ($CDCl_3$) δ 1.1–1.7 (m, 22 H), 1.97 (dd, 3 H, J = 1, 6 Hz), 3.30 (s, 1 H), 6.57 (dq, 1 H, J = 1, 15 Hz), 3.30 (s, 1 H), 6.57 (dq, 1 H, J = 1, 15 Hz), 7.18 (dq, 1 H, J = 6, 15 Hz); IR ($CDCl_3$) 3460, 1679, 1624 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 252 (M^+, 3), 184 (42), 183 (100), 109 (57), 97 (65), 95 (61), 84 (38), 83 (80), 81 (51), 69 (84), 67 (46), 57 (27), 55 (77), 43 (60), 41 (66).

Addition of Ethoxyethyl-Protected Cyanohydrins to Aldehydes and Ketones. Preparation of α′-Hydroxy Enones and γ-Lactones. General Procedure. α′-Hydroxy Enones. To a solution of 2.0 mmol of lithium diisopropylamide in 10 mL of dry THF/hexane (9:1), under N_2 and cooled to −78 °C (0 °C for reagent **4c**), is added 2.1 mmol of the ethoxyethyl-protected cyanohydrin. The bright yellow solution is stirred for 10 min after which time 1.5 mmol of the ketone or aldehyde is added followed by additional stirring for 10 min and then quenching of the reaction with water. The mixture is partitioned between ether and brine, extracted three times with ether, and concentrated in vacuo. The residue is then dissolved in 20 mL of 0.5 M H_2SO_4 (THF/H_2O, 1:1) and refluxed for 2–4 h. The mixture is again extracted with ether and then stirred with 20 mL of 10% aqueous NaOH. The mixture is extracted with ether, dried over $MgSO_4$, filtered, and concentrated in vacuo. Chromatography on silica gel followed by Kugelrohr distillation affords the pure α′-hydroxy enone.

γ-Lactones. The same reaction conditions are employed except the reaction is run at 0 °C. Once the reaction has been quenched,

the crude product is extracted with ether, and the extracts are concentrated in vacuo. Hydrolysis with 20 mL of 0.5 M H_2SO_4 (THF/H_2O, 1:1) at reflux for 2–4 h followed by the same workup, chromatography on silica gel, and Kugelrohr distillation affords the pure γ-lactone.

1-(1′-Hydroxycyclohexyl)-2-propen-1-one (40):[20] chromatography on silica gel (10% ether/hexane); Kugelrohr distillation, bp 100 °C (bath temperature) (0.05 torr); 72% yield; ^{1}H NMR (CCl_4) δ 1.0–2.0 (m, 10 H), 3.47 (s, 1 H), 5.76 (dd, 1 H, J = 3, 9 Hz), 6.41 (dd, 1 H, J = 3, 17 Hz), 6.92 (dd, 1 H, J = 9, 17 Hz); IR (neat) 3480, 1695, 1617 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 154 (M^+, 1), 99 (100), 81 (93), 57 (12), 56 (10), 55 (47), 43 (24), 41 (17).

4-Hydroxy-4-methyl-1-nonen-3-one (42): Kugelrohr distillation, bp 110–120 °C (bath temperature) (0.05 torr); 76% yield; ^{1}H NMR (CCl_4) δ 0.7–1.9 (m, 11 H), 1.28 (s, 3 H), 3.56 (br s, 1 H), 5.71 (dd, 1 H, J = 4, 8 Hz), 6.35 (dd, 1 H, J = 4, 16 Hz), 6.73 (dd, 1 H, J = 8, 16 Hz); IR (CCl_4) 3460, 1693, 1615 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 170 (M^+, absent), 129 (93), 71 (12), 69 (100), 57 (15), 56 (12), 55 (51), 45 (31), 43 (85), 41 (25).

1-(1′-Hydroxy-4′-*tert*-butylcyclohexyl)-2-propen-1-one (44): Kugelrohr distillation, bp 125–135 °C (bath temperature) (0.05 torr); 80% yield; ^{1}H NMR (CCl_4) δ 0.92 (s, 9 H), 1.55 (m, 9 H), 3.48 (br s, 1 H), 5.70 (dd, 1 H, J = 3, 9 Hz), 6.37 (dd, 1 H, J = 3, 16 Hz), 6.83 (dd, 1 H, J = 9, 16 Hz); IR (neat) 3460, 1686, 1612 cm^{-1}.

1-(1′-Hydroxycyclohexyl)-2-methyl-2-propen-1-one (46): Kugelrohr distillation, bp 110–115 °C (bath temperature) (0.05 torr); 83% yield; ^{1}H NMR (CCl_4) δ 1.4–1.9 (m, 10 H), 1.93 (d, 3 H, J = 1 Hz), 3.52 (br s, 1 H), 5.65 (m, 1 H), 6.00 (m, 1 H); IR (neat) 3450, 1660 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 168 (M^+, absent), 99 (89), 82 (25), 81 (100), 79 (38), 70 (78), 69 (27), 57 (32), 55 (68), 43 (64), 42 (27), 41 (71).

1-(1′-Hydroxycyclohexyl)-2-buten-1-one (48):[21] chromatography on silica gel (20% ether/hexane); Kugelrohr distillation, bp 100 °C (bath temperature) (0.05 torr); 68% yield; ^{1}H NMR (CCl_4) δ 1.0–1.9 (m, 10 H), 1.93 (dd, 3 H, J = 1, 6 Hz), 3.53 (s, 1 H), 6.40 (dq, 1 H, J = 1, 15 Hz), 7.03 (dq, 1 H, J = 6, 15 Hz); IR (CCl_4) 3475, 1690, 1636 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 168 (M^+, 1), 99 (100), 81 (63), 69 (16), 55 (21), 43 (17), 41 (18).

1-(1′-Hydroxy-4′-*tert*-butylcyclohexyl)-2-buten-1-one (49): chromatography on silica gel (10% ether/hexane); Kugelrohr distillation, bp 135–140 °C (bath temperature) (0.05 torr); 56% yield (recovered 43% starting material); ^{1}H NMR (CCl_4) δ 0.88 (s, 9 H), 1.53 (m, 9 H), 1.93 (dd, 3 H, J = 1, 6 Hz), 3.63 (s, 1 H), 6.42 (dq, 1 H, J = 1, 15 Hz), 7.03 (dq, 1 H, J = 6, 15 Hz); IR (neat) 3450, 1683, 1627 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 224 (M^+, absent), 155 (100), 137 (25), 121 (20), 119 (36), 117 (39), 95 (30), 81 (76), 69 (47), 57 (80), 41 (39).

1-Cyclohexyl-1-hydroxy-3-penten-2-one (50): chromatography on silica gel (25% ether/hexane); Kugelrohr distillation, bp 125 °C (bath temperature) (0.05 torr); 69% yield; ^{1}H NMR (CCl_4) δ 1.0–2.0 (m, 11 H), 1.93 (dd, 3 H, J = 1, 6 Hz), 3.37 (br d, 1 H), 4.03 (br d, 1 H), 6.08 (dq, 1 H, J = 1, 16 Hz), 6.95 (dq, 1 H, J = 6, 16 Hz); IR (neat) 3440, 1686, 1628 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 182 (M^+, 1), 95 (100), 83 (24), 70 (19), 69 (36), 67 (19), 55 (33), 41 (37).

1-Oxaspiro[4.5]decan-2-one (41):[22] chromatography on silica gel (15% ether/hexane); Kugelrohr distillation, bp 80–110 °C (bath temperature) (0.05 torr); 60% yield; ^{1}H NMR (CCl_4) δ 1.0–1.9 (m, 10 H), 2.03 (m, 2 H), 2.45 (m, 2 H); IR (CCl_4) 1775 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 154 (M^+, 27), 112 (19), 111 (100), 98 (25), 55 (27), 41 (21).

5-Methyl-5-pentyldihydro-2(3*H*)-furanone (43):[23] chromatography on silica gel (15% ether/hexane); Kugelrohr distillation, bp 110–120 °C (bath temperature) (0.05 torr); 43% yield; ^{1}H NMR (CCl_4) δ 0.90 (br t, 3 H), 1.33 (s, 3 H), 1.2–1.7 (m, 8 H), 2.03 (m, 2 H), 2.43 (m, 2 H); IR (CCl_4) 1770 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 170 (M^+, 1), 155 (3), 114 (2), 99 (100), 71 (7), 56 (6), 55 (8), 43 (27), 41 (9).

8-*tert*-Butyl-1-oxaspiro[4.5]decan-2-one (45):[24,34] chromatography on silica gel (15% ether/hexane); Kugelrohr distillation, bp 145–160 °C (bath temperature) (0.05 torr); 60% yield; ^{1}H NMR (CCl_4) δ 0.90 (s, 9 H), 1.0–2.0 (m, 9 H), 2.05 (m, 2 H), 2.37 (m, 2 H); IR (CCl_4) 1775 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 210 (M^+, 2), 154 (18), 111 (28), 57 (100), 56 (23), 55 (22), 41 (33).

3-Methyl-1-oxaspiro[4.5]decan-2-one (47):[25] chromatography on silica gel (15% ether/hexane); Kugelrohr distillation, bp 125–135 °C (bath temperature) (0.05 torr); 65% yield; ^{1}H NMR (CCl_4) δ 1.23 (d, 3 H), 1.1–2.0 (m, 10 H), 2.0–2.8 (m, 3 H); IR (CCl_4) 1768 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 168 (M^+, 10), 126 (17), 125 (100), 124 (19), 112 (19), 99 (22), 98 (17), 82 (24), 81 (35), 70 (16), 69 (22), 67 (22), 55 (76), 43 (17), 42 (25), 41 (31).

3-Methyl-1-oxaspiro[4.11]hexadecan-2-one (25):[15b,34] hydrolysis best with 70% aqueous acetic acid at 95–100 °C for 2 h; recrystallized from hexane/ether; 60% yield; mp 109–110 °C; ^{1}H NMR (CCl_4) δ 1.22 (d, 3 H), 1.0–1.8 (m, 22 H), 2.0–2.4 (m, 3 H); IR (CCl_4) 1772 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 252 (M^+, 30), 183 (23), 125 (75), 112 (47), 109 (29), 97 (32), 96 (28), 95 (51), 84 (35), 83 (35), 82 (40), 81 (53), 69 (64), 68 (30), 67 (44), 57 (25), 56 (29), 55 (100), 43 (38), 42 (32), 41 (72).

Conversion of the α-Addition Product 11 to the γ-Addition Product 13. A sample of **11** was prepared by the method described. Chromatography on silica gel (20% ether/hexane) followed by Kugelrohr distillation, bp 130 °C (bath temperature) (0.05 torr), yields 70% of **11**: ^{1}H NMR (CCl_4) δ 0.9–1.9 (m, 16 H), 2.15 (br s, 1 H), 3.57 (m, 2 H), 4.85 (m, 1 H), 5.2–6.3 (m, 3 H); IR (neat) 3480, 1635 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 253 (M^+, absent), 164 (15), 99 (65), 81 (54), 80 (11), 79 (11), 73 (99), 55 (63), 53 (17), 45 (100), 43 (53), 42 (19), 41 (36). To a −78 °C solution of lithium diisopropylamide (1.74 mmol) in 10 mL of dry THF/hexane (9:1) was added 265 mg (1.04 mmol) of **11** in 3 mL of dry THF. The mixture was stirred for several minutes at −78 °C at which point the bath was changed to a 0 °C bath. After 45 min the reaction was quenched with water. The mixture was extracted three times with ether, dried over $MgSO_4$, filtered, and concentrated in vacuo. Kugelrohr distillation, bp 140–160 °C (bath temperature) (0.05 torr), affords 230 mg (0.91 mmol, 87%) of **13**: ^{1}H NMR (CCl_4) δ 1.0–2.0 (m, 16 H), 2.33 (d, 2 H), 3.67 (m, 2 H), 5.20 (q, 1 H), 5.78 (t, 1 H); IR (neat) 3450, 2220, 1638 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 253 (M^+, absent), 154 (8), 111 (20), 99 (21), 81 (30), 74 (11), 73 (99), 67 (10), 55 (48), 53 (11), 45 (100), 44 (17), 43 (40), 42 (20), 41 (36).

Preparation of α′-Acetoxy Enones. General Procedure. To 10 mL of dry THF containing 5.0 mmol of the α′-hydroxy enone, under N_2, is added 10.0 mmol of acetic anhydride, 12.5 mmol of triethylamine, and 0.2 mmol of 4-(dimethylamino)-pyridine. The mixture is heated to reflux and the reaction followed by GC. Completion of the reaction usually requires 12–24 h; however, hindered alcohols require longer reaction times and/or higher concentrations. Once the reaction is complete, the mixture is concentrated in vacuo and chromatographed on silica gel. Kugelrohr distillation or recrystallization affords the pure α′-acetoxy enones.

1-(1′-Acetoxycyclohexyl)-2-buten-1-one (62):[34] chromatography on silica gel (15% ether/hexane); Kugelrohr distillation, bp 140–145 °C (bath temperature) (0.05 torr); 90% yield; ^{1}H NMR (CCl_4) δ 1.3–2.0 (m, 10 H), 1.83 (dd, 3 H, J = 1, 6 Hz), 2.00 (s, 3 H), 6.13 (dq, 1 H, J = 1, 15 Hz), 6.83 (dq, 1 H, J = 6, 15 Hz); IR (neat) 1740, 1700, 1633 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 210 (M^+, 1), 141 (11), 99 (100), 81 (20), 69 (52), 43 (31), 41 (15).

1-(1′-Acetoxycyclohexyl)-2-methyl-2-propen-1-one (63): chromatography on silica gel (10% ether/hexane); Kugelrohr distillation, bp 130–140 °C (bath temperature) (0.05 torr); 85%

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yield; ^{1}H NMR (CCl_4) δ 1.3–2.0 (m, 10 H), 1.77 (d, 3 H, J = 1 Hz), 1.93 (s, 3 H), 5.46 (m, 1 H), 5.75 (m, 1 H); IR (neat) 1733, 1674, 1625 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 210 (M^+, absent), 141 (54), 100 (16), 99 (100), 81 (65), 69 (57), 55 (14), 43 (81), 41 (49).

1-(1′-Acetoxycyclohexyl)-2-propene-1-one (64): chromatography on silica gel (20% ether/hexane); Kugelrohr distillation, bp 110–120 °C (bath temperature) (0.05 torr); 79% yield; ^{1}H NMR (CCl_4) δ 1.3–2.0 (m, 10 H), 2.07 (s, 3 H), 5.57 (dd, 1 H, J = 4, 9 Hz), 6.22 (dd, 1 H, J = 4, 17 Hz), 6.57 (dd, 1 H, J = 9, 17 Hz); IR (CCl_4) 1742, 1705, 1615 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 196 (M^+, absent), 141 (53), 100 (15), 99 (100), 81 (76), 79 (11), 55 (71), 43 (88), 41 (18).

1-(1′-Acetoxy-4′-*tert*-butylcyclohexyl)-2-buten-1-one (65):[34] chromatography on silica gel (5% ether/hexane); recrystallized from hexane; mp 76.5–77 °C; 70% yield; ^{1}H NMR (220 MHz, CCl_4) δ 0.87 (s, 9 H), 0.9–1.7 (m, 9 H), 1.86 (dd, 3 H, J = 2, 6 Hz), 2.05 (s, 3 H), 6.14 (dq, 1 H, J = 2, 15 Hz), 6.79 (dq, 1 H, J = 6, 15 Hz); IR (CCl_4) 1738, 1698, 1630 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 266 (M^+, 1), 197 (28), 156 (14), 155 (100), 137 (12), 81 (23), 69 (100), 67 (12), 57 (36), 55 (15), 43 (71), 41 (61); for X-ray crystal structure see ref 11.

1-(1′-Acetoxy-4′-*tert*-butylcyclohexyl)-2-propen-1-one (66):[34] chromatography on sillca gel (10% ether/hexane); Kugelrohr distillation, bp 140–145 °C (bath temperature) (0.05 torr); 90% yield; recrystallized from hexane; mp 61–62 °C; ^{1}H NMR (CCl_4) δ 0.88 (s, 9 H), 0.9–1.9 (m, 9 H), 2.05 (s, 3 H), 5.58 (dd, 1 H, J = 4, 9 Hz), 6.23 (dd, 1 H, J = 4, 17 Hz), 6.61 (dd, 1 H, J = 9, 17 Hz); IR (CCl_4) 1740, 1708, 1612 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 252 (M^+, 1), 197 (54), 155 (100), 137 (42), 95 (24), 81 (41), 69 (14), 67 (19), 57 (42), 55 (65), 43 (66), 41 (37).

1-(1′-Acetoxycycloheptyl)-2-buten-1-one (67):[34] chromatography on silica gel (15% ether/hexane); Kugelrohr distillation, bp 130 °C (bath temperature) (0.05 torr); 93% yield; ^{1}H NMR (CCl_4) δ 1.57 (m, 12 H), 1.88 (dd, 3 H, J = 1, 6 Hz), 2.03 (s, 3 H), 6.16 (dq, 1 H, J = 1, 15 Hz), 6.90 (dq, 1 H, J = 6, 15 Hz); IR (CCl_4) 1738, 1698, 1630 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 224 (M^+, absent), 155 (30), 114 (14), 113 (100), 95 (51), 69 (100), 67 (18), 55 (27), 53 (11), 43 (100), 41 (100).

1-(1′-Acetoxycyclododecyl)-2-buten-1-one (68):[34] Kugelrohr distillation, sublimes at 200–210 °C; recrystallized from ether/hexane; mp 154–155 °C; 93% yield; ^{1}H NMR ($CDCl_3$) δ 1.37 (m, 22 H), 1.83 (dd, 3 H, J = 1, 6 Hz), 2.05 (s, 3 H), 6.32 (dq, 1 H, J = 1, 15 Hz), 7.05 (dq, 1 H, J = 6, 15 Hz); IR ($CDCl_3$) 1735, 1700, 1632 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 294 (M^+, 1), 184 (31), 183 (100), 165 (16), 109 (24), 97 (15), 95 (26), 83 (51), 81 (17), 69 (85), 67 (14), 55 (30), 43 (59), 41 (33).

Preparation of Cyclopentenones from α′-Hydroxy (Method C) or α′-Trimethylsiloxy Enones (Method D). The α′-hydroxy enone (0.50 mmol) and *p*-toluenesulfonic acid monohydrate (0.10 mmol) are dissolved in 8 mL of dry toluene, and the mixture is heated to reflux. The reaction is refluxed until complete (GC or TLC). The mixture is then partitioned between ether and brine, basified with aqueous NaOH, extracted three times with ether, dried over $MgSO_4$, and concentrated in vacuo. Chromatography on silica gel followed by Kugelrohr distillation affords the pure cyclopentenone. The α′-trimethylsiloxy enones require 1.1 equiv of *p*-toluenesulfonic acid for conversion to the cyclopentenone; otherwise the same procedure is employed.

Preparation of Cyclopentenones from α′-Acetoxy Enones (Method E). A mixture of 5 mL of toluene and *p*-toluenesulfonic acid monohydrate (0.60 mmol) are refluxed through a Soxhlet extractor containing 4A molecular sieves for 4–6 h. The α′-acetoxy enone is then added and the reflux continued. The reaction is followed until complete (GC or TLC). The reaction mixture is then worked up in the same manner as above to afford the pure cyclopentenone.

Preparation of Cyclopentenones from γ-Lactones (Method F). The spirolactone was treated with 5 mL of a 1:10 (w/w) solution of P_2O_5 in methanesulfonic acid at 60 °C for 1–2 h. Afterward the reaction mixture was added dropwise to 25 mL of 50% aqueous K_2CO_3. After the mixture was stirred for 5 min, the product was extracted into ether. The ether layer was washed with brine, dried with $MgSO_4$, and Kugelrohr distilled to give cyclopentenones of greater than 95% purity (GC).

2,3,4,5,6,7-Hexahydro-3-methylinden-1-one (51).[2] **Method E**: chromatography on silica gel (20% ether/hexane); Kugelrohr distillation, bp 90–100 °C (bath temperature) (0.05 torr); 53% yield (method F, 94% yield); ^{1}H NMR (CCl_4) δ 1.15 (d, 3 H), 1.40–2.60 (m, 11 H); IR (neat) 1704, 1654 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 150 (M^+, 68), 135 (100), 122 (33), 107 (54), 93 (31), 91 (30), 79 (96), 77 (34), 41 (27), 39 (28).

2,3,4,5,6,7-Hexahydro-2-methylinden-1-one (52).[29] **Method E**: Kugelrohr distillation, bp (0.05 torr) 95–100 °C; yield 65% (method F, 76% yield); ^{1}H NMR (CCl_4) δ 1.10 (d, 3 H), 1.5–2.5 (m, 11 H); IR (neat) 1700, 1650 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 150 (M^+, 82), 135 (100), 122 (27), 108 (17), 107 (39), 94 (14), 93 (18), 91 (17), 79 (51), 77 (18), 41 (14).

2,3,4,5,6,7-Hexahydroinden-1-one (53).[26] **Method E**: chromatography on silica gel (30% ether/hexane); Kugelrohr distillation, bp 60–70 °C (bath temperature) (0.05 torr); 41% yield (method F, 89% yield); ^{1}H NMR (CCl_4) δ 1.5–2.5 (m, 12 H); IR (CCl_4) 1700, 1650 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 136 (M^+, 100), 135 (24), 108 (25), 94 (70), 93 (38), 91 (21), 79 (87), 77 (22).

2,3,4,5,6,7-Hexahydro-3-methyl-5-*tert*-butylinden-1-one (54). Method E: chromatography on silica gel (20% ether/hexane); Kugelrohr distillation, bp 140 °C (bath temperature) (0.05 torr); 85% yield; ^{1}H NMR (CCl_4) δ 0.92 (s, 9 H), 1.11 (d, 3 H), 1.1–2.7 (m, 10 H); IR (CCl_4) 1703, 1652 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 206 (M^+, 21), 150 (56), 121 (30), 119 (85), 117 (100), 57 (95), 47 (31), 41 (48).

2,3,4,5,6,7-Hexahydro-5-*tert*-butylinden-1-one (55). Method E: chromatography on silica gel (30% ether/hexane); Kugelrohr distillation, bp 140 °C (bath temperature) (0.05 torr); 66% yield; ^{1}H NMR (CCl_4) δ 0.93 (s, 9 H), 1.0–2.5 (m, 11 H); IR (CCl_4) 1700, 1654 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 192 (M^+, 70), 177 (15), 164 (18), 137 (20), 136 (100), 135 (45), 121 (19).

3,4,5,6,7,8-Hexahydro-3-methyl-(2*H*)-azulen-1-one (56).[31] **Method E**: chromatography on silica gel (20% ether/hexane); bp 70–90 °C (bath temperature) (0.05 torr); 60% yield; ^{1}H NMR (CCl_4) δ 1.13 (d, 3 H), 1.3–2.7 (m, 13 H); IR (neat) 1700, 1650 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 164 (M^+, 100), 149 (78), 136 (91), 122 (34), 121 (57), 108 (29), 107 (35), 93 (65), 91 (35), 79 (66), 77 (35), 41 (32).

15-Methylbicyclo[10.3.0]pentadec-1(12)-en-13-one (57).[15a] **Method E**: chromatography on silica gel (25% ether/hexane); Kugelrohr distillation, bp 185 °C (bath temperature) (0.05 torr); yield 91%; ^{1}H NMR (CCl_4) δ 1.0–2.9 (m, 23 H), 1.13 (d, 3 H); IR (CCl_4) 1700, 1632 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 234 (M^+, 100), 191 (72), 178 (38), 177 (69), 164 (30), 163 (68), 150 (36), 149 (61), 137 (45), 136 (33), 135 (55), 124 (69), 123 (49), 122 (56), 121 (37), 109 (62), 107 (33), 93 (33), 81 (31), 79 (47), 67 (34), 55 (46), 41 (64).

2,3,4,5-Tetrahydro-3-methylbenz[*e*]inden-1-one (58)[27] **and 3a,4,5,7a-Tetrahydro-3-methylbenz[*e*]inden-1-one (59). Method D**: isomers separated by chromatography on silica gel (15% ether/hexane); Kugelrohr distillation, bp 160 °C (bath temperature) (0.05 torr); recrystallize each isomer from hexane; mp (**58**) 103–104 °C, mp (**59**) 64–65.5 °C; 99% yield obtained as mixture of isomers in a ratio of 50:50. Spectral characteristics of **58** are as follows: ^{1}H NMR (CCl_4) δ 1.25 (d, 3 H), 1.9–3.1 (m, 7 H), 7.00 (m, 3 H), 8.10 (m, 1 H); IR (CCl_4) 1702, 1632 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 198 (M^+, 100), 183 (38), 170 (47), 155 (54), 153 (16), 141 (33), 129 (21), 128 (36). Spectral characteristics of **59** are as follows: ^{1}H NMR (CCl_4) δ 1.7–2.1 (m, 2 H), 2.12 (d, 3 H, J = 1 Hz), 2.3–2.6 (m, 2 H), 3.0–3.3 (m, 1 H), 3.47 (br d, 1 H), 5.90 (m, 1 H), 6.8–7.2 (m, 3 H), 7.3–7.5 (m, 1 H); IR (CCl_4) 1700, 1625 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 198 (M^+, 100), 197 (17), 183 (46), 180 (19), 165 (36), 156 (24), 155 (37), 141 (22), 129 (24), 128 (34), 115 (19), 55 (16); exact mass, found m/e 198.1049 (calcd for $C_{14}H_{14}O$, m/e 198.1045).

2,3,6,7-Tetrahydro-3,4,6,6-tetramethylinden-1-one (60) and 2,3,4,5,6,7-Hexahydro-3,6,6-trimethyl-4-methyleneinden-1-one (61). Method D: isomers separated by chromatography on silica gel (10% ether/hexane); Kugelrohr distillation of each isomer,

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bp 115 °C (bath temperature) (0.05 torr); 80% yield obtained as mixture of isomers **60** and **61** in a ratio of 70:30. Spectral characteristics of **60** are as follows: ^{1}H NMR (CCl_4) δ 0.93 (s, 3 H), 1.00 (s, 3 H), 1.12 (d, 3 H), 1.88 (d, 3 H, J = 1 Hz), 1.8–3.0 (m, 5 H), 5.63 (q, 1 H, J = 1 Hz); IR (CCl_4) 1689, 1641, 1578 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 190 (M^+, 22), 147 (5), 133 (100), 119 (6), 105 (7), 91 (6), 41 (6); UV λ_{max} 292 nm. Spectral characteristics of **61** are as follows: ^{1}H NMR (CCl_4) δ 0.90 (s, 3 H), 1.00 (s, 3 H), 1.22 (d, 3 H), 1.9–3.2 (m, 7 H), 5.21 (m, 1 H), 5.33 (m, 1 H); IR (CCl_4) 1695, 1629, 1598 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 190 (M^+, 80), 175 (57), 148 (27), 147 (52), 133 (100), 119 (28), 105 (49), 91 (40), 77 (23), 41 (34); UV λ_{max} 263 nm.

14-Methylbicyclo[10.3.0]pentadec-1(12)-en-13-one (26).[15b] **Method F**: Kugelrohr distillation, bp 165–170 °C (bath temperature) (0.05 torr); 85% yield; ^{1}H NMR (CCl_4) δ 1.0–2.7 (m, 23 H), 1.12 (d, 3 H); IR (CCl_4) 1700, 1638 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 234 (M^+, 100), 191 (77), 177 (80), 163 (55), 149 (31), 135 (21), 124 (23), 91 (21), 79 (30), 67 (22), 55 (33), 43 (21), 41 (58).

2-Methyl-3-butyl-2-cyclopentenone (69)[3a] **and 3-Pentyl-2-cyclopentenone (70).**[28] **Method F**: Kugelrohr distillation, bp 90–100 °C (bath temperature) (0.05 torr); 89% yield; obtained as a 93:7 mixture of **69** and **70**. Spectral characteristics of **69** contaminated with 7% **70** are as follows: ^{1}H NMR (CCl_4) δ 0.97 (br t, 3 H), 1.15 (m, 4 H), 2.05 (br s, 3 H), 1.92–2.7 (m, 6 H); IR (CCl_4) 1699, 1643 cm^{-1}; GC/MS (70 eV) of pure **69** m/e (relative intensity) 152 (M^+, 33), 137 (38), 123 (17), 110 (100), 109 (17), 95 (19), 67 (27), 41 (20). A pure sample of **70** was not obtained; however, spectral characteristics from the mixture are as follows: ^{1}H NMR (CCl_4) δ 6.17 (br s); GC/MS (70 eV) of pure **70** m/e (relative intensity) 152 (M^+, 42), 96 (100), 95 (28), 81 (49), 68 (23), 67 (21), 53 (20), 41 (31).

2,3,4,5-Tetrahydro-7-methoxy-3-methylbenz[*e*]inden-1-one (58b)[32,34] **and 3a,4,5,9b-Tetrahydro-7-methoxy-3-methylbenz[*e*]inden-1-one (59b). Method D**: Kugelrohr distillation, bp 170 °C (bath temperature) (0.05 torr); 99% yield obtained as mixture of isomers **58b** and **59b** in a ratio of 77:23; **58b** recrystallized from hexane; mp 92.5–93 °C. Spectral characteristics of **58b** are as follows: ^{1}H NMR (CCl_4) δ 1.15 (d, 3 H), 2.10–3.00 (m, 7 H), 3.76 (m, 3 H), 6.68 (m, 2 H), 8.13 (m, 1 H); IR (CCl_4) 1704, 1612 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 228 (M^+, 100), 214 (11), 213 (84), 200 (19), 185 (33), 171 (12), 141 (14), 115 (23); exact mass, found m/e 228.1151 (calcd for $C_{15}H_{16}O_2$, m/e 228.1151). A pure sample of **59b** was not obtained. Significant NMR characteristics of **59b** obtained from the combined spectrum of the two isomers are as follows: ^{1}H NMR (CCl_4) δ 2.05 (br s, 3 H), 3.75 (s, 3 H), 5.83 (br s, 1 H).

4-Methyl-2-phenyl-2-cyclopenten-1-one (23)[33] **and 3-Methyl-5-phenyl-2-cyclopenten-1-one (24). Method D**: isomers separated by chromatography on silica gel (50% ether/hexane); Kugelrohr distillation of each isomer, bp 125 °C (bath temperature) (0.05 torr); combined yield of 78% of separated isomers **23** and **24** in a ratio of 48:52. Spectral characteristics of **23** are as follows: ^{1}H NMR (220 MHz, CCl_4) δ 1.27 (d, 3 H), 2.06 (d, 1 H, J = 17 Hz), 2.70 (dd, 1 H, J = 8, 17 Hz), 2.93 (m, 1 H), 7.3–7.7 (m, 6 H); IR (CCl_4) 1706, 1598 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 172 (M^+, 62), 144 (21), 129 (100), 128 (31), 115 (17), 102 (29), 77 (14). Spectral characteristics of **24** are as follows: ^{1}H NMR (CCl_4) δ 2.15 (d, 3 H, J = 1 Hz), 2.3–3.3 (m, 2 H), 3.38 (dd, 1 H, J = 3, 7 Hz), 5.81 (q, 1 H, J = 1 Hz), 7.12 (m, 5 H); IR (CCl_4) 1700, 1627 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 172 (M^+, 100), 171 (15), 157 (38), 143 (19), 129 (75), 128 (30), 95 (13), 77 (12).

Preparation of 3-Furanones. General Procedure. The α'-hydroxy enone (0.5 mmol), *p*-toluenesulfonic acid (0.1 mmol), and 40 μL of methanol (1.0 mmol) are dissolved in 8 mL of toluene. The mixture is heated to reflux, and the reaction progress is followed by GC. The mixture is then partitioned between ether and water, extracted three times with ether, and dried over $MgSO_4$. Chromatography on silica gel followed by Kugelrohr distillation affords the pure 3-furanone.

2-Methyl-1-oxaspiro[4.5]decan-4-one (72):[30] chromatography on silica gel (10% ether/hexane); Kugelrohr distillation, bp 125–135 °C (bath temperature) (2 torr); 90% yield; ^{1}H NMR (CCl_4) δ 1.35 (d, 3 H), 1.50 (m, 10 H), 1.98 (dd, 1 H, J = 10, 18 Hz), 2.45 (dd, 1 H, J = 6, 18 Hz), 4.23 (m, 1 H); IR (CCl_4) 1754 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 168 (M^+, 22), 140 (28), 99 (50), 98 (100), 80 (29), 70 (33), 69 (48), 55 (74), 43 (39), 42 (66), 41 (57).

2,6-Dimethyl-1-oxaspiro[4.5]decan-4-one (73):[34] chromatography on silica gel (10% ether/hexane); Kugelrohr distillation, bp 85–90 °C (bath temperature) (0.05 torr); 78% yield; obtained as mixture of diastereomers; ^{1}H NMR (CCl_4) δ 0.70 (d, 3 H), 0.75 (d, 3 H), 1.34 (d, 3 H), 1.36 (d, 3 H), 1.0–1.7 (m, 22 H), 4.27 (m, 2 H) (the NMR spectrum reported is of the diastereomeric mixture); IR (CCl_4) 1740 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 182 (M^+, 11), 164 (11), 154 (48), 113 (17), 112 (100), 94 (19), 84 (12), 68 (19).

2-Methyl-1-oxaspiro[4.11]hexadecane-4-one (74): chromatography on silica gel (5% ether/hexane); Kugelrohr distillation, bp 165–170 °C (bath temperature) (0.05 torr); 80% yield; NMR (CCl_4) δ 1.30 (d, 3 H), 1.40 (m, 22 H), 2.00 (dd, 1 H, J = 10, 18 Hz), 2.48 (dd, 1 H, J = 6, 18 Hz), 4.27 (m, 1 H); IR (neat) 1750 cm^{-1}; mass spectrum (70 eV) m/e (relative intensity) 252 (M^+, 4), 224 (18), 183 (23), 182 (46), 125 (13), 112 (12), 111 (18), 98 (43), 97 (15), 71 (24), 69 (22), 58 (25), 55 (79), 43 (47), 42 (66), 41 (100).

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