Efficient and Flexible Syntheses of Paraconic Esters and Other Highly Substituted Furanone Derivatives from Methyl 2-Siloxycyclopropanecarboxylates†

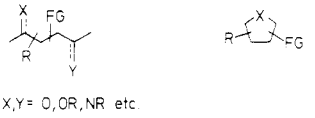
Christiane Brückner and Hans-Ulrich Reissig*

Institut für Organische Chemie der Universität Würzburg, Am Hubland, D-8700 Würzburg, FRG

Received September 10, 1987

Deprotonation of methyl 2-siloxycyclopropanecarboxylates **1** with lithium diisopropylamide and reaction of the resulting enolates with carbonyl compounds produce trifunctional cyclopropane derivatives. These primary adducts can only be isolated with good yields in exceptional cases. However, ring opening of the crude aldol adduct with fluoride reagents and subsequent oxidation with pyridinium chlorochromate makes accessible a variety of methyl 5-oxotetrahydrofuran-3-carboxylates (paraconic esters), which are synthesized by this route in a highly flexible and effective fashion. In addition, other transformations of the aldol adducts lead to various furan derivatives, e.g., α-methylene γ-lactones. Mechanistic points regarding the stereochemical features of the crucial addition to the enolate anion are discussed in detail.

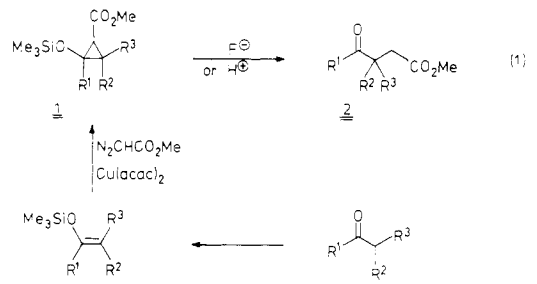
Because of their occurrence in natural products, other compounds of biological activity, or precursors for further transformations (e.g. to carbocycles), structural units displaying a substituent pattern with a 1–4 distance of heteroatoms are a synthetic challenge of general importance. Therefore acyclic systems with heterofunctions X and Y as well as heterocycles containing X, both carrying further substituents R and functional groups FG, should be made available by flexible chemo-, and regio-, and at the highest level stereoselective methods.[1]



X,Y = O, OR, NR etc.

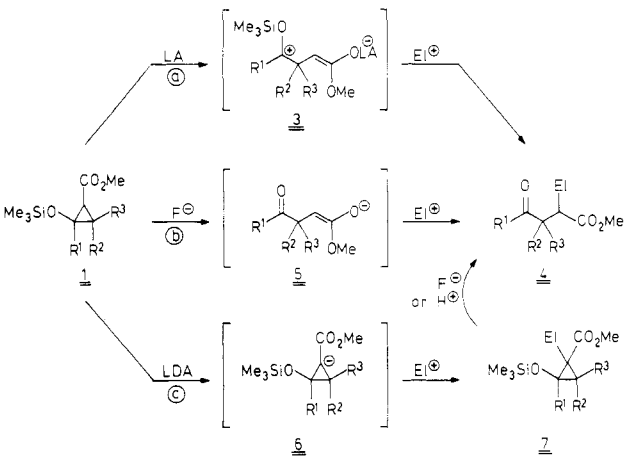
To assemble carbon chains with a 1–4 distance of functions X and Y by reactions via polar intermediates, one has to achieve umpolung of reactivity.[2] This can be accomplished by Michael-type additions of acyl anions,[3] by combination of enolates with enolium cations,[4] or by reactions of homo enolates with carbonyl compounds.[5] Based on earlier singular examples, Wenkert established certain oxycyclopropanes as valuable intermediates for the preparation of 1,4-dicarbonyl compounds and exploited their potential in natural product synthesis.[6]

This umpolung by means of the "cyclopropane trick"[2] is also operating with 2-siloxy-substituted methyl cyclopropanecarboxylates **1**, which are easily available from silyl enol ethers by a most flexible and effective protocol, even in large scale.[7] They can be cleaved by fluoride reagents or acids to a great variety of 4-oxoalkanoates **2** (eq 1).[8]



Considering the overall process, methyl diazoacetate has served as enolium cation equivalent. Further transformations of **1** by various methods to other compounds with the polarity pattern discussed here make donor–acceptor-substituted cyclopropanes **1** extremely versatile building blocks.[9]

Scheme I



For introduction of additional substituents or functional groups at C-2 of **1**, we have developed three routes leading to **4** (Scheme I): (a) Activation of **1** by Lewis acids forms zwitterions **3** (or their equivalents) which combine with apt electrophiles affording **4**.[10] (b) Desilylation with fluoride

* Present address: Institut für Organische Chemie der Technischen, Hochschule Darmstadt, Petersenstrasse 22, D-6100 Darmstadt, FRG.

† Dissertation Christiane Brückner, Universität Würzburg, 1986.

(1) For recent ingenious use of γ-lactones as templates for asymmetric synthesis, see: (a) Stork, G.; Rychnovsky, S. D. *Pure Appl. Chem.* **1986**, *58*, 767; *J. Am. Chem. Soc.* **1987**, *109*, 1564. (b) Hannessian, S.; Murray, P. J. *J. Am. Chem. Soc.* **1987**, *109*, 1170. (c) Ziegler, F. E.; Kneisley, A. *Heterocycles* **1987**, *25*, 105.

(2) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239.

(3) Reviews: (a) Lever, O. W. *Tetrahedron* **1976**, *32*, 1943. (b) Stetter, H. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 639. (c) Hase, T. A.; Koskimic, J. K. *Aldrichimica Acta* **1981**, *14*, 73. (d) Albright, J. D. *Tetrahedron* **1983**, *39*, 3207.

(4) The most convenient equivalents for enolium cations are α-halogen carbonyl compounds. See: House, H. O. *Modern Synthetic Reactions*, 2nd ed.; Benjamin: Menlo Park, CA, 1972.

(5) For a recent review, see: Hoppe, D. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 932.

(6) Wenkert, E. *Acc. Chem. Res.* **1980**, *13*, 27.

(7) Kunkel, E.; Reichelt, I.; Reissig, H.-U. *Liebigs Ann. Chem.* **1984**, 512.

(8) Kunkel, E.; Reichelt, I.; Reissig, H.-U. *Liebigs Ann. Chem.* **1984**, 802.

(9) For a recent review, see: Reissig, H.-U. *Top. Curr. Chem.* **1988**, *144*, 73.

(10) (a) Reissig, H.-U.; Lorey, H. *Liebigs Ann. Chem.* **1986**, 1914. (b) Reissig, H.-U.; Reichelt, I.; Lorey, H. *Liebigs Ann. Chem.* **1986**, 1924.

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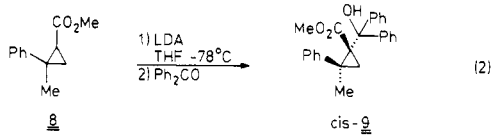
anions under aprotic conditions in the presence of D_2O or alkyl halides provides **4** via the intermediates γ-oxo ester enolate **5**.[8] Recently Marino and Laborde have explored this idea employing mainly Michael acceptors as electrophiles.[11] (c) The third route to compounds **4** goes via cyclopropane ester enolates **6**—easily generated with lithium diisopropylamide (LDA)—and needs an extra step to obtain **4** from the substituted cyclopropane **7**.[12] It is worth mentioning that these products **7** can also be starting materials for paths a and b, thus allowing stepwise introduction of *two* electrophiles[8,10] into 4-oxoalkanoates or derivatives thereof.[13]

So far only syntheses of cyclopropanes **7** have been described in detail for El = alkyl and thiomethyl, which occur in many examples with surprisingly high diastereoselectivity.[12] In this full account we want to disclose the scope and limitations of the additions of carbonyl compounds[14] to enolates **6**. This sequence affords trifunctional products whose potential for synthesis of furanon derivatives will be presented. In addition to this preparative point, mechanistic aspects regarding stereoselectivity are discussed.

Model Reaction

It was expected and confirmed in preliminary experiments that due to silyl group migration and subsequent cyclopropane ring-opening, isolation of primary adducts is not an easy task. On the other hand, the aldol-type reaction can principally be reversible, and formation of stereoisomers might further impede analysis and purification of products.

To avoid some of these complications and to examine the feasibility of the anticipated hydroxyalkylation, we deprotonated cyclopropane **8** having no siloxy function with LDA at −78 °C and then quenched it with benzophenone. After aqueous workup the crude reaction mixture was analyzed by ^1H NMR which shows signals of essentially *one* compound (>90:10). The crystalline product *cis*-**9** could be isolated in 78% yield (eq 2). Its



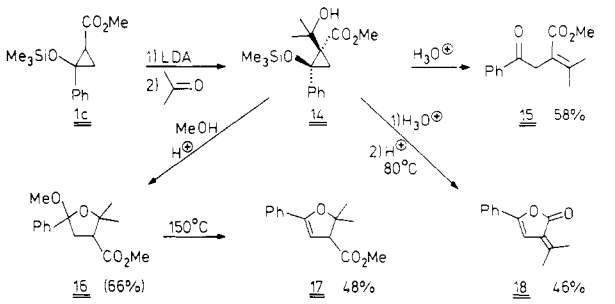
(2)

8 cis-9

stereochemistry is deduced from the high-field absorption of the methoxy group at 2.95 ppm. Notably benzophenone approaches the enolate exclusively, or at least with very high preference, at the less hindered side giving the cis compound. Similar stereoselectivity has been found for alkyl halides and dimethyl disulfide.[15]

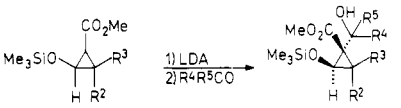
This model reaction demonstrates that the aldol addition of substituted methyl cyclopropanecarboxylates is possible even with the sluggish benzophenone and that it should be applicable to the corresponding siloxy derivatives. Special methods have to be employed, however, in the hydroxyalkylation of *unsubstituted* cyclopropanecarboxylates.[16]

Scheme II



Characterization of Primary Adducts from Siloxycyclopropanes

Several trimethylsiloxy-substituted cyclopropanes **1** were deprotonated with LDA and reacted with carbonyl compounds under similar conditions. However, only in exceptional cases could crystalline products be isolated in reasonable yields (eq 3). The stereochemistry of **10–13**



(3)

1a	R^2,R^3 = Me	R^4,R^5 = Me	10	64%
1a		R^4-R^5 = -$(CH_2)_5$-	11	30%
1b	R^2-R^3 = -$(CH_2)_5$-	R^4-R^5 = -$(CH_2)_5$-	12	31%
1b		R^4,R^5 = Ph	13	51%

is probably cis as drawn, since comparing ^1H and ^{13}C NMR data of compound **10** with the corresponding (*tert*-butyldimethylsiloxy)cyclopropane *cis*-**45** (vide infra) reveals almost identical chemical shifts. Remarkably the IR spectra of compounds **10–13** show two or three carbonyl frequencies (1740–1690 cm^{-1}), which are apparently the result of hydrogen bonds to the hydroxy group. In these cis compounds an intramolecular silyl shift is not possible—a fact that might have enhanced their stability and facilitated the isolation.

In contrast, the primary product *trans*-**14** synthesized from **1c** and acetone (Scheme II) could only be characterized by spectroscopic means. A methoxy signal at 3.12 ppm in the ^1H NMR spectrum is in accord with the suggested trans stereochemistry. Since attempts to purify **14** were frustrated by partial ring opening and dehydration, we deliberately transformed crude **14** to compounds **15–18** by different modes of straightforward workup procedures (Scheme II).

Whereas addition of acetone to the enolate of **1c** proceeds almost quantitatively, combination of the more hindered partners **1d** and benzophenone does not give satisfactory results. Although **1d** gives yields of 80–90% in the deprotonation/alkylation process,[12] addition of the **1d** enolate to benzophenone is incomplete. Water quench at low temperature affords ring-opened dehydrated compound **19** in at best 50% yield and starting material **1d**. Raising the temperature to 25 °C before aqueous workup does not improve conversion, but besides **1d** and **19** the unsaturated γ-lactone **20** is isolated in low quantity (Scheme III).

(11) Marino, J. P.; Laborde, E. *J. Org. Chem.* **1987**, *52*, 1.
(12) Reichelt, I.; Reissig, H.-U. *Liebigs Ann. Chem.* **1984**, 531.
(13) In all three routes to **4** illustrated in Scheme I cyclopropane **1** can be regarded as a homo enolate equivalent, since the electrophile El is finally found β to the carbonyl group liberated in these processes (d^3 reactivity according to ref 2). Of course, the necessity for the activating ester function questions this classification to some extent.
(14) For a preliminary report, see: Brückner, C.; Reissig, H.-U. *J. Chem. Soc., Chem. Commun.* **1985**, 1512.
(15) Reichelt, I., Reissig, H.-U. *Chem. Ber.* **1983**, *116*, 3895.
(16) For a discussion of the problems, see ref 15 and (a) Wemple, J. *Tetrahedron Lett.* **1975**, 3255. (b) Pinnick, H. W.; Chang, Y.-H.; Foster, S. C.; Govindan, M. *J. Org. Chem.* **1980**, *45*, 4508. (c) Kai, Y.; Knochel, P.; Kwiatkowski, S.; Dunitz, J. D.; Oth, J. F. M.; Seebach, D.; Kalinowski, H.-O. *Helv. Chim. Acta* **1982**, *65*, 137. (d) Paquette, L. A.; Blankenship, C.; Wells, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 6442. (e) Häner, R.; Maetzke, T.; Seebach, D. *Helv. Chim. Acta* **1986**, *69*, 1655.

Table I. Synthesis of γ-Lactols According to eq 4

cyclopropane	R^1	R^2	R^3	R^4	R^5	reagent	product	yield, %
1a	H	Me	Me	Me	Me	TBAF[a]	**23**	48
1a	H	Me	Me	$-(CH_2)_5-$		TBAF	**24**	50
1a	H	Me	Me	Ph	Ph	$NEt_3 \cdot 3HF$	**25**	46
1a	H	Me	Me	Ph	H	HCl	**26**	21
1a	H	Me	Me	CHMePh	H	TBAF	**27**	69
1b	H	$-(CH_2)_5-$		$-(CH_2)_5-$		TBAF	**28**	62[b]
1b	H	$-(CH_2)_5-$		Ph	Ph	$NEt_3 \cdot 3HF$	**29**	26
1c	Ph	H	H	Me	Me	TBAF	**30**	85[c]
1c	Ph	H	H	Ph	Ph	$NEt_3 \cdot 3HF$	**31**	32

[a] Tetra-*n*-butylammonium fluoride. [b] Yield based on isolated primary adduct **12**. [c] Yield for crude product (>90% pure according to ^1H NMR spectroscopy).

Table II. Synthesis of Paraconic Esters According to eq 6

cyclopropane	R^2	R^3	R^4	R^5	product	yield, %	cis:trans
1a	Me	Me	Ph	Ph	**32**	70	
1a	Me	Me	Me	Me	**33**	67	
1a	Me	Me	$-(CH_2)_5-$		**34**	54	
1b	$-(CH_2)_5-$		Me	Me	**35**	43	
1b	$-(CH_2)_5-$		$-(CH_2)_5-$		**36**	51	
1b	$-(CH_2)_5-$		Ph	Ph	**37**	27	
1a	Me	Me	Ph	H	**38**	57	2:3
1a	Me	Me	Me	H	**39**	52	1:2
1a	Me	Me	CHMePh	H	**40**[a]	52	1:3
1a	Me	Me	CH=CHMe	H	**41**	38	1:3
1b	$-(CH_2)_5-$		Me	H	**42**	51	1:1

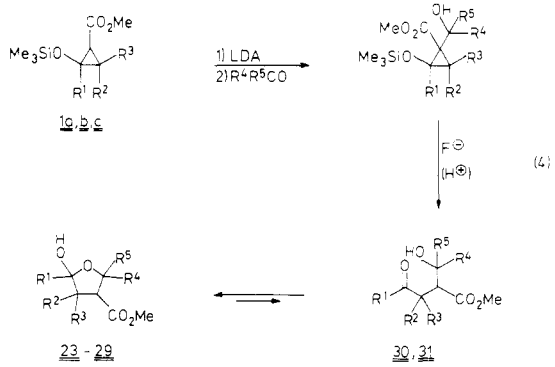
[a] Four isomers due to the exocyclic center of chirality.

With the more reactive benzaldehyde as electrophile complete consumption of **1d** is observed again. Crystalline primary adduct **21** with undefined stereochemistry could be isolated although in low yield only. Acetaldehyde also adds smoothly to the enolate of **1d**, but since the spectra of the primary product were not conclusive, ring opening and dehydration have deliberately been executed with acid to provide a 3:1 *E*/*Z* mixture of **22** in >80% overall yield.

The examples above indicate that the projected aldol addition *via* enolates of type **6** can be performed with cyclopropanes having differing substituent patterns. However, to establish this route as a synthetically valuable method, it is necessary to elaborate alternative procedures to attain more stable reaction products with efficiency.

Ring Cleavage to γ-Lactols

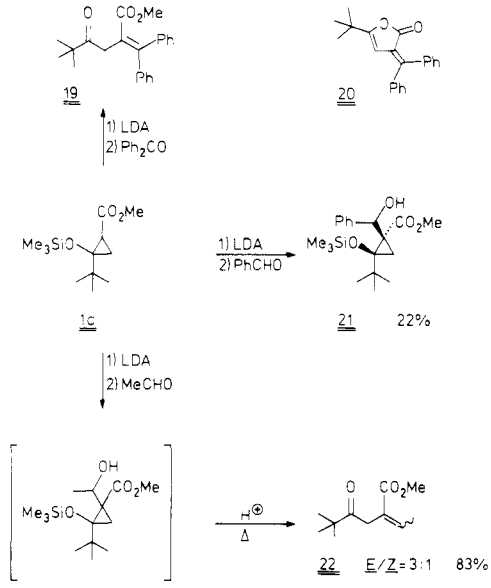
Deprotection and ring opening of methyl 2-siloxycyclopropanecarboxylates **1** to γ-oxo esters **2** can be accomplished under mild conditions with acids or fluoride sources.[8] Similarly, crude hydroxyalkylated cyclopropanes are transformed to γ-lactols **23–29** starting with **1a** and **1b**, respectively, or to the acyclic tautomers **30** and **31**, if cyclopropane **1c** ($R^2 = R^3 = H$) is the precursor (eq 4, Table I).



(4)

Tetra-*n*-butylammonium fluoride (TBAF) is the reagent of choice, since acidic conditions cause side reactions for substrates with R^4, R^5 = alkyl. The rather low yield for **26** and **29** (Table I) might therefore be improvable. Taking into account the possible formation of stereoisomers, the average yield of 50%—referring to purified crystalline material in most cases—is satisfactory for a two-step sequence. Nevertheless, it was desirable to search for methods which remove the anomeric hydroxyl group and lead to preparatively more valuable products.[17]

Scheme III

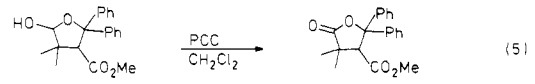


Oxidation to Paraconic Esters

For removal of the hydroxyl function in γ-lactols, the oxidation to γ-lactones was envisaged—a method obviously restricted to compounds with R^1 = H. Therefore, the isolated γ-lactol **25** was treated with 1.5 equiv of pyridinium chlorochromate (PCC)[18] in methylene chloride.[19]

(17) A reductive transformation to other tetrahydrofuran derivatives is described in the following paper: Brückner, C.; Reissig, H.-U. *J. Org. Chem.*, following paper in this issue.

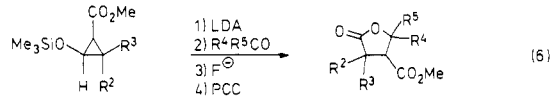
Because of the high steric hindrance a reaction time of 90 h is required to bring about the anticipated oxidation to the paraconic ester **32** which was formed as exclusive product (eq 5). Having established the feasibility of this



(5)

25 **32** 67%

process, we converted siloxycyclopropanes **1** to paraconic esters without efforts to purify intermediate aldol adducts and γ-lactols (eq 6). Results of these unoptimized experiments are compiled in Table II.



(6)

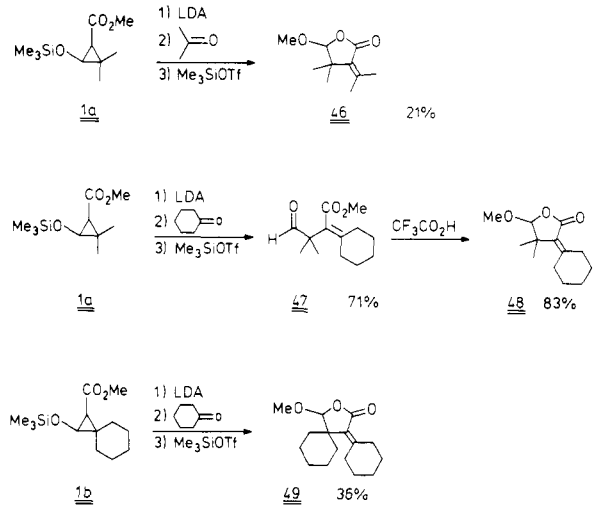
1a, **b** **32** - **42**

Satisfactory overall yields are gained for aromatic as well as for aliphatic ketones and aldehydes. Enolization of the carbonyl component apparently does not play a role. Only with the sluggish electrophile benzophenone, addition to the enolates seems to be incomplete since small amounts (10–20%) of hydrolyzed starting material could be detected. As demonstrated with **34** and **35**, isomeric lactones can be synthesized by a suitable choice of starting materials. With crotonaldehyde only products resulting from 1,2-addition could be identified.

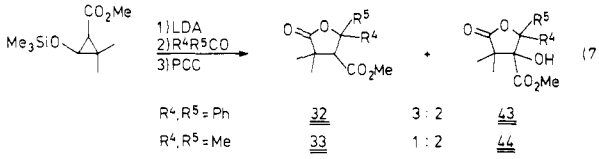
Aldehydes as electrophiles afford the paraconic esters as the expected mixtures of cis and trans isomers. The ratio is determined in the ring-cleaving step and very likely untouched during the oxidation procedure. If desired, these isomers could be separated through chromatography. In four of five examples the trans compound predominates. The stereochemistry of these γ-lactones can be defined by means of ^{1}H NMR spectroscopy showing a vicinal coupling constant for 4-H and 5-H of ~10 Hz in trans compounds and of ~5 Hz in the cis series.[20] However, stereochemical determinations based solely on coupling constants are not always unambiguous in five-membered heterocycles.[21] Fortunately, our assignments are confirmed by the relative chemical shifts of several characteristic signals. Of particular significance are the methoxy protons in **38** with a singlet at higher field in *cis*-**38** with respect to that of *trans*-**38**. Paraconic esters **32–42** show a typical IR absorption in the range of 1780–1800 cm^{-1} for cis compounds and of 1780–1790 cm^{-1} for the trans isomers.

In summary, the sequence illustrated in eq 6 is very flexible compared to other known methods[22] regarding substituents R^2–R^5. Although it operates with reasonable efficiency, we nevertheless tried to abbreviate the procedure. Since PCC is acidic (pH 1.75 for a 0.01 M solution),[23]

Scheme IV



it should be a suitable reagent to bring about the cyclopropane cleavage before oxidizing the generated γ-lactol. This would save an extra step for ring cleavage. However, treating the unpurified adducts prepared from **1a** and benzophenone with PCC does not only afford the expected product **32** but also the hydroxylated γ-lactone **43** (eq 7).

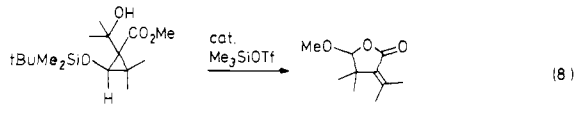


(7)

Analogously, the two γ-lactones **33** and **44** are formed, if acetone is the electrophile introduced. These unexpected oxygenated hexasubstituted γ-lactones **43** and **44**, respectively, could be isolated in pure form through chromatography. The mechanism of their formation is yet unclear, but preliminary experiments reveal that a hydroxyalkyl function at C-1 of the siloxycyclopropane is a prerequisite for this oxidative ring opening[24] found by serendipity.

Rearrangement to α-Methylene γ-Lactones

To confirm the stereochemistry of the adduct **45**—obtained from **1e** and acetone (see next section)—we attempted its isomerization to the thermodynamically more stable *cis*-**45**. By treatment of **45** with a catalytical amount of trimethylsilyl triflate we observed smooth and quantitative formation of α-methylene γ-methoxy γ-lactone **46** (eq 8). Apparently trifluoromethanesulfonic acid—liberated under the reaction conditions—causes desilylation, ring cleavage, and dehydration giving **46** as most stable compound.



(8)

45 **46** 84%

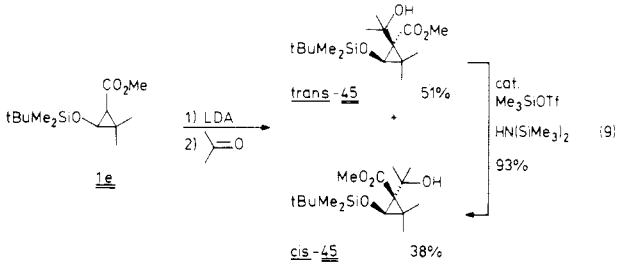
This surprising rearrangement could be utilized to prepare a few of these highly substituted α-methylene γ-lactones[25] as depicted in the unoptimized examples of

(18) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.
(19) Compare oxidation of similar compounds: (a) Pratt, A. J.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1982**, 1115. (b) Ueno, Y.; Chino, K.; Watanabe, M.; Moriya, O.; Okawara, M. *J. Am. Chem. Soc.* **1982**, *104*, 5564.
(20) See for example: Hussain, S. A. M. T.; Ollis, W. D.; Smith, C.; Stoddart, J. F. *J. Chem. Soc., Perkin Trans 1* **1975**, 1480, and references in ref 21.
(21) See discussion in: Jaime, C.; Ortuno, R. M.; Font, J. *J. Org. Chem.* **1986**, *51*, 3946.
(22) (a) van Tamelen, E. E.; Rosenberg-Bach, S. *J. Am. Chem. Soc.* **1958**, *80*, 3079. (b) Minami, N.; Kuwajima, I. *Tetrahedron Lett.* **1977**, 1423. (c) Shono, T.; Hamaguchi, H.; Nishiguchi, I.; Sasaki, M.; Miyamoto, T.; Miyamato, M.; Fujita, S. *Chem. Lett.* **1981**, 1217. (d) Pohmakotr, M.; Reutrakul, V.; Phongpradit, T.; Chansri, A. *Chem. Lett.* **1982**, 687. (e) Lawlor, J. M.; McNamee, M. B. *Tetrahedron Lett.* **1983**, *24*, 2211. (f) Mulzer, J.; deLasalle, P.; Chucholowski, A.; Blaschik, U.; Brüntrup, G.; Jibril, I.; Huttner, G. *Tetrahedron* **1984**, *40*, 2211. (g) Mulzer, J.; Chucholowski, A. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 655.
(23) Battacharjee, M.; Chandhuri, M. K.; Dasgupta, H. S.; Roy, N. *Synthesis* **1982**, 588.
(24) For the oxidation of silyl enol ethers with Cr(VI), see: Lee, T. V.; Toczek, J. *Tetrahedron Lett.* **1982**, *23*, 2917.

Scheme IV. Starting from the trimethylsilyl derivative **1a**, γ-lactone **46** is isolated in low yield. By employing cyclohexanone as electrophile, the initially isolated product **47** was transformed to the final goal **48** by treatment with trifluoroacetic acid. Spirocyclopropane **1b** makes available the spiro-γ-lactone **49** in moderate yield. Although not verified by experiment, it can be foreseen that a substitution pattern with R^2 and $R^3 \neq H$ is required for synthesis of this type of α-methylene γ-methoxy γ-lactones (compare formation of γ-lactones **18** and **20**, Schemes II and III).

Mechanistic Aspects of the Aldol Addition

Endocyclic Stereoselectivity. Besides the preparative features enclosed in the sections above, we were also interested in the stereochemical characteristics of the hydroxyalkylation step, which was to compare with the reactions of ester enolates **6** with other electrophiles. To determine the stereoselectivity with respect to the face differentiation of the electrophile, we chose cyclopropane **1e** as model compound carrying the *tert*-butyldimethylsilyl group which makes products less sensitive and facilitates isolation and characterization. After deprotonation of **1e** with LDA and reaction with acetone under standard conditions, the crude product was investigated by high-field NMR spectroscopy. Besides 11% of unchanged starting material **1e**, two products **45** were detected in 51% and 38% (eq 9). Most significantly, the 2-H signal in the



(9)

^1H NMR spectrum appears at 3.73 ppm for the major isomer, while that of the other adduct shows up at 3.49 ppm. Taking into account our experience in the relative chemical shifts of related cyclopropanes obtained by enolate alkylation,[12] we tentatively assigned the stereochemistry as drawn in eq 9. To prove this hypothesis, the isomers were separated through chromatography, and the assumed *trans*-**45** was exposed to trimethylsilyl triflate catalysis in the presence of hexamethyldisilazane resulting in complete isomerization to *cis*-**45**.

This (Lewis) acid-catalyzed process—discovered several years ago[26]—establishes the thermodynamic equilibrium of methyl 2-siloxycyclopropanecarboxylates **1** and serves as a valuable tool for stereochemical assignments.[7] The conversion *trans*-**45** → *cis*-**45** is the first example with an additional 1-hydroxyalkyl group. Because of the dominance of steric effects, and as the 1-(2-hydroxy-isopropyl) substituent ought be more bulky compared to the methoxy carbonyl group, the equilibrium should be completely on the side of *cis*-**45** as observed. Therefore the assignment shown in eq 9 has very high probability.

In contrast to alkylations, the aldol addition of ester enolates can be a reversible reaction and the stereochemical outcome could be a matter of thermodynamic control. Therefore experiments quenching the reaction mixture (eq 9) with water after 5 min and in a third run after 10 s at −78 °C have been performed. We uniformly found a product ratio of ~5:4 in favor of *trans*-**45**, however, with more unconsumed starting material **1e**.

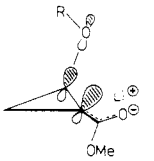


Figure 1. Pyramidal ester enolate as a consequence of a proposed cis anomeric effect.

Having ascertained the structures of adducts **45** and the kinetic control of their formation, one has to state that acetone attacks the more hindered side of the enolate (cis to the *tert*-butyldimethylsiloxy group) with slight but unequivocal preference ($\Delta\Delta G^{\ddagger}$ = 0.1 kcal/mol). However an even more pronounced unusual behavior of this ester enolate has been found with smaller electrophiles like iodomethane, giving almost exclusive *contrasteric alkylation* (ratio of diastereomers 96:4).[12] We have attributed this effect steering electrophiles cis to the β-oxygen function at C-2 to an anomeric effect,[27] which stabilizes a pyramidal enolate[28] with the more extended orbital lobe at C-1 cis to the C–O bond at C-2. Since the assumption of this cis anomeric effect[29] is based solely on product ratios, its speculative character should be emphasized (Figure 1).

This stereoelectronic effect of a siloxy group[30] is dominating compared to its steric effect, as long as rather small electrophiles are employed.[12] For this reason it is surprising that with acetone still a small preference for the contrasterical addition forming the *trans*-cyclopropane can be recorded.

As mentioned above, the primary adduct **10** with a trimethylsiloxy group—synthesized from **1a** and acetone—has cis stereochemistry according to NMR data. The yield of 64% indicates that the stereoselectivity must be reversed here (cis:trans > 64:36). This is no apparent contradiction to the results of eq 9, since the enolate from **1a** exhibits also lower trans selectivity in the reaction with iodomethane (90:10).[12] The origin for the stronger stereoelectronic effect of the *tert*-butyldimethylsiloxy group compared to a trimethylsiloxy unit is so far obscure.

As depicted in Scheme II, cyclopropane **1c** and acetone combine to trans adduct **14** (>90:10 according to ^1H NMR). Formation of this aldol product is now clearly favored for stereoelectronic *and* steric reasons (phenyl group larger than siloxy group[31]).

Exocyclic Stereoselectivity. Reaction of cyclopropane **1f** with a prochiral electrophile like benzaldehyde can afford four diastereomers. The experiment provides only two isomers **50** in a ratio of 3:1 (eq 10). As in alkylation reactions, it is probable that the enolate generated from **1f** incorporates carbonyl compounds exclusively cis to the siloxy group.[12] Again stereoelectronic and steric effects are cooperating. Therefore the isomers of **50** should only

(25) Recent reviews: (a) Hoffman, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 294. (b) Petragnani, N.; Ferraz, H. M. C.; Silva, G. V. J. *Synthesis* **1986**, 157. (c) Sarma, J. C.; Sharma, R. P. *Heterocycles* **1986**, *24*, 441.

(26) Reissig, H.-U., Böhm, I. *Tetrahedron Lett.* **1983**, *24*, 715.

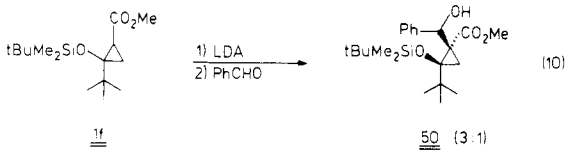
(27) The possibility of an anomeric effect has briefly been mentioned in ref 12. For a more detailed discussion, see ref 9. Also see: Padwa, A.; Wannamaker, M. W. *Tetrahedron Lett.* **1986**, *27*, 2555. Padwa, A.; Wannamaker, M. W.; Dyszlewski, A. D. *J. Org. Chem.* **1987**, *52*, 4760.

(28) Reissig, H.-U.; Böhm, I. *J. Am. Chem. Soc.* **1982**, *104*, 1735.

(29) General discussion of the anomeric effect: Deslongchamps, P. *Stereoelectronic Effects* in *Organic Chemistry*; Pergamon Press: Oxford, 1983. Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer Verlag: Heidelberg, 1983.

(30) Alkoxy groups display a similar though less pronounced effect: see ref 15.

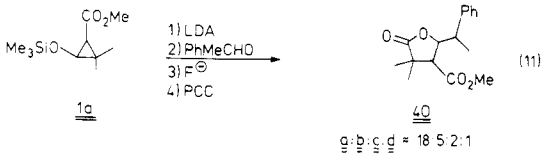
(31) Siloxy groups might have a similar size as alkoxy groups. For steric substituent parameters, see: (a) Knorr, R. *Chem. Ber.* **1980**, *113*, 2441. (b) Fujita, T.; Nishioka, T. *Prog. Phys. Org. Chem.* **1976**, *12*, 49.



1f 50 (3:1)

differ at the exocyclic stereocenter—a hypothesis that is in accordance with the very high similarity of the ^{13}C NMR data. Only signals for C-1 and for the benzylic carbon, respectively, show differences of more than 1 ppm. Unfortunately attempts to remove the hydroxyl group and to gain a single compound, thus proving our assignment, were not successful. Though the ratio of 3:1 implies a reasonable diastereoselection, we are not able to determine the relative stereochemistry with the data at hand.[32] Since this configurational relation between C-1 and the center in the side chain is probably of no meaning for the cis/trans ratio in ring-opened products, we did not insist on clarifying this point.

In contrast, Cram/anti-Cram-type diastereoselectivity is completely transferred to the subsequent products. Therefore the reaction between the enolate of **1a** and the chiral aldehyde 2-phenylpropanal—already presented in Table II without discussing this aspect—should be analyzed again under this point of view. At the stage of the isolated paraconic esters **40**, all four possible diastereomers **a**, **b**, **c**, and **d** could be detected in a ratio of approximately 18:5:2:1 by high-field ^1H NMR spectroscopy (eq 11).



1a 40

a:b:c:d ≈ 18:5:2:1

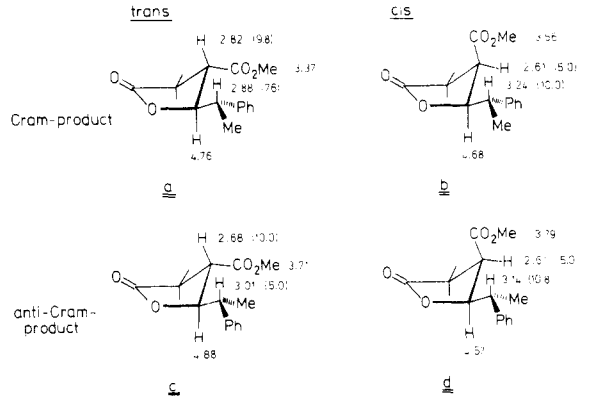
According to the 2-H/3-H vicinal coupling constants of 9.8 Hz and 10 Hz, respectively, isomers **a** and **c** should have trans configuration, whereas in **b** and **d** this coupling value is only 5 Hz and therefore the cis stereochemistry has to be assumed.

The cis/trans ratio, however, does not tell anything about the diastereoselectivity of the enolate reaction. Close inspection of the other ^1H NMR data reveals that the major isomer **a** is very likely to result from a Cram-type addition. The coupling constant of 2-H/3-H and 2-H/1′-H suggests an envelope conformation[21] of the γ-lactone ring, with the bulky 2-substituent in pseudoequatorial position and a twisted anti conformation of this side chain (Figure 2). The phenyl group is located rather close to the 3-CO_2Me substituent and causes a clear upfield shift of these protons to 3.37 ppm. Usually the ester signals in such lactones appear at ~3.7 ppm (e.g. in **39**).

According to this assignment, the other trans isomer **c** must have the inverse relative configuration with respect to C-2 and C-1′ (anti-Cram product). The 5-Hz coupling between 2-H and 1′-H implies a more twisted side chain.

The differences between cis isomers **b** and **d** are less pronounced. Both show large values for the coupling of 2-H and 1′-H, revealing almost perfect anti conformations (fully staggered). The close distance between the ester group and 1′-H is expressed in chemical shifts at relatively low field for the latter proton. On the other hand, isomer **b** shows the methoxy singlet at 3.56 ppm. This small but distinct upfield shift might again reflect the proximity of the phenyl group, whereas in **d** these substituents are remote, resulting in a CO_2Me signal at low field. Therefore

(32) This ratio might be governed by the E/Z configuration of the enolate double bond, which is presently unknown.



a b c d

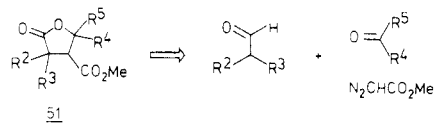
Figure 2. Proposed configurations and conformations of methyl 5-oxotetrahydrofuran-3-carboxylates **40a–d** (characteristic chemical shifts shown in ppm, coupling constants given in hertz as values in parentheses).

we tentatively assign to diastereomer **b** the configuration as illustrated in Figure 2 and assume that **b** is also result of a Cram addition. The remaining minor product **d** should be formed by anti-Cram reaction.

Summing up, a Cram/anti-Cram selectivity of approximately 8:1 has been determined. This is surprisingly high, since 2-phenylpropanal shows selectivities in the range of ~3:1 with other lithium ester enolates.[33] It is perhaps not too speculative to attribute the higher ratio observed in this work to the bulkiness of the ester enolate generated from cyclopropane **1a**.

Conclusions

The results presented in this account illustrate that application of route c (Scheme I) using carbonyl compounds as electrophiles leads to very versatile trifunctional adducts, which are precursors to several classes of furanone derivatives. Therefore one of the goals envisioned in the introductory paragraph—syntheses of functionalized five-membered heterocycles—has been attained with fair success. The most efficient and broad way to use cyclopropanes **1** for this purpose is their three-step conversion to paraconic esters. Analyzing the product **51**, one can state its genesis from two different carbonyl compounds and methyl diazoacetate. Their chemo- and regioselective fusion guarantees high flexibility.



51

Regarding starting cyclopropanes **1**, different substituent patterns are compatible although incomplete adduct formation can be a problem if enolate **6** *and* the electrophile are too hindered (see, e.g., Scheme III or **37** in Table II).[34] Thus the method is nicely supplementary to the Lewis acid promoted C–C bond forming ring opening via route a (Scheme I), which is advantageous in particular for systems with rather bulky substituents. On the other hand, route c described in detail here, gives satisfactory results in most

(33) (a) Heathcock, C. H. *The Aldol Addition Reaction* in *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, p 111. (b) Evans, D. A.; Nelson, J. V.; Taber, T. R. "Stereoselective Aldol Condensations" in *Topics in Stereochemistry*; Allinger, N. L., Eliel, E. L., Wilen, S. H., Eds.; Wiley: New York, 1982; Vol. 13, p 1.

(34) The enolate of methyl 2,3,3-trimethyl-2-(trimethylsiloxy)cyclopropanecarboxylate gave only very low conversions with acetone or benzaldehyde as electrophile. The enolate formation is not the problematic step, since reaction with allyl bromide occurred smoothly to provide the alkylation product **52** in 78% yield.

cases also for highly substituted compounds. Aliphatic, aromatic, and α,β-unsaturated aldehydes or ketones can be employed as electrophiles. One apparent drawback of our method so far is its lack of stereocontrol with regard to cis/trans selectivity. This disadvantage is outweighed, however, by the easy availability of starting materials required and the simplicity of the procedures. The syntheses of different furanone derivatives described here underline again the high versatility of siloxycyclopropanes 1 as precursors to polyfunctional acyclic compounds,[35] carbocycles,[11,36] and heterocyclic systems.[9,17,37]

Experimental Section

IR spectra (wavenumbers given in cm^{-1}) were recorded in CCl_4 on a Perkin-Elmer 157 G or a Beckman Acculab 4. ^1H NMR spectra were obtained in $CDCl_3$ solution (or in C_6H_6 solution if indicated) on a Varian T 60, Varian EM 360, or Bruker WM 400 spectrometer [internal reference $CHCl_3$ = 7.25 ppm]. ^{13}C NMR spectra were recorded on a Bruker WM 400 spectrometer [internal reference $CDCl_3$ = 77.0 ppm]. UV spectra were obtained on a Perkin Elmer 330 spectrophotometer. Mass spectra (MS) were recorded with a Varian MAT CH 7 (70 eV) spectrometer.

Melting points were determined with a Kofler-Heiztischmikroskop apparatus (Fa. Reichert) and were corrected. Boiling points refer to the temperature in a Büchi Kugelrohroven. Radial chromatography was performed with a "Chromatotron" (Harrison Research, Model 7924) using silica gel plates.

All reactions employing *n*-butyllithium (standardized according to ref 38) were performed in dry reaction vessels under a slight pressure of dry nitrogen. Solvents and reagents were added by syringe. Tetrahydrofuran was distilled from potassium/benzophenone immediately before usage. Diisopropylamine and dichloromethane were distilled from calcium hydride and stored over molecular sieves. Cyclopropanes **1a–f** and **8** were synthesized according to published procedures.[7,15] Carbonyl compounds were distilled before usage. All other commercially available materials were applied without further purification.

General Procedure for Hydroxyalkylation of Methyl Cyclopropanecarboxylates. Synthesis of Primary Adducts (Procedure A). Diisopropylamine (1.5 equiv) in tetrahydrofuran (20 mL for 4 mmol of **8** or **1**) were treated at −78 °C with 1.5 equiv of *n*-butyllithium for 20 min. Then 1.0 equiv of the corresponding methyl cyclopropanecarboxylate **8** or **1** was added via syringe and stirred for 2 h at −78 °C. To the resulting enolate solution were added 1.5 equiv of the carbonyl compound (solids dissolved in THF). After being stirred at this temperature for 1.5–2 h, saturated aqueous ammonium chloride solution (20 mL for 4 mmol of **8** or **1**) was added, and the resulting mixture was warmed up to room temperature and extracted thrice with *tert*-butyl methyl ether. The organic phase was dried over magnesium sulfate, filtered, and concentrated. After inspection of the obtained crude product by ^1H NMR spectroscopy the material was either purified by distillation, crystallization, or chromatography or it was subjected to further reactions without purification.

Methyl *cis*-1-(Hydroxydiphenylmethyl)-2-methyl-2-phenylcyclopropanecarboxylate (*cis*-(9)). Cyclopropane **8** (0.760 g, 4.00 mmol) and benzophenone (0.823 g, 4.50 mmol) gave 1.17 g (78%) of *cis*-**9** as colorless crystals (mp 134–135 °C, from pentane/chloroform): ^1H NMR δ 7.85–6.95 (m, 15 H, Ph), 5.7 (br s, 1 H, OH), 2.95 (s, 3 H, CO_2Me), 1.85, 2.73 (AB system, J = 6 Hz, 2 H, CH_2), 1.25 (s, 3 H, Me); IR 3460 (br, OH), 3060–2850 (C–H), 1705 (CO_2Me). Anal. Calcd for $C_{25}H_{24}O_3$: C, 80.63; H, 6.49. Found: C, 80.83; H, 6.56.

Methyl *cis*-1-(1-Hydroxy-1-methylethyl)-3,3-dimethyl-2-(trimethylsiloxy)cyclopropanecarboxylate (10). Cyclopropane **1a** (2.16 g, 10.0 mmol) and acetone (0.85 g, 15.0 mmol) provided 1.76 g (64%) of **10** as colorless crystals (mp 72–75 °C, from petroleum ether; sublimation at 50 °C/20 mm afforded the analytical sample: mp 78–79 °C): ^1H NMR δ 3.66 (s, 3 H, CO_2Me), 3.55 (s, 1 H, 2-H), 1.62 (br s, 1 H, OH), 1.40, 1.35, 1.32, 1.03 (4 s, 3 H each, Me), 0.13 (s, 9 H, $OSiMe_3$); ^1H NMR (C_6H_6) δ 3.81 (s, 1 H, 2-H), 3.34 (s, 3 H, CO_2Me), 1.40 (s, 6 H, Me), 1.28, 1.25 (2 s, 3 H each, Me), 0.30 (s, 9 H, $OSiMe_3$); ^{13}C NMR δ 170.0, 50.7 (s, q, CO_2Me), 71.0 (s, $HOCMe_2$), 59.6 (d, C-2), 44.7 (s, C-1), 30.6, 28.9 (2 q, $HOCMe_2$), 25.1 (s, C-3), 19.7, 19.2 (2 q, 3-Me), −0.3 (q, $OSiMe_3$); IR 3610 (OH), 2980–2940 (C–H), 1735, 1720 (CO_2Me). Anal. Calcd for $C_{13}H_{26}O_4Si$: C, 56.90; H, 9.55. Found: C, 57.12; H, 9.97.

Methyl *cis*-1-(1-Hydroxycyclohexyl)-3,3-dimethyl-2-(trimethylsiloxy)cyclopropanecarboxylate (11). Cyclopropane **1a** (0.864 g, 4.00 mmol) and cyclohexanone (0.589 g, 6.00 mmol) gave 0.382 g (30%) of **11** as colorless crystals (mp 82–83 °C, from petroleum ether): ^1H NMR (C_6H_6) δ 3.88 (s, 1 H, 2-H), 3.34 (s, 3 H, CO_2Me), 2.3–0.9 [m, 11 H, $(CH_2)_5$, OH], 1.46, 1.30 (2 s, 3 H each, Me), 0.32 (s, 9 H, $OSiMe_3$); IR 3610 (OH), 2940–2860 (C–H), 1735, 1715 (CO_2Me). Anal. Calcd for $C_{16}H_{30}O_4Si$: C, 61.12; H, 9.54. Found: C, 61.36; H, 9.86.

Methyl *cis*-1-(1-Hydroxycyclohexyl)-2-(trimethylsiloxy)spiro[2.5]octanecarboxylate (12). Cyclopropane **1b** (0.512 g, 2.00 mmol) and cyclohexanone (0.294 g, 3.00 mmol) provided 0.220 g (31%) of **12** as colorless crystals (mp 100–102 °C, from petroleum ether): ^1H NMR (C_6H_6) δ 3.93 (s, 1 H, 2-H), 3.46 (s, 3 H, CO_2Me), 2.2–0.9 (m, 21 H), 0.32 (s, 9 H, $OSiMe_3$); IR 3620 (OH), 2930, 2860 (C–H), 1740, 1725 (CO_2Me). Anal. Calcd for $C_{19}H_{34}O_4Si$: C, 64.35; H, 9.66. Found: C, 65.47; H, 10.24. Because of unavoidable traces of ring cleavage products in the sample, we did not obtain more satisfactory analyses values.

Methyl *cis*-1-(Hydroxydiphenylmethyl)-2-(trimethylsiloxy)spiro[2.5]octanecarboxylate (13). Cyclopropane **1b** (1.02 g, 4.00 mmol) and benzophenone (1.09 g, 6.00 mmol) provided 0.896 g (51%) of **13** as colorless crystals (mp 138–142 °C, from petroleum ether). The crude product contained 22% of **1b**. **13**: ^1H NMR δ 7.9–7.1 (m, 10 H, Ph), 4.20, 4.02 (2 s, 1 H each, OH, 2-H), 3.34 (s, 3 H, CO_2Me), 1.85–1.2 (m, 10 H), 0.37 (s, 9 H, $OSiMe_3$); IR 3400 (OH), 3060, 3030, 2930, 2850 (C–H), 1755, 1725, 1690 (CO_2Me). Due to the very facile ring opening of **13** we could not obtain satisfactory analyses values.

Methyl *trans*-1-(1-Hydroxy-1-methylethyl)-2-phenyl-2-(trimethylsiloxy)cyclopropanecarboxylate (14). Cyclopropane **1c** (1.05 g, 4.00 mmol) and acetone (0.270 g, 4.80 mmol) provided 1.32 g of crude product **14**: ^1H NMR δ 7.3 (br s, 5 H, Ph), 3.42 (br s, 1 H, OH), 3.12 (s, 3 H, CO_2Me), 2.25, 1.97 (AB system, J = 7 Hz, CH_2), 1.90, 1.41 (2 s, 3 H each, Me), 0.05 (s, 9 H, $OSiMe_3$). Crude aldol adduct **14** was treated with 5 mL of hydrochloric acid (ca. 15% in water) for 16 h at room temperature. After aqueous workup thermolysis at 150 °C and distillation (150 °C/0.02 mm) gave 0.543 g (58%) of **methyl 2-isopropylidene-4-oxo-4-phenylbutanoate (15).** Crystallization from *tert*-butyl methyl ether/petroleum ether afforded 0.273 g of colorless crystals (mp 85–88 °C; sublimation at 70 °C/0.01 mm provided the sample for analysis, mp 92–93 °C): ^1H NMR δ 8.1 (m, 5 H, Ph), 4.11 (s, 2 H, CH_2), 3.69 (s, 3 H, CO_2Me), 2.26, 1.88 (2 s, 3 H each, Me); ^{13}C NMR δ 196.6 (s, C-4), 167.8, 50.8 (s, q, CO_2Me), 149.3 (s, CMe_2), 132.6 (s, C-2), 136.4, 128.2, 127.7, 120.3 (s, 3 d, Ph), 39.3 (t, C-3), 23.0, 22.9 (2 q, Me); IR 3070–2840 (C–H), 1730 (CO_2Me), 1705 (CO), 1645 (C=C). Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.38; H, 6.94. Found: C, 72.71; H, 6.87.

Methyl 2,2-Dimethyl-5-phenyl-2,3-dihydrofuran-3-carboxylate (17). Crude primary adduct **14** (4.00 mmol) was treated with 5 mL of HCl in methanol. Aqueous workup with $NaHCO_3$ provided 0.700 g (66%) of crude **16**: ^1H NMR δ 8.1–7.2 (m, 5 H, Ph), 3.70 (s, 3 H, CO_2Me), 3.05 (s, 3 H, OMe), 3.5–2.4 (m, 3 H), 1.67, 1.29 (2 s, 3 H each, Me). Distillation at 150 °C/0.01 mm gave 0.446 g (48%) of **17** as a pale yellow liquid: ^1H NMR δ 8.2–7.2 (m, 5 H, Ph), 5.29 (d, J = 3 Hz, 1 H, 4-H), 3.73 (br s, 4 H, CO_2Me, 3-H), 1.63, 1.40 (2 s, 3 H each, Me), purity ca. 90%. Attempts to purify the sensitive enol ether were not successful.

(35) Grimm, E. L.; Zschiesche, R.; Reissig, H.-U. *J. Org. Chem.* **1985**, *50*, 5543.

(36) (a) Zschiesche, R.; Grimm, E. L.; Reissig, H.-U. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1086. (b) Zschiesche, R.; Reissig, H.-U. *Liebigs Ann. Chem.* **1987**, 387.

(37) (a) Pyridazinone derivatives: Reichelt, I.; Reissig, H.-U. *Synthesis* **1984**, 786. (b) γ-Lactones: Grimm, E. L.; Reissig, H.-U. *J. Org. Chem.* **1985**, *50*, 242. (c) Thiophene derivatives: Brückner, C., Reissig, H.-U. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 588. Brückner, C.; Reissig, H.-U. *Liebigs Ann. Chem.*, in press. (d) Pyrrole derivatives: Brückner, C.; Suchland, B.; Reissig, H.-U. *Liebigs Ann. Chem.*, in press. (e) Pyrroline *N*-oxides: Zschiesche, R.; Reissig, H.-U. *Tetrahedron Lett.*, in press.

(38) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.

3-Isopropylidene-5-phenyl-2(3*H*)-furanone (18). Crude primary adduct **14** (4.00 mmol) was treated with 10 mL of 2 N HCl. After extractive workup and concentration, the resulting mixture was dissolved in 20 mL of benzene. Addition of a small amount of toluenesulfonic acid, reflux at a water separator for 4 h, and distillation at 160 °C/0.02 mm provided 0.372 g (46%) of **18**. Crystallization from diethyl ether gave yellow crystals (mp 104–108 °C, mp 108–109 °C[39]): ^{1}H NMR δ 8.1–7.2 (m, 5 H, Ph), 6.45 (s, 1 H, 4-H), 2.45, 2.16 (2 s, 3 H each, Me); IR 2920, 2850 (C–H), 1780 (CO), 1640 (C=C); UV (MeOH) λ_{max} (log ϵ) 335 (3.94), 225 nm (3.95).

Methyl 2-(Diphenylmethylene)-5,5-dimethyl-4-oxohexanoate (19) and 5-*tert*-Butyl-3-(diphenylmethylene)-2(3*H*)-furanone (20). Cyclopropane **1b** (0.488 g, 2.00 mmol) and benzophenone (0.412 g, 2.25 mmol) afforded after 16 h at −78 °C a ca. 1:1 mixture of starting material **1d** and **19**[10b] (^{1}H NMR analysis). In a second run the reaction mixture was allowed to warm up to room temperature before the aqueous quenching procedure. Now 0.157 g (10%) of **20** was isolated as yellow crystals (mp 165–167 °C, from diethyl ether/petroleum ether; mp 172–175 °C[10b]).

Methyl *trans*-2-*tert*-Butyl-1-(hydroxyphenylmethyl)-2-(trimethylsiloxy)cyclopropanecarboxylate (21). Cyclopropane **1d** (0.976 g, 4.00 mmol) and benzaldehyde (0.477 g, 4.50 mmol) gave 0.308 g (22%) of **21** as colorless crystals (mp 91–93 °C, from petroleum ether; the sampe for analysis was sublimed at 80 °C/0.01 mm, mp 96–98 °C): ^{1}H NMR δ 7.2 (m, 5 H, Ph), 4.75 (d, J = 4.5 Hz, 1 H, 1-CH), 3.65 (d, J = 4.5 Hz, 1 H, OH), 3.35 (s, 3 H, CO_2Me), 1.68, 1.23 (AB system, J = 7.5 Hz, 2 H, 3-H), 0.91 (s, 9 H, *t*-Bu), 0.22 (s, 9 H, $OSiMe_3$); IR 3570, 3510 (OH), 3050, 3010, 2950–2860 (C–H), 1730, 1705 (CO_2Me). Anal. Calcd for $C_{19}H_{30}O_4Si$: C, 65.10; H, 8.62. Found: C, 65.80; H, 8.82.

Methyl (*E*/*Z*)-2-Ethylidene-5,5-dimethyl-4-oxohexanoate (22). Cyclopropane **1d** (0.976 g, 4.00 mmol) and acetaldehyde (0.264 g, 6.00 mmol) afforded 1.20 g of crude product, which was dissolved in 20 mL of benzene. Addition of a trace of toluenesulfonic acid, reflux for 16 h on a water separator, concentration, and distillation (100 °C/0.02 mm) gave 0.656 g (83%) of **22** as a 3:1 *E*/*Z* mixture: ^{1}H NMR δ 7.04, 6.02 (2 q, J = 7.5 Hz both, 0.75 H and 0.25 H, =CH), 3.65 (s, 3 H, CO_2Me), 3.52 (br s, 2 H, 3-H), 2.05, 1.71 (2 d, J = 7.5 Hz both, 0.75 H and 2.25 H, Me), 1.17 (s, 9 H, *t*-Bu); IR 2950–2850 (C–H), 1760 (CO_2Me), 1710 (CO), 1670 (C=C). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 65.72; H, 9.39.

General Procedure for Ring Opening of Cyclopropanes. Synthesis of γ-Lactols (Procedure B). The corresponding cyclopropane was dissolved in tetrahydrofuran or dichloromethane (ca. 15 mL for 4 mmol) and stirred with 2 equiv of $NEt_3 \cdot 3HF$[40] (1 h at room temperature) or with 1.2 equiv of tetra-*n*-butylammonium fluoride·$3H_2O$ (TBAF) (1 h at 0 °C, 1.5 h at room temperature). Addition of petroleum ether/water, extractive workup with THF or dichloromethane, drying over $MgSO_4$, and concentration afforded the crude material which was either purified or subjected to further reactions as indicated in the specific experiments.

Methyl 5-Hydroxy-2,2,4,4-tetramethyltetrahydrofuran-3-carboxylate (23). According to procedure B primary adduct **10** (0.274 g, 1.00 mmol) was treated with TBAF. Distillation of the crude product at 100 °C/0.02 mm, crystallization from petroleum ether, and sublimation at 40 °C/0.02 mm provided 0.096 g (48%) of **23** as colorless crystals (mp 50–52 °C): ^{1}H NMR (C_6H_6) δ 4.96 (s, 1 H, 5-H), 3.70 (s, 1 H, OH), 3.40 (s, 3 H, CO_2Me), 3.25 (s, 1 H, 3-H), 1.68, 1.50, 1.42, 1.34 (4 s, 3 H each, Me); IR 3605, 3400 (OH), 2980–2830 (C–H), 1745 (CO_2Me). Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.37; H, 8.96. Found: C, 59.83; H, 9.27.

Execution of procedures A and B, starting from **1a** and acetone, gave **23** in a 90% overall yield (colorless liquid, >95% pure according to ^{1}H NMR spectroscopy).

Methyl 2-Hydroxy-3,3-dimethyl-1-oxaspiro[5.4]decane-4-carboxylate (24). Following procedure A, cyclopropane **1a** (0.432 g, 2.00 mmol) and cyclohexanone (0.294 g, 3.00 mmol) provided a crude product which was treated with TBAF (procedure B). Filtration of a solution of the resulting product through a short pad of Al_2O_3 and recrystallization from *tert*-butyl methyl ether/petroleum ether gave 0.227 g (50%) of **24** as colorless crystals (mp 76–78 °C). ^{1}H NMR spectroscopy revealed that **24** was a 1:1 mixture of cis/trans isomers: ^{1}H NMR δ 4.91 (s, 1 H, 2-H), 4.81 (s, 1 H, OH), 3.79, 3.63 (2 s, 1.5 H each, CO_2Me), 2.86, 2.64 (2 s, 0.5 H each, 4-H), 1.9–1.2 (m, 10 H), 1.20, 1.07 (2 s, 3 H each, Me); IR 3630, 3450 (OH), 2950, 2860 (C–H), 1745, 1720 (CO_2Me). Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.61; H, 9.48.

Methyl 5-Hydroxy-4,4-dimethyl-2,2-diphenyltetrahydrofuran-3-carboxylate (25). Following procedures A and B (NEt_3·HF), cyclopropane **1a** (2.16 g, 10.0 mmol) and benzophenone (2.05 g, 11.0 mmol) gave a crude product which afforded after recrystallization from chloroform/petroleum ether 1.51 g (46%) of **25** as colorless crystals (mp 123–127 °C; the analytical sample was recrystallized again: mp 133–135 °C): ^{1}H NMR δ 7.8–7.0 (m, 10 H, Ph), 5.20 (s, 1 H, 5-H), 5.0 (br s, 1 H, OH), 4.01 (s, 1 H, 3-H), 3.45 (s, 3 H, CO_2Me), 1.32, 1.05 (2 s, 3 H each, Me); IR 3400 (OH), 3050–3005, 2960–2840 (C–H), 1720 (CO_2Me). Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.59; H, 6.79. Found: C, 73.79; H, 6.67.

***cis*-Methyl 5-Hydroxy-4,4-dimethyl-2-phenyltetrahydrofuran-3-carboxylate (26).** Cyclopropane **1a** (0.864 g, 4.00 mmol) and benzaldehyde (0.477 g, 4.50 mmol) were subjected to procedure A; however, the mixture was directly quenched with 5 mL of hydrochloric acid (ca. 15% in water, 16 h, room temperature). Extractive workup, distillation (150 °C/0.01 mm), and crystallization from chloroform/*tert*-butyl methyl ether/petroleum ether provided 0.211 g (21%) of **26** as colorless crystals (mp 95–96 °C): ^{1}H NMR δ 7.6–7.2 (m, 5 H, Ph), 5.75 (d, J = 13.5 Hz, 1 H, OH), 5.59 (d, J = 6 Hz, 1 H, 2-H), 5.05 (d, J = 13.5 Hz, 1 H, 5-H), 3.20 (s, 3 H, CO_2Me), 3.12 (d, J = 6 Hz, 1 H, 3-H), 1.33, 1.16 (2 s, 3 H each, Me); IR 3400 (OH), 3010, 2900–2840 (C–H), 1740 (CO_2Me). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.24. Found: C, 67.09; H, 7.23.

Methyl 5-Hydroxy-4,4-dimethyl-2-(1-phenylethyl)tetrahydrofuran-3-carboxylate (27). Following procedures A and B (TBAF), cyclopropane **1a** (0.864 g, 4.00 mmol) and 2-phenylpropanal (0.817 g, 6.00 mmol) gave 1.27 g of semicrystalline product. Crystallization from *tert*-butyl methyl ether/petroleum ether provided 0.321 g (29%) of **27** (mp 107–115 °C), which was a 1:2 mixture of diastereomers according to ^{1}H NMR spectroscopy: ^{1}H NMR δ 7.22 (s, 5 H, Ph), 4.95 (s, 1 H, 5-H), 4.53 (t, J = 10 Hz, 1 H, 2-H), 3.40, 3.29 (2 s, 1 H and 2 H, CO_2Me), 3.10 (mc, 2 H, OH and C*H*MePh), 2.83 (d, J = 10 Hz, 1 H, 3-H), 1.42 (d, J = 7.5 Hz, 3 H, CH*Me*Ph), 1.12, 0.93 (2 s, 3 H each, Me); IR 3620, 3450 (OH), 3090, 3070, 3030, 2970–2850 (C–H), 1740, 1715 (CO_2Me). Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.05; H, 7.97. Found: C, 69.22; H, 8.38.

Kugelrohr distillation of the mother liquid gave an additional 0.443 g (40%) of **27** as mixture of diastereomers.

Methyl 15-Hydroxy-14-oxadispiro[5.1.5.2]pentadecane-7-carboxylate (28). Primary adduct **12** (86 mg, 0.24 mmol) was treated with TBAF (procedure B), giving after sublimation (120 °C/0.02 mm) 42 mg (62%) of **28** as a crystalline solid (mp 83–90 °C). ^{1}H NMR spectroscopy reveals a cis:trans ratio of 4:6: ^{1}H NMR δ 5.35 (s, 1 H, 15-H), 4.98 (br s, 1 H, OH), 3.69, 3.64 (2 s, 1.2 and 1.8 H, CO_2Me), 2.79 (s, 1 H, 7-H), 2.0–1.0 (m, 20 H); IR 3610 (OH), 2930, 2850 (C–H), 1745 (CO_2Me). Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.05; H, 9.28. Found: C, 68.29; H, 9.48.

Methyl 1-Hydroxy-3,3-diphenyl-2-oxaspiro[5.4]decane-4-carboxylate (29). Following procedures A and B (NEt_3·3HF), cyclopropane **1b** (1.02 g, 4.00 mmol) and benzophenone (1.09 g, 6.00 mmol) provided 1.46 g of semicrystalline material. Recrystallization from *tert*-butyl methyl ether/petroleum ether gave 0.74 (26%) of **29** as colorless crystals (mp 139–143 °C): ^{1}H NMR δ 7.8–7.2 (m, 10 H, Ph), 5.4 (br s, 1 H, OH), 5.35 (s, 1 H, 1-H), 4.28 (s, 1 H, 4-H), 3.49 (s, 3 H, CO_2Me), 1.9–1.2 (m, 10 H); IR 3420 (OH), 3070–3030, 2940–2860 (C–H), 1725 (CO_2Me). Anal. Calcd for $C_{23}H_{26}O_4$: C, 75.38; H, 7.15. Found: C, 75.59; H, 7.25.

Methyl 2-(1-Hydroxy-1-methylethyl)-4-oxo-4-phenylbutanoate (30). Following procedures A and B (TBAF), cyclopropane **1c** (1.06 g, 4.00 mmol) and acetone (0.346 g, 6.00 mmol) gave 1.10 g (85%) of **30**, which was >90% pure according to ^{1}H NMR spectroscopy: ^{1}H NMR δ 8.2–7.2 (m, 5 H, Ph), 3.73 (s, 3

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(40) (a) Hünig, S.; Wehner, G. *Synthesis* **1975**, 180. (b) Franz, R. *J. Fluorine Chem.* **1980**, *15*, 423.

H, CO_2Me), 3.7–2.5 (m, 4 H, OH, 4-H, 3-H), 1.35 (s, 6 H, Me). Attempts to purify **30** by distillation or chromatography failed.

Methyl 2-(Hydroxydiphenylmethyl)-4-oxo-4-phenylbutanoate (31). According to procedures A and B (NEt_3·3HF), cyclopropane **1c** (1.06 g, 4.00 mmol) and benzophenone (0.873 g, 4.80 mmol) gave after recrystallization from chloroform/petroleum ether 0.478 g (32%) of **31** as colorless crystals (mp 148–150 °C, mp 150–151 °C[10b]).

Oxidation with Pyridinium Chlorochromate. Synthesis of Paraconic Esters (Procedure C). Pyridinium chlorochromate (PCC) (2–3 equiv) was suspended in dichloromethane (ca. 20 mL for 8 mmol) and after addition of the corresponding γ-lactol the resulting mixture was stirred for several days (the reaction times are given in the individual experiments). Dilution with *tert*-butyl methyl ether and filtration through a pad of Florisil or Al_2O_3 (occasionally this operation had to be repeated) gave the crude product, which was purified by distillation, crystallization, or chromatography.

Methyl 4,4-Dimethyl-2,2-diphenyl-5-oxotetrahydrofuran-3-carboxylate (32). γ-Lactol **25** (0.326 g, 1.00 mmol) and PCC (0.323 g, 1.50 mmol) were stirred for 90 h (procedure C). Recrystallization from chloroform/*tert*-butyl methyl ether/petroleum ether gave 0.126 g (67%) of **32** (mp 138 °C, mp 138 °C[41]): ^1H NMR δ 7.8–7.1 (m, 10 H, Ph), 4.09 (s, 1 H, 3-H), 3.22 (s, 3 H, CO_2Me), 1.28, 0.98 (2 s, 3 H each, Me); IR 3040–3000, 2920–2840 (C–H), 1790 (C=O), 1740 (CO_2Me).

Starting with cyclopropane **1a** (0.864 g, 4.00 mmol) and benzophenone (1.10 g, 6.00 mmol) and following procedures A, B (NEt_3·3HF), and C (12.0 mmol of PCC, 90 h), one isolated after recrystallization (chloroform/petroleum ether) 0.895 g (70%) of **32** (mp 135–138 °C).

Methyl 2,2,4,4-Tetramethyl-5-oxotetrahydrofuran-3-carboxylate (33). Applying procedures A, B (TBAF), and C (4.00 mmol of PCC, 4 days), cyclopropane **1a** (0.432 g, 2.00 mmol) and acetone (0.170 g, 3.00 mmol) gave after distillation (90 °C/0.02 mm) 0.266 g (67%) of **33** as a colorless liquid: ^1H NMR δ 3.70 (s, 3 H, CO_2Me), 2.93 (s, 1 H, 3-H), 1.52, 1.50, 1.38, 1.33 (4 s, 3 H each, Me); IR 2970–2830 (C–H), 1780 (C=O), 1750 (CO_2Me). Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.96; H, 8.05. Found: C, 60.19; H, 8.43.

Methyl 3,3-Dimethyl-2-oxo-1-oxaspiro[5.4]decane-4-carboxylate (34). Following procedures A, B (TBAF), and C (4.00 mmol of PCC, 6 days), cyclopropane **1a** (0.432 g, 2.00 mmol) and cyclohexanone (0.294 g, 3.00 mmol) provided after distillation and recrystallization (petroleum ether) 0.259 g (54%) of **34** as colorless crystals (mp 58–60 °C): ^1H NMR δ 3.65 (s, 3 H, CO_2Me), 2.78 (s, 1 H, 4-H), 1.9–1.4 (m, 10 H), 1.27 (s, 6 H, Me); IR 2950, 2860 (C–H), 1780 (C=O), 1740 (CO_2Me). Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.97; H, 8.39. Found: C, 65.30; H, 8.66.

Methyl 3,3-Dimethyl-1-oxo-2-oxaspiro[5.4]decane-4-carboxylate (35). Applying procedures A, B (TBAF), and C (8.00 mmol of PCC, 6 days), cyclopropane **1b** (1.02 g, 4.00 mmol) and acetone (0.348 g, 6.00 mmol) afforded after distillation 0.417 g (43%) of **35**, which slowly crystallized (mp 57–60 °C): ^1H NMR δ 3.73 (s, 3 H, CO_2Me), 3.01 (s, 1 H, 3-H), 2.2–1.6 (m, 10 H), 1.52, 1.49 (2 s, 3 H each, Me); IR 2970–2850 (C–H), 1770 (C=O), 1745 (CO_2Me). Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.97; H, 8.38. Found: C, 65.17; H, 8.67.

Methyl 15-Oxo-14-oxadispiro[5.1.5.2]pentadecane-7-carboxylate (36). Applying procedures A, B (TBAF), and C (8.00 mmol of PCC, 1 day), cyclopropane **1b** (1.02 g, 4.00 mmol) and cyclohexanone (0.589 g, 6.00 mmol) gave after distillation and recrystallization (*tert*-butyl methyl ether/petroleum ether) 0.509 g (51%) of **36** as colorless crystals (mp 88–90 °C): ^1H NMR δ 3.75 (s, 3 H, CO_2Me), 2.93 (s, 1 H, 7-H), 2.2–0.8 (m, 20 H); IR 2940, 2860 (C–H), 1770 (C=O), 1750 (CO_2Me). Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.53; H, 8.62. Found: C, 68.43; H, 8.97.

Methyl 1-Oxo-3,3-diphenyl-2-oxaspiro[5.4]decane-4-carboxylate (37). Following procedure A, cyclopropane **1b** (0.512 g, 2.00 mmol) benzophenone (0.549 g, 3.00 mmol) gave 0.964 g of crude product containing ca. 27% of **1b**. This mixture was subjected to procedures B (NEt_3·3HF) and C (4.00 mmol of PCC, 4 days), affording 0.194 g (27%) of **37** as colorless crystals (mp 165–167 °C). With respect to consumed **1b**, the yield was 36%. **37**: ^1H NMR δ 7.9–7.1 (m, 10 H, Ph), 4.33 (s, 1 H, 4-H), 3.20 (s, 3 H, CO_2Me), 1.9–1.1 (m, 10 H); IR 3060–3020, 2940–2860 (C–H), 1790 (C=O), 1745 (CO_2Me). Anal. Calcd for $C_{23}H_{24}O_4$: C, 75.81; H, 6.64. Found: C, 76.19; H, 6.82.

Methyl 4,4-Dimethyl-5-oxo-2-phenyltetrahydrofuran-3-carboxylate (38). Following procedures A, B (NEt_3·3HF), and C (20.0 mmol of PCC, 2 days), cyclopropane **1b** (2.16 g, 10.0 mmol) and benzaldehyde (1.59 g, 15.0 mmol) gave after distillation (150 °C/0.02 mm) 1.41 g (57%) of **38**. This cis/trans mixture (2:3) was separated by means of flash chromatography (Al_2O_3, cyclohexane/ethyl acetate 10:1) to provide pure *cis*-**38** (mp 111–113 °C) and *trans*-**38** (mp 77–78 °C).

***cis*-38**: ^1H NMR δ 7.36 (s, 5 H, Ph), 5.78 (d, J = 6 Hz, 1 H, 2-H), 3.38 (d, J = 6 Hz, 1 H, 3-H), 3.26 (s, 3 H, CO_2Me), 1.48, 1.30 (2 s, 3 H each, Me); IR 3060–3020, 2970–2840 (C–H), 1800 (C=O), 1750 (CO_2Me).

***trans*-38**: ^1H NMR δ 7.39 (s, 5 H, Ph), 5.70 (d, J = 10 Hz, 1 H, 2-H), 3.71 (s, 3 H, CO_2Me), 3.06 (d, J = 10 Hz, 1 H, 3-H), 1.43, 1.21 (2 s, 3 H each, Me); IR 3060–3030, 2970–2840 (C–H), 1790 (C=O), 1745 (CO_2Me).

Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.72; H, 6.49. Found for *cis*-**38**: C, 67.67; H, 6.53. Found for *trans*-**38**: C, 67.63; H, 6.53.

Methyl 2,4,4-Trimethyl-5-oxotetrahydrofuran-3-carboxylate (39). According to procedures A, B (TBAF), and C (8.00 mmol of PCC, 3 days), cyclopropane **1a** (0.864 g, 4.00 mmol) and acetaldehyde (0.246 g, 6.00 mmol) afforded after distillation (100 °C/0.02 mm) 0.384 g (52%) of **39**. Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.57. Found: C, 58.40; H, 7.88. This mixture of cis/trans isomers (1:2) could be separated through column chromatography (cyclohexane/ethyl acetate 10:1).

***cis*-39**: ^1H NMR δ 4.74 (quint, J = 6 Hz, 1 H, 2-H), 3.71 (s, 3 H, CO_2Me), 2.99 (d, J = 6 Hz, 1 H, 3-H), 1.42 (d, J = 6 Hz, 3 H, Me), 1.36, 1.24 (2 s, 3 H each, Me); IR 2990–2850 (C–H), 1780 (C=O), 1745 (CO_2Me).

***trans*-39**: ^1H NMR δ 4.69 (qd, J = 6 Hz, J = 10 Hz, 1 H, 2-H), 3.72 (s, 3 H, CO_2Me), 2.67 (d, J = 10 Hz, 1 H, 3-H), 1.39 (d, J = 6 Hz, 3 H, Me), 1.34, 1.09 (2 s, 3 H each, Me); IR 2970–2840 (C–H), 1770 (C=O), 1740 (CO_2Me).

Methyl 2-(1-Phenylethyl)-4,4-dimethyl-5-oxotetrahydrofuran-3-carboxylate (40). Cyclopropane **1a** (0.864 g, 4.00 mmol) and 2-phenylpropanal (0.817 g, 6.00 mmol) were subjected to procedures A, B (TBAF), and C (8.00 mmol of PCC, 6 days) and afforded 0.808 g of semicrystalline crude material. Kugelrohr distillation (160 °C/0.02 mm) provided 0.587 g (52%) of **40** as a mixture of four diastereomers **a**, **b**, **c**, and **d** (ratio according to ^1H NMR spectroscopy: 18:5:2:1). The major isomer **a** could be enriched to ca. 90% purity by recrystallization from *tert*-butyl methyl ether/petroleum ether (0.367 g, 33%, mp 96–99 °C). For ^1H NMR data, see Table III. **40a**: ^{13}C NMR δ 179.1 (s, C=O), 169.3, 51.6 (s, q, CO_2Me), 140.4, 128.4, 128.3, 127.2 (s, 3 d, Ph), 81.7 (d, C-2), 55.8 (d, C-3), 44.9 (d, CHMePh), 43.6 (s, C-4), 24.6, 21.1, 17.2 (3 q, Me); IR 3090–3030, 2980–2850 (C–H), 1785 (C=O), 1745 (CO_2Me). Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.29. Found: C, 69.34; H, 7.55.

Methyl 4,4-Dimethyl-5-oxo-2-(1-propenyl)tetrahydrofuran-3-carboxylate (41). Applying procedures A, B (TBAF), and C (8.00 mmol of PCC, 4 days), cyclopropane **1a** (0.864 g, 4.00 mmol) and crotonaldehyde gave after distillation (90 °C/0.02 mm) 0.319 g (38%) of **41** as a 1:3 mixture of cis/trans isomers.

***cis*-41**: ^1H NMR δ 5.98 (dq, J = 6.3 Hz, J = 15 Hz, 1 H, =C*H*Me), 5.46 (dd, J = 7 Hz, J = 15 Hz, 1 H, —C*H*=), 3.68 (s, 3 H, CO_2Me), 30.8 (d, J = 6 Hz, 1 H, 3-H), 1.74 (d, J = 6.3 Hz, 3 H, Me), 1.35, 1.22 (2 s, 3 H each, Me); signal for 2-H hidden by other signals.

***trans*-41**: ^1H NMR δ 5.98 (dq, J = 6.3 Hz, J = 15 Hz, 1 H, =C*H*Me), 5.46 (dd, J = 7 Hz, J = 15 Hz, 1 H, —C*H*=), 5.06 (dd, J = 7 Hz, J = 10 Hz, 1 H, 2-H), 3.75 (s, 3 H, CO_2Me), 2.87 (d, J = 10 Hz, 1 H, 3-H), 1.74 (d, J = 6.3 Hz, 3 H, Me), 1.35, 1.12 (2 s, 3 H each, Me).

IR: 3040, 2980–2860 (C–H), 1790 (C=O), 1745 (CO_2Me). Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.79; H, 7.71.

Methyl 3-Methyl-1-oxo-2-oxaspiro[5.4]decane-4-carboxylate (42). Cyclopropane **1b** (1.02 g, 4.00 mmol) and acetaldehyde (0.264 g, 6.00 mmol) were subjected to procedures A, B (TBAF), and C (8.00 mmol of PCC, 3 days), and afforded

(41) Bourelle-Warnier, F.; Gastambide, B. *C.R. Acad. Sci., Ser. C* **1968**, *266*, 1384.

Table III. ^{1}H NMR Spectral Data of Paraconic Esters 40a–d[a,b]

proton	40a		40b		40c		40d	
	δ	J	δ	J	δ	J	δ	J
Ph mc	7.25		7.25		7.25		7.25	
2-H dd	4.76	9.8	4.68	5.0	4.88	10.0	4.57	5.0
		7.6		10.0		5.0		10.8
CO_2Me s	3.37		3.56		3.71		3.79	
1′-H dq	2.88	7.6	3.24	10.0	3.01	5.0	3.14	10.8
		6.9		6.5		7.3		7.3
3-H d	2.82	9.8	2.61	5.0	2.68	10.0	2.61	5.0
1′-Me d	1.45	6.9	1.46	6.5	1.41	7.3	1.38	7.3
4-Me 2 s	1.29		1.33		1.17		1.36	
	1.08		1.13		1.11		1.24	

[a] Determined in $CDCl_3$ at 400 MHz, δ in ppm, J in hertz. [b] **40a:40b:40c:40d** = 18:5:2:1.

after distillation (100 °C/0.02 mm) 0.459 g (51%) of **42**. The 1:1 cis/trans mixture could be separated by means of flash chromatography (Al_2O_3, cyclohexane/ethyl acetate 10:1) into *cis*-**42** (mp 67–70 °C) and *trans*-**42** (mp 80–81 °C).

***cis*-42**: ^{1}H NMR δ 4.72 (quint, J = 6 Hz, 1 H, 2-H), 3.72 (s, 3 H, CO_2Me), 3.20 (d, J = 6 Hz, 1 H, 3-H), 2.0–1.0 (m, 10 H), 1.40 (d, J = 6 Hz, 3 H, Me); IR 2990–2860 (C–H), 1785 (C=O), 1745 (CO_2Me).

***trans*-42**: ^{1}H NMR δ 4.78 (qd, J = 6 Hz, J = 10 Hz, 1 H, 2-H), 3.76 (s, 3 H, CO_2Me), 2.66 (d, J = 10 Hz, 1 H, 3-H), 2.0–1.0 (m, 10 H), 1.40 (d, J = 6 Hz, 3 H, Me); IR 2990–2860 (C–H), 1785 (C=O), 1745 (CO_2Me).

Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.69; H, 8.02. Found for *cis*-**42**: C, 63.86; H, 8.26. Found for *trans*-**42**: C, 64.01; H, 8.28.

Methyl 3-Hydroxy-4,4-dimethyl-5-oxo-2,2-diphenyltetrahydrofuran-3-carboxylate (43). Following procedure A, cyclopropane **1a** (0.864 g, 4.00 mmol) and benzophenone (0.824 g, 4.50 mmol) gave 0.977 g of crude product which contained ca. 15% unchanged **1a**. Oxidation (procedure C, 12.0 mmol of PCC, 2 days) provided a 3:2 mixture of **32** and **43** that was separated by means of column chromatography (Al_2O_3, cyclohexane/ethyl acetate 12:1). The fraction containing **43** was recrystallized from chloroform/petroleum ether to give 0.197 g (15%) of **43** as colorless crystals (mp 186–191 °C): ^{1}H NMR δ 8.0–7.1 (m, 10 H, Ph), 4.40 (s, 1 H, OH), 3.29 (s, 3 H, CO_2Me), 1.09, 0.93 (2 s, 3 H each, Me); ^{13}C NMR δ 177.6, 174.0 (2 s, C=O), 143.1, 141.4, 128.3, 128.1, 127.5, 127.2, 126.3, 123.6 (2 s, 6 d, Ph), 87.5, 86.1 (2 s, C-2, C-3), 52.8 (q, OMe), 46.2 (s, C-4), 21.6, 20.4 (2 s, Me); IR 3480 (OH), 3060, 2980–2850 (C–H), 1795 (C=O), 1730 (CO_2Me); MS, m/z (rel intensity) 341 (0.1, M + H^+), 183 (100). Anal. Calcd for $C_{20}H_{20}O_5$: C, 70.56; H, 5.92. Found: C, 70.33; H, 5.95.

Methyl 3-Hydroxy-2,2,4,4-tetramethyl-5-oxotetrahydrofuran-3-carboxylate (44). Analogously to the synthesis of **43**, cyclopropane **1a** (0.864 g, 4.00 mmol) and acetone (0.261 g, 4.50 mmol) gave a 1:2 mixture of **33** and **44**. Chromatography (cyclohexane/ethyl acetate 12:1) and recrystallization from *tert*-butyl methyl ether/petroleum ether provided 0.146 g (18%) of **44** as colorless crystals (mp 85–86 °C): ^{1}H NMR δ 3.89 (s, 3 H, CO_2Me), 3.78 (s, 1 H, OH), 1.55, 1.41, 1.37, 1.16 (4 s, 3 H each, Me); IR 3500 (OH), 3000–2860 (C–H), 1785 (C=O), 1730 (CO_2Me). Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.55; H, 7.45. Found: C, 55.52; H, 7.46.

5-Methoxy-4,4-dimethyl-3-isopropylidene-4,5-dihydro-2-(3*H*)-furanone (46). Cyclopropane **45** (0.165 g, 0.52 mmol) was treated in 5 mL of dichloromethane with one drop of trimethylsilyl triflate (ca. 0.03 mmol) and stirred at room temperature for 1 h. After addition of triethylamine (50 mg, 0.50 mmol), filtration through a short pad of Al_2O_3, and distillation (100 °C/0.02 mm), 81 mg (84%) of **46** was obtained as a colorless liquid: ^{1}H NMR δ 4.62 (s, 1 H, 5-H), 3.38 (s, 3 H, OMe), 2.15, 1.87 (2 s, 3 H each, $=CMe_2$), 1.18, 1.13 (2 s, 3 H each, Me); IR 3000–2840 (C–H), 1760 (C=O), 1655 (C=C). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.20; H, 8.75. Found: C, 64.80; H, 8.93.

Starting with cyclopropane **1a** (0.864 g, 4.00 mmol) and acetone (0.346 g, 6.00 mmol), there was obtained after application of procedure A and subsequent treatment with $Me_3SiOSO_2CF_3$ (0.129 g, 0.58 mmol, 4 days at room temperature) and Kugelrohr distillation (80 °C/0.02 mm) 153 mg (21%) of **46**.

Methyl 2-Cyclohexylidene-3,3-dimethyl-4-oxobutanoate (47). Following procedure A, cyclopropane **1a** (0.864 g, 4.00 mmol) and cyclohexanone (0.588 g, 6.00 mmol) gave 1.49 g of crude product which was dissolved in 5 mL of dichloromethane and stirred with $Me_3SiOSO_2CF_3$ (60 mg, 0.25 mmol) for 90 min. Addition of triethylamine (0.10 mL), filtration (Al_2O_3), and distillation (120 °C/0.02 mm) afforded 0.637 g (71%) of **47** as a colorless liquid: ^{1}H NMR δ 9.50 (s, 1 H, 4-H), 3.68 (s, 3 H, CO_2Me), 2.2–1.7, 1.7–1.2 (2 m, 4 H and 6 H), 1.16 (s, 6 H, Me); IR 2980–2860, 2800, 2710 (C–H), 1725 (C=O, CO_2Me), 1640 (C=C). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.98. Found: C, 69.96; H, 9.42.

3-Cyclohexylidene-5-methoxy-4,4-dimethyl-4,5-dihydro-2-(3*H*)-furanone (48). Aldehyde **47** (0.135 g, 0.60 mmol) was dissolved in 2 mL of dichloromethane and treated with 10 drops of trifluoroacetic acid for 24 h. Filtration (Al_2O_3) and distillation (110 °C/0.02 mm) gave 0.112 g (83%) of **48** as a colorless liquid: ^{1}H NMR δ 4.69 (s, 1 H, 5-H), 3.44 (s, 3 H, OMe), 3.1–2.8, 2.5–2.2, 1.8–1.5 (3 m, 2 H, 2 H, and 6 H); IR 2970–2850 (C–H), 1755 (C=O), 1640 (C=C). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.98. Found: C, 70.05; H, 9.35.

4-Cyclohexylidene-1-methoxy-2-oxaspiro[5.4]decan-3-one (49). According to procedure A, cyclopropane **1b** (1.02 g, 4.00 mmol) and cyclohexanone (0.588 g, 6.00 mmol) gave 1.46 g of crude product. This was dissolved in 5 mL of dichloromethane and stirred for 1 h with $Me_3SiOSO_2CF_3$ (0.120 g, 0.54 mmol). Addition of triethylamine (0.100 g), filtration (Al_2O_3), and radial chromatography (cyclohexane/ethyl acetate 10:1) provided 0.373 g (36%) of **49** as colorless crystals (mp 74–75 °C): ^{1}H NMR δ 5.01 (s, 1 H, 1-H), 3.49 (s, 3 H, OMe), 3.2–2.8, 2.6–2.4, 2.2–1.3 (3 m, 2 H, 2 H, and 16 H); IR 2930, 2850 (C–H), 1755 (C=O), 1630 (C=C). Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.68; H, 9.14. Found: C, 72.94; H, 9.34.

Methyl 2-(*tert*-Butyldimethylsiloxy)-1-(1-hydroxy-1-methylethyl)-3,3-dimethylcyclopropanecarboxylate (45). Following procedure A (2 h, −78 °C), cyclopropane **1e** (1.03 g, 4.00 mmol) and acetone (0.346 g, 6.00 mmol) provided 1.13 g of crude product. After filtration (Al_2O_3), ^{1}H and ^{13}C NMR spectra were recorded which reveal the presence of 51% *trans*-**45**, 38% *cis*-**45**, and 11% **1e**. Distillation (100 °C/0.02 mm) gave 0.896 g (71%; considering consumed **1e** the yield was 80%) of *cis*/*trans*-**45** as a colorless liquid.

Similar experiments with shorter reaction times results in the following approximate ratios of compounds: 5 min/−78 °C 50% *trans*-**45**, 40% *cis*-**45**, 10% **1e**; 10 s/−78 °C 40% *trans*-**45**, 35% *cis*-**45**, 25% **1e**.

Radial chromatography (cyclohexane/ethyl acetate 10:1) allowed separation of the isomers.

***cis*-45**: colorless crystals (mp 84–86 °C): ^{1}H NMR δ 3.49 (s, 1 H, 2-H), 3.56 (s, 3 H, CO_2Me), 1.42, 1.31, 1.14, 1.10 (4 s, 3 H each, Me), 0.86 (s, 9 H, CMe_3), 0.04 (s, 6 H, $SiMe_2$), OH proton hidden by other signals; ^{13}C NMR δ 170.2, 51.4 (s, q, CO_2Me), 73.2 (s, $COHMe_2$), 64.5 (d, C-2), 45.0 (s, C-1), 30.9, 29.0 (2 q, $COHMe_2$), 25.6, 18.2 (q, s, CMe_3), 19.7, 19.4 (2 q, Me), −5.6 (q, $SiMe_2$); the signal for C-3, which should show up at ca. 25 ppm, is hidden by other signals.

***trans*-45**: colorless liquid (bp 100 °C/0.02 mm); ^{1}H NMR δ 4.74 (s, 1 H, OH), 3.73 (s, 1 H, 2-H), 3.58 (s, 3 H, CO_2Me), 1.38, 1.26, 1.24, 0.93 (4 s, 3 H each, Me), 0.83 (s, 9 H, CMe_3), 0.08, 0.06 (2 s, 3 H each, $SiMe_2$); ^{13}C NMR δ 171.7, 50.7 (s, q, CO_2Me), 72.2 (s, $COHMe_2$), 65.1 (d, C-2), 42.4 (s, C-1), 32.2, 28.2 (2 q, $COHMe_2$), 25.7, 18.0 (q, s, CMe_3), 19.9, 14.6 (2 q, Me), −5.2 (q, $SiMe_2$); the signal for C-3, which should show up at ca. 25 ppm, is hidden by other signals.

IR: 3650 (OH), 2950–2850 (C–H), 1735, 1720 (CO_2Me).

Anal. Calcd for $C_{16}H_{32}O_4Si$: C, 60.71; H, 10.19. Found for *cis*-**45**: C, 60.33; H, 10.34. Found for *trans*-**45**: C, 60.88; H, 10.19.

Isomerization of *trans*-45. Cyclopropane *trans*-**45** (0.165 g, 0.50 mmol, containing ca. 10% **1e**) in 5 mL of dichloromethane was stirred with $Me_3SiOSO_2CF_3$ (50 mg, 0.22 mmol) and hexamethyldisilazane (0.1 mL) for 20 h at room temperature. Filtration (Al_2O_3) and distillation (100 °C/0.02 mm) gave 0.153 g (93%) of *cis*-**45** (containing ca. 10% **1e**).

Methyl 2-*tert*-Butyl-2-(*tert*-butyldimethylsiloxy)-1-(hydroxyphenylmethyl)cyclopropanecarboxylate (50). Applying procedure A, cyclopropane **1f** (0.572 g, 2.00 mmol) and benzaldehyde (0.636 g, 6.00 mmol) afforded 0.821 g of crude **50** which was analyzed by high-field NMR spectroscopy: ^{1}H NMR δ 7.6–7.4 (m, 5 H, Ph), 5.13, 4.99 (2 s, 0.25 H and 0.75 H, C*H*OHPh), 3.72 (s, 1 H, OH), 3.41, 3.38 (2 s, 2.25 H and 0.75 H, CO_2Me), 1.82, 1.47 (AB system, J = 7.3 Hz, 1.5 H, 3-H), 1.72, 1.42 (AB system, J = 7.5 Hz, 0.5 H, 3-H), 1.09, 1.08, 1.04 (3 s, 18 H, CMe_3), 0.37, 0.34, 0.35, 0.26 (4 s, 2 H, 2 H, 1 H, and 1 H, $OSiMe_2$); ^{13}C NMR δ 171.1 (170.9), 51.3 (51.1) (s, q, CO_2Me), 140.7 (142.4), 127.8, 125.5, 125.3 (127.2, 127.0, 126.5) (s, 3 d, Ph), 74.9 (73.3) (d, *C*HOHPh), 72.0 (72.2) (s, C-2), 41.2 (42.5) (s, C-1), 36.1 (36.3) (s, *C*Me_3), 26.9, 26.1 (26.8, 26.3) (2 q, C*Me*$_3$), 20.2 (19.6) (t, C-3), 18.6 (18.7) (s, Si*C*Me_3), –1.1 (–2.7) (q, $SiMe_2$), values in parentheses refer to the signals of the minor isomer.

Attempts to remove the benzylic hydroxyl group by hydrogenolysis (H_2, Pd/C) or to convert this functional group to a carbonyl group (PCC) failed.

Methyl *trans*-1-Allyl-2,3,3-trimethyl-2-(trimethylsiloxy)cyclopropanecarboxylate (52). According to the published procedure,[12] methyl 2,3,3-trimethyl-2-(trimethylsiloxy)cyclopropanecarboxylate[7] (0.460 g, 2.00 mmol) and allyl bromide (0.363 g, 3.00 mmol) gave 0.419 g (78%) of **52** as a colorless liquid (bp 80 °C/0.02 mm): ^{1}H NMR δ 5.95–5.5, 5.1–4.8 (2 m, 1 H and 2 H, CH=CH_2), 3.52 (s, 3 H, CO_2Me), 2.6–2.1 (m, 2 H, CH_2), 1.38, 1.07, 1.00 (3 s, 3 H each, Me), 0.04 (s, 9 H, $OSiMe_3$); IR 3085, 2980–2890 (C–H), 1730 (CO_2Me). Anal. Calcd for $C_{14}H_{26}O_3Si$: C, 62.18; H, 9.69. Found: C, 62.20; H, 10.03.

Acknowledgment. We are most grateful for generous support of this work by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the Universitätsbund Würzburg, and the Karl-Winnacker-Stiftung (Hoechst AG).

Diastereoselective Syntheses of Highly Substituted Methyl Tetrahydrofuran-3-carboxylates by Reactions of γ-Lactols with Silylated Nucleophiles†

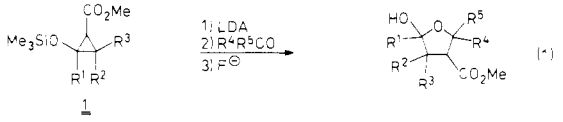
Christiane Brückner, Hiltrud Holzinger, and Hans-Ulrich Reissig*

Institut für Organische Chemie der Universität Würzburg, Am Hubland, D-8700 Würzburg, FRG

Received September 10, 1987

Hydroxyalkylation of enolates generated from methyl 2-siloxycyclopropanecarboxylates **1** followed by fluoride-induced ring opening gives γ-lactols as key intermediates. Their reduction with triethylsilane/BF_3·OEt_2 affords methyl tetrahydrofuran-3-carboxylates **3**, **5**, and **6–13** in good overall yield. The bicyclic furan derivative **13** is formed as essentially one diastereomer. Under the influence of BF_3·OEt_2, several γ-lactols are also reacted with a range of silylated nucleophiles. By this methodology the anomeric hydroxyl group can be substituted by a cyano, allyl, allenyl, or trimethylsilylethynyl unit to give the highly substituted tetrahydrofuran derivatives **15–18**, **21**, **23**, **25**, and **27**. In many examples this C–C bond-forming process occurs with excellent diastereoselectivity. Mechanistic features as well as the stereochemical outcome are discussed. Neighboring group participation by the ester function might be responsible for the surprisingly high trans/cis ratios in the resulting tetrahydrofuran-3-carboxylates.

In the preceding publication[1] we have demonstrated that starting from methyl 2-siloxycyclopropanecarboxylates **1** and carbonyl compounds, a large variety of paraconic esters as well as other furanone derivatives are available in good overall yield. Key intermediates are γ-lactols (or their open chain isomers), which are attained by hydroxyalkylation of the corresponding ester enolate and subsequent ring cleavage with fluoride reagents (eq 1). Whereas the oxidation of these γ-lactols to paraconic esters is necessarily limited to derivatives with R^1 = H, substitution of the anomeric hydroxyl group should also be applicable for compounds with $R^1 \neq$ H. In this full account[2] we want to disclose our results concerning the Lewis acid promoted reactions of these γ-lactols with several silylated nucleophiles, which lead to a diversity of highly substituted and functionalized tetrahydrofuran-3-carboxylates.



Reduction of γ-Lactols with Triethylsilane

At first we applied the combination of triethylsilane/BF_3·OEt_2, which is known to reduce less substituted γ- and δ-lactols.[3,4] To our pleasure the pure γ-lactols **2** and **4**

* Present address: Institut für Organische Chemie der Technischen Hochschule Darmstadt, Petersenstrasse 22, D-6100 Darmstadt, FRG.

† Dissertation Christiane Brückner, Universität Würzburg, 1986.

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