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†

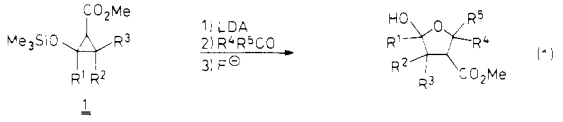
Christiane Brückner, Hiltrud Holzinger, and Hans-Ulrich Reissig*

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.

(1) Brückner, C.; Reissig, H.-U. *J. Org. Chem.*, preceding paper in this issue.

(2) For preliminary reports, see: (a) Brückner, C.; Reissig, H.-U. *J. Chem. Soc., Chem. Commun.* **1985**, 1512. (b) Brückner, C.; Lorey, H.; Reissig, H.-U. *Angew. Chem., Int. Ed. Engl.* **1986**, 556.

(3) (a) Kraus, G. A.; Frazier, K. A.; Roth, B. D.; Taschner, M. J.; Neuenschwander, K. *J. Org. Chem.* **1981**, *46*, 2417. (b) Kraus, G. A.; Molina, M. T.; Walling, J. A. *J. Org. Chem.* **1987**, *52*, 1273. (c) Babirad, S. A.; Wang, Y.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 1370.

(4) Review on Ionic Hydrogenation: Kursanov, D. N.; Parnes, Z. N.; Loim, M. M. *Synthesis* **1974**, 633.

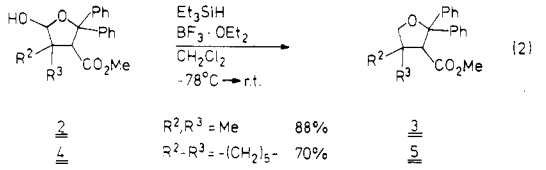
0022-3263/88/1953-2450$01.50/0

Table I. Synthesis of Methyl Tetrahydrofuran-3-carboxylates According to eq 3

cyclopropane	R^1	R^2	R^3	R^4	R^5	product	yield, %	cis:trans
1a	H	Me	Me	Ph	Ph	**3**	47	
1a	H	Me	Me	Me	Me	**6**	71	
1b	H	$-(CH_2)_5-$		$-(CH_2)_5-$		**7**	48	
1a	H	Me	Me	Me	H	**8**	51	1:3
1a	H	Me	Me	Ph	H	**9**	79	2:3
1a	H	Me	Me	CHMePh	H	**10**[a]	71	1:2
1b	H	$-(CH_2)_5-$		Me	H	**11**	54	1:1
1c	Ph	H	H	Me	Me	**12**	54	1:1
1d	$-(CH_2)_4-$		H	Me	Me	**13**	66	>9:1

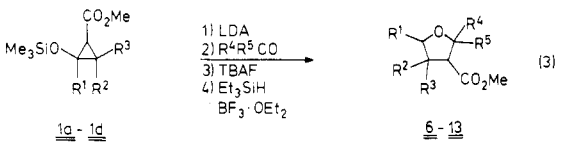
[a] Four isomers due to the exocyclic center of chirality.

react smoothly to give the expected methyl tetrahydrofuran-3-carboxylates **3** and **5**, respectively (eq 2).



(2)

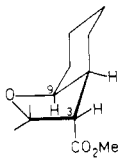
Having estabilished that this crucial step even works with rather crowded substrates such as **2** and **4**, we tried to gain the desired tetrahydrofuran derivatives without purification of the precursors, which is in many cases tedious and inefficient.[1] Thus siloxycyclopropanes **1a–d** are hydroxyalkylated and ring opened with fluoride, and the resulting crude γ-lactols are treated with the reducing agent (eq 3). As disclosed in Table I this protocol affords methyl tetrahydrofuran-3-carboxylates **3** and **6–13** in very reasonable overall yields for a three-step sequence.



(3)

Addition of aldehydes to the enolates of **1a** or **1b** results in mixtures of cis/trans isomers (**8–11**). The ratio of diastereomers is established during the ring-opening step with fluoride and is plausibly not changed under the conditions of the final reduction. Transformation of the intermediate γ-lactols to paraconic esters has given very similar cis/trans ratios.[1] This holds also true for the example incorporating the chiral aldehyde 2-phenylpropanal. Now a mixture of four diastereomers **10a–d** is found, whose approximate ratio of 12:5:1:1 could be determined by high-field ^1H NMR spectroscopy. This ratio is again in reasonable agreement with that found in the corresponding oxidation experiment.[1] Therefore the two major isomers **10a** and **10b** are presumably the result of a Cram-type addition to the chiral aldehyde. They differ only in the site of the 3-methoxycarbonyl group (cis/trans isomers). The NMR data of these two isomers are in accord with these assignments.

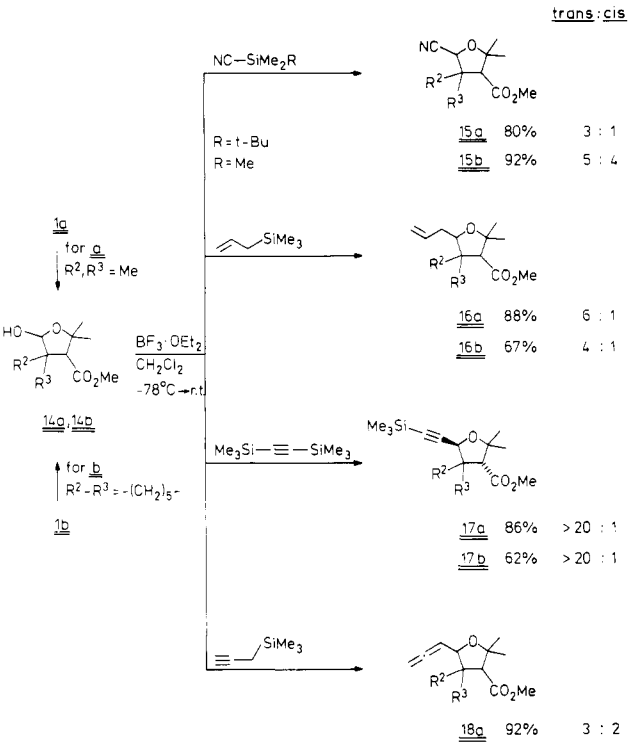
For furan derivative **12** the cis/trans ratio refers to the relative configuration at C-3 and C-5. It reflects the stereoselectivity of the reduction with the silane. Thus this step is virtually unselective in the case leading to **12**. In contrast, the bicyclic siloxycyclopropane **1d** provides furan derivative **13** as essentially one of four possible diastereomers (>90% selectivity). Most characteristic signals in the ^1H NMR spectrum of **13** are the broad quartet at 4.09 ppm ($J \approx 6$ Hz) for the bridgehead 9-H and the doublet at 2.76 ppm ($J = 7.5$ Hz) for 3-H. If one assumes a chair/envelope conformation for the bicyclic furan derivative, the configuration of **13** as illustrated in the formula is highly probable. Whereas the location of the ester



13

function is determined in the ring cleavage with fluoride, which might produce the thermodynamically most stable γ-lactol, the reduction brings about the cis fusion of the two rings. Apparently delivery of hydride proceeds more easily to the convex side of the intermediate oxonium ion (see Discussion below).

Scheme I



Substitution with Silylated C-Nucleophiles

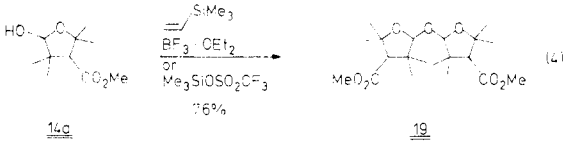
Synthetically even more valuable would be the introduction of C-nucleophiles at the anomeric center to afford "*C*-glycosyl" compounds. Indeed, this process is possible with several silanes as illustrated in Scheme I. The γ-lactols **14a** and **14b**, both available in good yield from the corresponding cyclopropanes **1a** or **1b**, respectively, react smoothly with cyanotrialkylsilanes, allyltrimethylsilane, bis(trimethylsilyl)acetylene, and propargyltrimethylsilane. The latter nucleophile cleanly transfers an allenyl group

to the heterocycle. The allylation process has also been executed without purification of the intermediate γ-lactol, as already demonstrated for the reduction with triethylsilane. Thus cyclopropane **1a** gives **16a** in this three-step sequence, in 56% overall yield.

Since BF_3·OEt_2 works fine with these nucleophiles, we have so far not investigated the effect of other Lewis acids on yield and stereochemical course of the substitution. The C–C bond formation occurs in excellent yield in all examples and with a very high trans/cis ratio for **17a** and **17b**. Whereas the diastereoselectivity is good in the allyltransfer process, it is considerably lower with the cyanosilanes and essentially zero for propargylsilane. For **15a** we obtained the same 3:1 ratio of isomers regardless of whether we used *tert*-butylcyanodimethylsilane or the corresponding trimethylsilyl derivative. The spectroscopic data confirm the α-cyano ether structure of **15a** and **15b** and disprove the imaginable formation of isocyanides.[5]

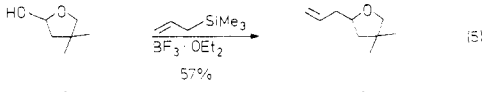
The cis/trans assignments are based on arguments comparing chemical shifts. Characteristic is, for example, the low-field shift of the ^1H NMR signals of 3-H and 5-H by 0.11 and 0.73 ppm, respectively, on going from *cis*-**15a** to *trans*-**15a**. Similar effects can be observed for other pairs of diastereomers. These assignments are supported by ^{13}C NMR data, which show in general signals for the cis isomers at higher field compared to the corresponding trans compounds. This is attributed to more severe steric compression of substituents in the cis compounds.[6]

With the less reactive trimethylvinylsilane we did not observe any vinylation at C-5. Instead, the double acetal **19** is found (eq 4). This product, resulting from condensation of γ-lactol **14a**, is also formed when **14a** is treated with 0.25 equiv of trimethylsilyl triflate. As indicated by the very few signals (6 lines) in the ^1H NMR spectrum of **19**, out of six possible diastereomers **19** must be one whose structure involves an element of symmetry. Formation of **19** also proceeds in experiments employing (trimethylsiloxy)propene as nucleophile. Very likely protodesilylation of the more sensitive silyl enol ether occurs under the conditions applied.



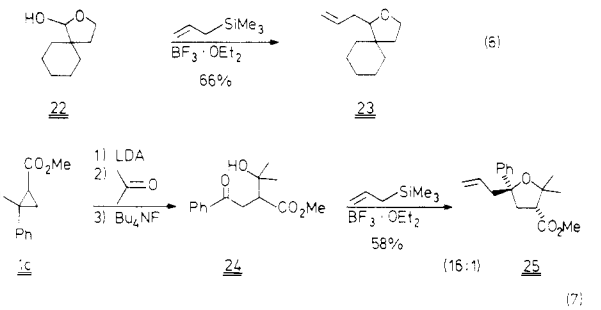
14a 19

Equations 5 and 6 demonstrate that less substituted γ-lactols such as **20** or **22** are also capable of reacting with allylsilane providing 2-allyltetrahydrofuran derivatives **21** and **23**, respectively, in good yields. The starting materials have also been prepared from cyclopropanes **1a** and **1b** by modified reductive procedures.[7,8]



20 21

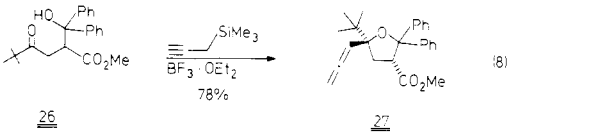
The α-hydroxyalkylated γ-oxoalkanoate **24**, gained from cyclopropane **1c** and acetone, is an open-chain tautomer of a γ-lactol. Therefore reaction of unpurified **24** with allyltrimethylsilane in the presence of BF_3·OEt_2 provides the tetrahydrofuran derivative **25** in reasonable overall efficiency. The stereoselectivity is considerably higher compared to the related reduction with triethylsilane (see **1c** → **12**, Table I).



22 23

1c 24 25

Compound **26** can also be prepared from a 2-siloxysubstituted methyl cyclopropanecarboxylate, although in this case only the complementary Lewis acid methodology[9] gives satisfying yields (see Discussion in the preceding paper[1]). The allylation and cyanation of **26** have already been described.[9] Similar to those reactions treatment of **26** with propargyltrimethylsilane/BF_3·OEt_2 takes place with excellent diastereoselectivity, providing the highly substituted methyl 5-allenyltetrahydrofuran-3-carboxylate **27** in very good yield. Although the NMR



26 27

data of tetrahydrofuran derivative **27** do not allow an unambiguous stereochemical assignment, we attribute the trans configuration to the compound as depicted. This is highly plausible with respect to the results obtained in other examples. Attempts to add bis(trimethylsilyl)-acetylene to **26** were not successful. Very likely this nucleophile is too unreactive to compete with other acid-induced transformations of **26**.[9]

Discussion

Lewis acid promoted additions of nucleophiles to acetals[10] or α-halogeno ethers[11] are known and have found new applications in asymmetric synthesis quite recently.[12] The reaction of *N*-acyliminium ions with silylated nucleophiles, often performed in an intramolecular fashion, is also related to the reaction discussed in this work.[13] Therefore good mechanistic evidence is existent for eq 9: the Lewis acid abstracts the hydroxyl group of the γ-lactol to form the cyclic oxonium ion **28**; the nucleophile then attacks

(5) (a) Gassman, P. G.; Haberman L. M. *Tetrahedron Lett.* **1985**, *26*, 4971. (b) Carr, S. A.; Weber, W. P. *Synth. Commun.* **1985**, *15*, 775. (c) Imi, K.; Yanagihara, N.; Utimoto, K. *J. Org. Chem.* **1987**, *52*, 1013 and references cited therein.

(6) Kalinowski, H.-O.; Berger, S.; Braun, S. *^{13}C-NMR-Spektroskopie*; Georg Thieme Verlag: Stuttgart, 1984.

(7) Bretsch, W.; Reissig, H.-U. *Liebigs Ann. Chem.* **1987**, 175.

(8) Grimm, E. L.; Reissig, H.-U. *J. Org. Chem.* **1985**, *50*, 242.

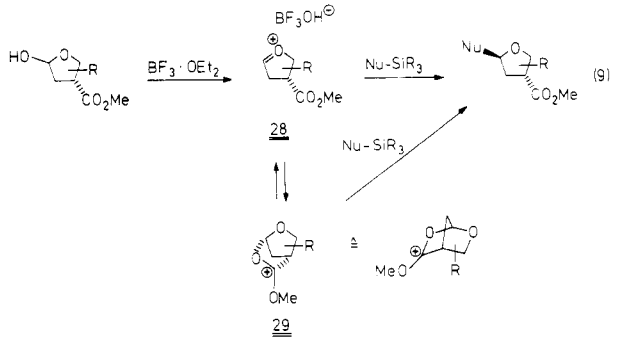
(9) Reissig, H.-U.; Reichelt, I.; Lorey, H. *Liebigs Ann. Chem.* **1986**, 1924.

(10) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, 1983.

(11) (a) Hosomi, A.; Sakata, Y.; Sakurai, H. *Chem. Lett.* **1983**, 405. (b) Reetz, M. T.; Müller-Starke, H. *Liebigs Ann. Chem.* **1983**, 1726. For other references, see ref 10.

(12) Review: Seebach, D.; Imwinkelried, R.; Weber, T. "EPC Syntheses with C,C Bond formation via Acetals and Enamines" in *Modern Synthetic Methods 1986*; Scheffold, R., Ed.; Springer-Verlag: Berlin, 1986; Vol. 4, p 191.

(13) Reviews: (a) Shono, T. *Tetrahedron* **1984**, *40*, 811. (b) Speckamp, W. N.; Hiemstra, H. *Tetrahedron* **1985**, *41*, 4367. For some more recent applications, see: (c) Renaud, P.; Seebach, D. *Helv. Chim. Acta* **1987**, *69*, 1704. (d) Thaning, M.; Wistrand, L.-G. *Helv. Chim. Acta* **1987**, *69*, 1711. (e) Klaver, W. J.; Hiemstra, H.; Speckamp, N. *Tetrahedron Lett.* **1987**, *28*, 1581.



from the more accessible face of **28** leading after desilylation to the product. Although we cannot exclude an activation of the silylated nucleophile by the BF_3OH^-, participation of the anion in the C–C bond-forming step seems rather unlikely.

In many examples the stereoselectivity is surprisingly high. Considering the puckered and relatively flexible conformation of **28**, one would not expect such large steric discrimination of its sides due to the 3-carbomethoxy function (1,3-induction). Therefore a neighboring group effect of this substituent might participate, giving the bicyclic oxonium ion **29**. This would be attacked by the nucleophile under inversion at the bridgehead carbon, thereby affording the trans product. This type of assistance is well known in sugar chemistry where the formation of acyl oxonium ions is a clever strategy to control stereochemistry at the anomeric center.[14]

Comparing the silylated nucleophiles employed in their stereodifferential power, the propargyl system seems to be the least selective reagent besides triethylsilane. The attacking terminal carbon is sterically unimpeded and therefore this slim nucleophile might be rather reactive and relatively unselective. The same holds true for the cyanide transfer process, which might take place via the trialkyl isocyanide present in small equilibrium concentrations.[15] Whereas allyltrimethylsilane shows good reactivity and selectivity, the disilylated acetylene acts rather sluggishly (no addition to **26**) but with high stereoselectivity. Here one trimethylsilyl group has to come over the five-membered ring during attack of the nucleophile on oxonium ion **28**. This leads to severe steric interaction with the substituents and to excellent face differentiation.[16]

When the stereochemical outcome of the different γ-lactols and the equivalent α-hydroxyalkylated γ-oxoalkanoates used is compared, the following sequence of selectivity can in general be found: **14b ≤ 14a < 24 < 26**. Group R^1 at the anomeric center determines the degree of stereoselectivity most importantly. Thus replacing R^1 = H by R^1 = Ph or *t*-Bu distinctly enhances the trans/cis ratio. This can be rationalized by the decreased reactivity of the oxonium ions involved due to steric and electronic effects.

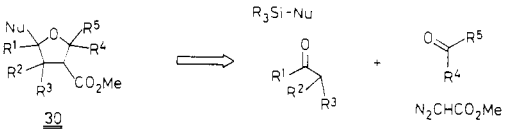
Conclusion

The large number of recent reports dealing with the substitution on anomeric centers witness the current interest in this reaction type. In particular, sugar derivatives are being investigated in much detail to elaborate selective syntheses of *C*-glycosyl compounds. However, usually the substitution at the anomeric carbon is performed with "good" leaving groups like halogen, OR (R = alkyl, acyl), $NHCOCl_3$, or SR.[17-19] According to the leaving group quality of these substituents, preparation and handling of these intermediates can often be troublesome and inefficient.

Whereas the substitution of *free* hydroxyl groups in cyclic hemiacetals by hydride has already been studied,[3] the related reaction with C-nucleophiles has only been applied in a few special cases.[20] Our broad investigation disclosed here demonstrates that a range of silylated nucleophiles can be coupled to γ-lactols with very good success to provide highly substituted tetrahydrofuran derivatives under mild conditions. Thus in many instances the special activation of hemiacetals is not necessary. This should also be valid for δ-lactols and sugar derivatives. Only sensitive nucleophiles which are prone to protodesilylation seem to require protection and activation of the hydroxyl group to be substituted.

The diastereoselectivity of C–C bond formation is excellent in many examples and should even be enhanced if higher substituted nucleophiles are employed. Since the unsaturated nucleophiles incorporated in the tetrahydrofuran ring can serve as a handle for further transformations, the procedures outlined here might help to achieve stereoselective synthesis of this class of heterocycles. Tetrahydrofuran derivatives are subject to numerous current efforts in asymmetric synthesis.[21]

The retrosynthetic analysis of **30** shows its genesis from the nucleophile, two distinct carbonyl compounds, and methyl diazoacetate. Three of these precursors can widely



be varied as demonstrated, and therefore high flexibility with regard to the substituents is garanteed, which is characteric for many reactions employing methyl 2-sil-

(14) Reviews: (a) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155. (b) Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212.

(15) Durig, J. R.; George, W. O.; Li, Y. S.; Carter, R. O. *J. Mol. Struct.* **1973**, *16*, 47.

(16) With O,O- and N,O-acetals bis(trimethylsilyl)acetylene also displays excellent diastereoselectivity: see ref 12 and 13c.

(17) (a) Glycosylchlorides: Hosomi, A.; Sakata, Y.; Sakurai, H. *Tetrahedron Lett.* **1984**, *25*, 2383. (b) New applications of glycosyl fluorides: Posner, G. H.; Haines, S. R. *Tetrahedron Lett.* **1985**, *26*, 1823.

(18) For leading references on allylation and cyanation of *O*-acyl and *O*-alkyl glycosyl compounds, see: (a) Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976. (b) Cupps, T. L.; Wise, D. S.; Townsend, L. B. *J. Org. Chem.* **1982**, *47*, 5115. (c) Kozikowski, A. P.; Sorgi, K. L. *Tetrahedron Lett.* **1982**, *23*, 2281. (d) Danishefsky, S.; Kerwin, J. F. *J. Org. Chem.* **1982**, *47*, 3805. (e) Giannis, A.; Sandhoff, K. *Tetrahedron Lett.* **1985**, *26*, 1479. (f) Bennek, J. A.; Gray, G. R. *J. Org. Chem.* **1987**, *52*, 892. (g) Utimoto, K.; Wakabayashi, Y.; Horiie, T.; Inoue, M.; Shishiyama, Y.; Obayashi, M.; Nozaki, H. *Tetrahedron* **1983**, *39*, 967. (h) Farkas, J.; Fric, I. *Collect. Czech. Chem. Commun.* **1985**, *50*, 1291.

(19) Use of trichloroacetimidates: (a) Hoffmann, M. G.; Schmidt, R. R. *Liebigs Ann. Chem.* **1985**, 2403 and ref 14b. Use of thioglycosides: (b) Stewart, A. O.; Williams, R. M. *J. Am. Chem. Soc.* **1985**, *107*, 4289. (c) Keck, G. E.; Kachensky, D. F.; Enholm, E. J. *J. Org. Chem.* **1985**, *50*, 4317.

(20) To our best knowledge only one single example, namely, reaction of allyltrimethylsilane with 2,3,4,6-tetrabenzylglucopyranose, has been reported. See ref 18a. After submission of our manuscript a report appeared describing stereoselective reactions of γ-lactols with organometallic reagents: Tomooka, T.; Matsuzawa, K.; Suzuki, K.; Tsuchihashi G. *Tetrahedron Lett.* **1987**, *28*, 6339.

(21) Reviews: (a) Semple, J. E.; Joullié, M. M. *Heterocycles* **1980**, *14*, 1825. (b) Bartlett, P. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, Chapter 6. For recent work in this area, see: (c) Mukaiyama, T.; Hayashi, M.; Ichikawa, J. *Chem. Lett.* **1986**, 1157. (d) Still, W. C.; Romero, A. G. *J. Am. Chem. Soc.* **1986**, *108*, 2105. (e) Schreiber, S. L.; Sammakia, T.; Hulin, B.; Schulte, G. *J. Am. Chem. Soc.* **1986**, *108*, 2106. (f) Williams, D. R.; White, F. H. *Tetrahedron Lett.* **1986**, *27*, 2195. (g) Dolle, R. E.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1985**, *107*, 1691. (h) Frauenrath, H.; Runsink, J. *J. Org. Chem.* **1987**, *52*, 2707. (i) Hopkins, M. H.; Overman, L. E. *J. Am. Chem. Soc.* **1987**, *109*, 4748. (j) Herrinton, P. M.; Hopkins, M. H.; Mishra, P.; Brown, M. J.; Overman, L. E. *J. Org. Chem.* **1987**, *52*, 3712.

oxycyclopropanecarboxylates as key building blocks.[22]

Experimental Section

For general information see the preceding paper.[1] Triethylsilane (Fluka AG), allyltrimethylsilane (Fluka AG), and bis(trimethylsilyl)acetylene (Aldrich) were used as supplied; propargyltrimethylsilane was synthesized according to ref 23. $BF_3{\cdot}OEt_2$ was distilled from calcium hydride.

Procedures A (hydroxyalkylation) and B (ring opening with fluoride) were outlined in detail in the preceding paper.[1]

General Procedure for Reactions of γ-Lactols with Triethylsilane and Silylated Nucleophiles (Procedure C). After dissolving 1.0 equiv of the γ-lactol in dry dichloromethane (15 mL for 4 mmol), 1.1 equiv of the silane was added at −78 °C. The homogeneous mixture was treated with 1.1 equiv of $BF_3{\cdot}OEt_2$ and stirred at −78 °C for 45 min and at room temperature for 3 h (deviations in stoichiometry and reaction times are indicated in the specific experiments). Addition of water, extraction with dichloromethane, and drying over $MgSO_4$ provided the crude product which was purified by distillation, chromatography, or crystallization.

Methyl 4,4-Dimethyl-2,2-diphenyltetrahydrofuran-3-carboxylate (3). According to procedure C, γ-lactol **2** (0.489 g, 1.50 mmol) was treated with triethylsilane (0.195 g, 1.65 mmol). The crude product was recrystallized from petroleum ether to provide 0.409 g (88%) of **3** as colorless needles (mp 80–81 °C): ^{1}H NMR δ 7.8–7.1 (m, 10 H, Ph), 4.20, 3.81 (AB system, J = 8 Hz, 2 H, 5-H), 3.90 (s, 1 H, 3-H), 3.38 (s, 3 H, CO_2Me), 1.21, 1.00 (2 s, 3 H each, Me); IR 3070, 3030, 2960, 2880 (C–H), 1750, 1735 (CO_2Me). Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.12; H, 7.31.

Starting from cyclopropane **1a** (0.864 g, 4.00 mmol) and benzophenone (1.10 g, 6.00 mmol) and following procedures A, B ($NEt_3{\cdot}3HF$), and C (Et_3SiH), there was obtained after recrystallization 0.587 g (47%) of **3** which was pure according to ^{1}H NMR spectroscopy.

Methyl 3,3-Diphenyl-2-oxaspiro[5.4]decane-4-carboxylate (5). Following procedure C, γ-lactol **4** (0.260 g, 0.710 mmol) and triethylsilane (0.091 g, 0.780 mmol) provided after recrystallization from petroleum ether 0.179 g (70%) of **5** as colorless crystals (mp 104 °C): ^{1}H NMR δ 7.7–6.9 (m, 10 H, Ph), 4.19, 3.90 (AB system, J = 8 Hz, 2 H, 1-H), 3.95 (s, 1 H, 4-H), 3.26 (s, 3 H, CO_2Me), 1.7–1.1 (m, 10 H); IR 3070–3010, 2980–2850 (C–H), 1745, 1725 (CO_2Me). Anal. Calcd for $C_{23}H_{26}O_3$: C, 78.82; H, 7.48. Found: C, 79.26; H, 7.85.

Methyl 2,2,4,4-Tetramethyltetrahydrofuran-3-carboxylate (6). According to procedures A, B (TBAF), and C (Et_3SiH), cyclopropane **1a** (0.432 g, 2.00 mmol) and acetone (0.170 g, 3.00 mmol) gave 0.396 g of crude product. Distillation (90 °C/0.02 mm) afforded 0.264 g (71%) of **6** as a colorless liquid: ^{1}H NMR δ 3.64 (s, 3 H, CO_2Me), 3.53 (br s, 2 H, 5-H), 2.52 (s, 1 H, 3-H), 1.36, 1.30, 1.18, 1.11 (4 s, 3 H each, Me); IR 2960–2840 (C–H), 1740 (CO_2Me). Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.47; H, 9.95. Found: C, 64.27; H, 10.06.

Methyl 14-Oxadispiro[5.1.5.2]pentadecane-7-carboxylate (7). Following procedures A, B (TBAF), and C (Et_3SiH), cyclopropane **1b** (0.512 g, 2.00 mmol) and cyclohexanone (0.294 g, 3.00 mmol) afforded 0.632 g of crude product. Radial chromatography (cyclohexane/ethyl acetate 20:1) and distillation (110 °C/0.02 mm) provided 0.257 g (48%) of **7** as colorless crystals (mp 51–53 °C): ^{1}H NMR δ 3.74 (br s, 2 H, 15-H), 3.69 (s, 3 H, CO_2Me), 2.52 (s, 1 H, 7-H), 1.9–1.1 (m, 20 H). Anal. Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 72.32; H, 10.12.

Methyl *cis*- and *trans*-2,4,4-Trimethyltetrahydrofuran-3-carboxylate (8). According to procedures A, B (TBAF), and C (Et_3SiH), cyclopropane **1a** (0.864 g, 4.00 mmol) and acetaldehyde (0.264 g, 6.00 mmol) provided after distillation (80 °C/0.02 mm) 0.348 g (51%) of **8** as a mixture of cis/trans isomers (1:3): ^{1}H NMR δ 4.6–4.5 (m, 1 H, 2-H), 3.75 (s, 3 H, CO_2Me), 3.65 (br s, 2 H, 5-H), 2.72 (d, J = 6 Hz, 0.25 H, 3-H), 2.41 (d, J = 8.5 Hz, 0.75 H, 3-H), 1.40 (d, J = 6 Hz, 3 H, 2-Me), 1.33, 1.13 (2 s, 3 H each, Me); IR 2970–2880 (C–H), 1740 (CO_2Me). Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.91; H, 9.50.

Methyl *cis*- and *trans*-4,4-Dimethyl-2-phenyltetrahydrofuran-3-carboxylate (9). Following procedures A, B ($NEt_3{\cdot}3HF$), and C (Et_3SiH), cyclopropane **1a** (2.16 g, 10.0 mmol) and benzaldehyde (1.59 g, 15.0 mmol) gave 2.37 g of crude product. Distillation (100 °C/0.02 mm) provided 1.85 g (79%) **9** as a mixture of cis/trans isomers (2:3): ^{1}H NMR *cis*-**9** δ 7.3 (m, 5 H, Ph), 5.49 (d, J = 6.5 Hz, 1 H, 2-H), 4.20, 3.76 (AB system, J = 7.5 Hz, 2 H, 5-H), 3.22 (s, 3 H, CO_2Me), 3.06 (d, J = 6.5 Hz, 1 H, 3-H), 1.35, 1.14 (s, 3 H each, Me); *trans*-**9** δ 7.3 (m, 5 H, Ph), 5.38 (d, J = 9 Hz, 1 H, 2-H), 3.88 (br s, 2 H, 5-H), 3.72 (s, 3 H, CO_2Me), 2.77 (d, J = 9 Hz, 1 H, 3-H), 1.31, 1.19 (2 s, 3 H each, Me); IR 3060–3020, 2960, 2840 (C–H), 1740 (CO_2Me). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.76; H, 7.74. Found: C, 71.91; H, 7.43.

Methyl 4,4-Dimethyl-2-(1-phenylethyl)tetrahydrofuran-3-carboxylates (10a–d). According to procedures A, B (TBAF), and C (Et_3SiH, 16 h at room temperature), cyclopropane **1a** (0.864 g, 4.00 mmol) and 2-phenylpropanal (0.817 g, 6.00 mmol) gave after distillation (120 °C/0.02 mm) 0.880 g (71%) of **10** as a mixture of diastereomers (approximately 12:5:1:1). ^{1}H NMR (400 MHz): **10a** δ 7.3–7.05 (m, 5 H, Ph), 4.42 (dd, J = 8.25 Hz, J = 8.5 Hz, 1 H, 2-H), 3.34 (s, 3 H, CO_2Me), 2.79 (qd, J = 6.9 Hz, J = 8.25 Hz, 1 H, 1′-H), 2.40 (d, J = 8.5 Hz, 1 H, 3-H), 1.37 (d, J = 6.9 Hz, 3 H, Me), 1.08, 0.94 (2 s, 3 H each, Me); **10b** δ 7.3–7.05 (m, 5 H, Ph), 4.38 (dd, J = 5.5 Hz, J = 10.25 Hz, 1 H, 2-H), 3.47 (s, 3 H, CO_2Me), 2.93 (qd, J = 6.7 Hz, J = 10.25 Hz, 1 H, 1′-H), 2.28 (d, J = 5.5 Hz, 1 H, 3-H), 1.38 (d, J = 6.7 Hz, 3 H, Me), 1.26, 1.17 (2 s, 3 H each, Me); signals for 5-H of all isomers appear as multiplet at 3.5–3.7 ppm. The following signals were assigned to the two minor isomers: **10c** δ 4.52 (dd, J = 6.3 Hz, J = 8.8 Hz, 1 H, 2-H), 2.43 (d, J = 8.8 Hz, 1 H, 3-H); **10d** δ 4.32 (dd, J = 5.3 Hz, J = 10.3 Hz, 1 H, 2-H); the other signals of the minor isomers are hidden by signals of the major isomers.

^{13}C NMR **10a** (values in parentheses refer to signals of **10b**): δ 172.0, 51.0 (50.5) (s, q, CO_2Me), 142.8, 128.1, 127.4, 126.5 (128.5, 128.3) (s, 3 d, Ph), 85.6 (86.1) (d, C-2), 80.3 (79.0) (t, C-5), 58.9 (57.4) (d, C-3), 45.4 (d, C-1′), 43.6 (43.7) (s, C-4), 26.4, 22.1, 18.0 (28.2, 21.5, 17.5) (3 q, Me).

IR: 3090–3030, 2960–2870 (C–H), 1735 (CO_2Me).

Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.26; H, 8.45. Found: C, 72.96; H, 8.67.

Methyl *cis*- and *trans*-3-Methyl-2-oxaspiro[5.4]decane-4-carboxylate (11). Following procedures A, B (TBAF), and C (Et_3SiH), cyclopropane **1b** (1.02 g, 4.00 mmol) and acetaldehyde (0.260 g, 6.00 mmol) provided 0.627 g of crude product. Distillation (100 °C/0.02 mm) afforded 0.460 g (54%) of **11** as a 1:1 mixture of cis/trans isomers, which could be separated by radial chromatography (cyclohexane/ethyl acetate 10:1).

***cis*-11**: ^{1}H NMR δ 4.38 (quint, J = 6 Hz, 1 H, 3-H), 3.92, 3.67 (AB system, J = 8.5 Hz, 2 H, 1-H), 3.70 (s, 3 H, CO_2Me), 2.78 (d, J = 6 Hz, 1 H, 4-H), 1.8–0.9 (m, 10 H), 1.22 (d, J = 6 Hz, 3 H, Me); IR 2930, 2860 (C–H), 1740 (CO_2Me).

***trans*-11**: ^{1}H NMR δ 4.27 (qd, J = 6.5 Hz, J = 9 Hz, 1 H, 3-H), 3.83, 3.67 (AB system, J = 9 Hz, 2 H, 1-H), 3.72 (s, 3 H, CO_2Me), 2.23 (d, J = 9 Hz, 1 H, 4-H), 1.8–1.0 (m, 10 H), 1.25 (d, J = 6.5 Hz, 3 H, Me); IR 2980–2860 (C–H), 1735 (CO_2Me).

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.26; H, 9.49.

Methyl *cis*- and *trans*-2,2-Dimethyl-5-phenyltetrahydrofuran-3-carboxylate (12). According to procedures A, B (TBAF), and C (Et_3SiH, 6 h at room temperature), cyclopropane **1c** (1.32 g, 5.00 mmol) and acetone (0.435 g, 7.50 mmol) provided 0.974 g of crude product. Distillation (110 °C/0.02 mm) afforded 0.634 g (54%) of **12** as a 1:1 mixture of cis/trans isomers. Traces of methyl 4-oxo-4-phenylbutanoate could be removed by radial chromatography (cyclohexane/ethyl acetate 15:1). **12**: ^{1}H NMR δ 7.35 (mc, 5 H, Ph), 5.3–4.85 (m, 1 H, 5-H), 3.68 (s, 3 H, CO_2Me), 3.2–1.9 (m, 3 H, 4-H, 3-H), 1.53, 1.48, 1.23 (3 s, 1.5 H, 1.5 H, 3 H, Me); IR 3070, 3030, 2980–2830 (C–H), 1745 (CO_2Me). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.76; H, 7.74. Found: C, 72.10; H, 7.75.

Methyl 2,2-Dimethyl-1-oxabicyclo[4.3.0]nonane-3-carboxylate (13). According to procedures A, B (TBAF), and C (Et_3SiH), cyclopropane **1d** (0.824 g, 4.00 mmol) and acetone (0.350 g, 6.00 mmol) gave 0.727 g of crude product. Distillation (150 °C/0.02 mm) affords 0.475 g (66%) of **13** as a colorless liquid:

(22) See preceding paper and references cited therein. For a recent review, see: Reissig, H.-U. *Top. Curr. Chem.* **1988**, *144*, 73.

(23) Masson, J.-C.; LeQuan, M.; Cadiot, P. *Bull. Soc. Chim. Fr.* **1967**, 777.

^{1}H NMR (400 MHz) δ 4.09 (br q, $J \approx 6$ Hz, 1 H, 9-H), 3.69 (s, 3 H, CO_2Me), 2.76 (d, $J = 7.5$ Hz, 1 H, 3-H), 2.64 (br td, $J \approx 7$ Hz, $J \approx 12$ Hz, 1 H, 4-H), 1.48, 1.12 (2 s, 3 H each, Me), 1.8–1.2 (m, 8 H); IR 2980–2860 (C–H), 1740 (CO_2Me); ^{13}C NMR δ 173.0, 51.6 (CO_2Me), 81.2 (s, C-2), 76.1 (d, C-9), 57.6 (d, C-3), 40.8 (d, C-4), 31.1, 24.9 (2 q, 2-Me), 29.4, 27.8, 22.3, 21.6 (4 t, C-5, C-6, C-7, C-8). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.49. Found: C, 67.41; H, 9.77.

Methyl *cis*- and *trans*-5-Cyano-2,2,4,4-tetramethyltetrahydrofuran-3-carboxylate (15a). Following procedure C (*t*-$BuMe_2SiCN$) γ-lactol **14a** (0.404 g, 2.00 mmol) provided after distillation (100 °C/0.02 mm) 0.338 g (80%) of **15a** as a 1:3 cis/trans mixture: ^{1}H NMR δ 4.41, 4.30 (2 s, 0.75 H and 0.25 H, 5-H), 3.71 (s, 3 H, CO_2Me), 2.92, 2.19 (2 s, 0.75 H and 0.25 H, 3-H), 1.57–1.22 (8 s, 12 H, Me); ^{13}C NMR *trans*-**15a** (values in parentheses refer to signals *cis*-**15a**) δ 169.7 (169.3), 51.5 (s, q, CO_2Me), 117.4 (s, CN), 84.6 (83.5) (s, C-2), 75.9 (75.1) (d, C-5), 60.8 (61.9) (d, C-3), 46.4 (46.3) (s, C-4), 30.8, 25.7, 24.7, 21.7 (29.5, 25.5, 25.3, 19.3) (4 q, Me); IR 2980–2850 (C–H), 1745 (CO_2Me). Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.52; H, 8.10; N, 6.62. Found: C, 62.83; H, 8.31; N, 6.62.

Starting with cyclopropane **1a** (0.864 g, 4.00 mmol) and acetone (0.346 g, 6.00 mmol) there was obtained after execution of procedures A, B (TBAF), and C (Me_3SiCN) and distillation 0.407 g (48%) of **15a** as a 1:3 cis/trans mixture.

Methyl *cis*- and *trans*-5-Allyl-2,2,4,4-tetramethyltetrahydrofuran-3-carboxylate (16a). Following procedure C (allyltrimethylsilane), γ-lactol **14a** (0.808 g, 4.00 mmol) gave 0.897 g of crude product. Distillation (100 °C/0.02 mm) provided 0.796 g (88%) of **16a** as a colorless oil (cis/trans 1:6): ^{1}H NMR δ 6.15–5.65, 5.25–5.00 (2 m, 1 H and 2 H, $CH{=}CH_2$), 3.81, 3.46 (dd, both $J = 6$ Hz, $J = 7.5$ Hz, 0.84 H and 0.16 H, 5-H), 3.65 (s, 3 H, CO_2Me), 2.60 (s, 1 H, 3-H), 2.19 (mc, 2 H, 5-CH_2), 1.40, 1.27, 1.06 (3 s, 12 H, Me); ^{13}C NMR *trans*-**16a** (values in parentheses refer to signals of *cis*-**16a**) δ 171.7 (170.7), 50.7 (s, q, CO_2Me), 135.7 (135.6), 115.8 (d, t, $CH{=}CH_2$), 84.2 (84.6) (d, C-5), 79.6 (s, C-2), 64.6 (63.9) (d, C-3), 44.9 (s, C-4), 34.1 (33.4) (t, 5-CH_2), 31.2, 25.0, 24.4, 22.5 (30.5, 26.1, 24.7, 16.4) (4 q, Me); IR 3080, 2980–2870 (C–H), 1740 (CO_2Me), 1640 (C=C). Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.79. Found: C, 68.69; H, 9.79.

Starting from cyclopropane **1a** (0.864 g, 4.00 mmol) and acetone (0.346 g, 6.00 mmol) and applying procedures A, B, and C, 0.507 g (56%) of **16a** was obtained.

Methyl *trans*-2,2,4,4-Tetramethyl-5-[2-(trimethylsilyl)ethynyl]tetrahydrofuran-3-carboxylate (17a). Execution of procedure C with bis(trimethylsilyl)acetylene (0.511 g, 3.00 mmol, 16 h at room temperature) and γ-lactol **14a** (0.202 g, 1.00 mmol) gave 0.266 g of crude product. Distillation (100 °C/0.1 mm) provided 0.242 mg (86%) of **17a** as a colorless oil: ^{1}H NMR δ 4.32 (s, 1 H, 5-H), 3.63 (s, 3 H, CO_2Me), 2.79 (s, 1 H, 3-H), 1.45, 1.21, 1.14 (3 s, 3 H, 3 H, and 6 H, Me), 0.12 (s, 9 H, $OSiMe_3$); IR (film) 3050–2800 (C–H), 2170 (C≡C), 1755 (CO_2Me). Anal. Calcd for $C_{15}H_{26}O_3Si$: C, 63.78; H, 9.28. Found: C, 63.53; H, 9.67.

Methyl *cis*- and *trans*-5-Allenyl-2,2,4,4-tetramethyltetrahydrofuran-3-carboxylate (18a). Performance of procedure C with propargyltrimethylsilane (0.164 g, 1.46 mmol, 16 h at room temperature) and γ-lactol **14a** (0.202 g, 1.00 mmol) gave 0.263 g of crude product. Distillation (90 °C/0.02 mm) provided 0.207 g (92%) of **18a** as a colorless mixture of cis/trans isomers (2:3): ^{1}H NMR δ 5.3–4.6 (m, 3 H, $CH{=}C{=}CH_2$), 4.24, 3.72 (2 dt, both $J = 8$ Hz, $J = 1.5$ Hz, 0.6 H and 0.4 H, 5-H), 3.62 (s, 3 H, CO_2Me), 2.62, 2.59 (2 s, 1 H, 3-H), 1.36, 1.34, 1.25, 1.06, 1.05, 0.99 (6 s, 12 H, Me); IR (film) 3050–2800 (C–H), 1955 ($CH{=}C{=}CH_2$), 1740 (CO_2Me). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.91; H, 9.59.

3,3,3′,3′,5,5,5′5′-Octamethyl-4,4′-bis(methoxycarbonyl)-2,2′-bis(tetrahydrofuranyl) Ether (19). γ-Lactol **14a** (0.202 g, 1.00 mmol) and trimethylsilyl triflate (0.060 g, 0.270 mmol) were stirred in 5 mL of dry dichloromethane for 1 h at room temperature. Addition of triethylamine (0.100 g, 1.00 mmol) and filtration through a short pad of Al_2O_3 (eluation with petroleum ether) provided after concentration 0.147 g (76%) of **19** as colorless crystals (mp 90–96 °C). The sample for analysis was purified by sublimation (80 °C/0.02 mm, mp 93–96 °C): ^{1}H NMR δ 4.91 (s, 2 H, 2-H, 2′-H), 3.70 (s, 6 H, CO_2Me), 2.94 (s, 2 H, 4-H, 4′-H), 1.45, 1.30, 1.13 (3 s, 24 H, Me); IR 2980–2870 (C–H), 1745 (CO_2Me); MS, *m/z* (rel intensity) 371 (0.06, M^+ – Me), 185 (100). Anal. Calcd for $C_{20}H_{34}O_7$: C, 62.15; H, 8.86. Found: C, 62.57; H, 9.23.

Methyl *cis*- and *trans*-1-Cyano-3,3-dimethyl-2-oxaspiro[5.4]decane-4-carboxylate (15b). Applying procedure C (16 h at room temperature) to γ-lactol **14b** (0.242 g, 1.00 mmol) and cyanotrimethylsilane (0.198 g, 2.00 mmol) provided 0.255 g of crude product. Distillation (120 °C/0.02 mm) gave 0.230 g (92%) of **15b** as colorless liquid. The cis/trans ratio is approximately 6:7. **15b**: ^{1}H NMR δ 4.66, 4.51 (2 s, 0.45 H and 0.55 H, 1-H), 3.65 (s, 3 H, CO_2Me), 2.85, 2.68 (2 s, 0.45 H and 0.55 H, 4-H), 2.1–1.1, 1.49, 1.4, 1.38, 1.22 (m, 4 s, 16 H); IR 2980, 2940, 2860 (C–H), 1745 (CO_2Me). Anal. Calcd for $C_{14}H_{21}O_3N$: C, 66.91; H, 8.42; N, 5.57. Found: C, 67.00; H, 8.52; N, 5.73.

Methyl *cis*- and *trans*-1-Allyl-3,3-dimethyl-2-oxaspiro[5.4]decane-3-carboxylate (16b). Applying procedure C, γ-lactol **14b** (0.968 g, 4.00 mmol) and allyltrimethylsilane (0.498 g, 4.40 mmol) provided 1.42 g of crude product. Radial chromatography (cyclohexane/ethyl acetate 10:1) and distillation (110 °C/0.02 mm) afforded 0.578 g (54%) of **16b** as a colorless cis/trans mixture (1:4): ^{1}H NMR (400 MHz) δ 5.9–5.85, 5.3–5.0 (2 m, 1 H and 2 H, $CH{=}CH_2$), 3.9–3.8, 3.75–3.65 (2 m, 0.2 H and 0.8 H, 1-H), 3.65 (s, 3 H, CO_2Me), 2.86, 2.78 (2 s, 0.2 H and 0.8 H, 4-H), 2.65–2.55, 2.3–2.2 (2 m, 1 H each, 1-CH_2), 1.95–1.1 (m, 10 H), 1.41, 1.38, 1.27, 1.17 (4 s, 0.6 H, 2.4 H, 2.4 H, 0.6 H, Me); ^{13}C NMR *trans*-**16b** (values in parentheses refer to signals of *cis*-**16b**) δ 172.2, 51.0 (s, q, CO_2Me), 136.6 (136.2), 115.8 (d, t, $CH{=}CH_2$), 87.1 (84.1) (d, C-1), 81.0 (79.8) (s, C-3), 62.5 (60.1) (d, C-4), 50.0 (49.7) (s, C-5), 39.1, 35.7, 28.3, 25.6, 23.3 (33.5, 29.8, 25.4, 23.5, 22.0) (5 t, CH_2), 31.7, 27.3 (32.0, 26.0) (2 q, Me); IR 3080, 2980–2860 (C–H), 1740 (CO_2Me), 1640 (C=C). Anal. Calcd for $C_{16}H_{26}O_3$: C, 72.13; H, 9.83. Found: C, 71.77; H, 10.00.

Methyl *trans*-3,3-Dimethyl-1-[2-(trimethylsilyl)ethynyl]-2-oxaspiro[5.4]decane-4-carboxylate (17b). According to procedure C (16 h at room temperature), γ-lactol **14b** (0.242 g, 1.00 mmol) and bis(trimethylsilyl)acetylene (0.511 mg, 3.00 mmol) gave 0.234 g of crude product. Distillation (160 °C/0.02 mm) afforded 0.200 g (62%) of **17b** as a colorless liquid: ^{1}H NMR δ 4.59 (s, 1 H, 1-H), 3.65 (s, 3 H, CO_2Me), 2.88 (s, 1 H, 4-H), 2.1–1.1, 1.48, 1.22 (m, 2 s, 16 H), 0.18 (s, 9 H, $OSiMe_3$); IR (film) 3050–2800 (C–H), 2170 (C≡C), 1740 (CO_2Me). Anal. Calcd for $C_{18}H_{30}O_3Si$: C, 67.03; H, 9.38. Found: C, 67.38; H, 9.03.

2-Allyl-4,4-dimethyltetrahydrofuran (21). According to procedure C (16 h at room temperature), γ-lactol **20** (0.628 g, 5.40 mmol)—prepared by Dibal reduction of dihydro-4,4-dimethyl-2(3*H*)-furanone[7]—was treated with allyltrimethylsilane (2.46 g, 21.6 mmol). Distillation (90 °C/5 mm) provided 0.432 g (57%) **21** as colorless liquid: ^{1}H NMR δ 6.2–5.4, 5.2–4.75 (2 m, 1 H and 2 H, $CH{=}CH_2$), 4.01 (ddt, $J = 6$ Hz, $J = 9$ Hz, $J = 7$ Hz, 1 H, 2-H), 3.51, 3.40 (AB system, $J = 8.5$ Hz, 2 H, 5-H), 2.45–2.05 (m, 2 H, 2-CH_2), 1.63, 1.43 (AB part of an ABX system, $J_{AB} = 12$ Hz, $J_{AX} = 6$ Hz, $J_{BX} = 9$ Hz, 2 H, 4-H), 1.07 (s, 6 H, Me); IR 3080, 3000–2800 (C–H), 1640 (C=C). Anal. Calcd for $C_9H_{16}O$: C, 77.10; H, 11.50. Found: C, 77.20; H, 12.00.

1-Hydroxy-2-oxaspiro[5.4]decane (22). Cyclopropane **1b** (2.56 g, 10.0 mmol) was dissolved in 20 mL of dry tetrahydrofuran and treated with 25 mL of Dibal solution (1 M in cyclohexane, 30 min at −78 °C, 2 h at room temperature).[8,24] After workup with sodium tartrate solution, one obtained 1.86 g of material which was dissolved in 20 mL of tetrahydrofuran and refluxed for 7 h with 20 mL of 2 N NaOH. Extraction with *tert*-butyl methyl ether provided 0.869 g of crude **22**. Distillation (120 °C/0.02 mm) afforded 0.751 g (48%) of **22** as colorless oil, which was ~90% pure according to ^{1}H NMR spectroscopy: ^{1}H NMR δ 5.04 (s, 1 H, 1-H), 4.3–3.4 (m, 3 H, 3-H, OH), 2.1–1.25 (m, 12 H); IR 3400 (br, OH), 2930, 2850 (C–H), 1725 (weak, C=O). Anal. Calcd for $C_9H_{16}O_2$: C, 69.20; H, 10.32. Found: C, 68.98; H, 10.51.

1-Allyl-2-oxaspiro[5.4]decane (23). According to procedure C (16 h at room temperature), γ-lactol **22** (0.703 g, 4.50 mmol) and allyltrimethylsilane (1.09 g, 9.60 mmol) provided 0.688 g of crude product. Distillation (110 °C/0.02 mm) gave 0.530 g (66%) of **23** as a colorless liquid: ^{1}H NMR δ 6.3–5.55, 5.35–4.9 (m, 1 H and 2 H, $CH{=}CH_2$), 4.2–3.6 (m, 2 H, 3-H), 3.45 (t, $J = 6$ Hz, 1

(24) Preparation of **22** follows ref 7 but diisobutylaluminum hydride is used for the reduction of the ester group instead of $LiAlH_4$.

H, 1-H), 2.45-2.1, 2.1-1.1 (2 m, 2 H and 14 H, 2-CH_2, CH_2); IR (film) 3080, 3000-2800 (C-H), 1640 (C=C). Anal. Calcd for $C_{12}H_{20}O$: C, 80.39; H, 10.69. Found: C, 79.34, H, 10.81.

Methyl 5-Allyl-2,2-dimethyl-5-phenyltetrahydrofuran-3-carboxylate (25). Following procedures A, B (TBAF), and C (allyltrimethylsilane), cyclopropane **1c** (1.32 g, 5.00 mmol) and acetone (0.435 g, 7.50 mmol) gave 1.13 g of crude product. Distillation (140 °C/0.02 mm) afforded 0.799 g (58%) of **25**. Traces of methyl 4-oxo-4-phenylbutanoate could be removed by radial chromatography (cyclohexane/ethyl acetate 10:1). **25**: ^{1}H NMR (400 MHz) δ 7.4-7.15 (m, 5 H, Ph), 5.71, 5.01 (2 mc, 1 H and 2 H, CH=CH_2), 3.66, 3.64 (2 s, 2.8 H and 0.2 H, CO_2Me), 3.06 (dd, J = 7.8 Hz, J = 12.5 Hz, 1 H, 3-H), 2.72 (t, J = 12.5 Hz, 1 H, 4-H), 2.53 (dd, J = 7.8 Hz, J = 12.5 Hz, 1 H, 4-H), 2.45 (dd, J = 6.8 Hz, J = 13.8 Hz, allylic coupling J = 2.5 Hz, 1 H, 5-CH), 2.35 (dd, J = 7.5 Hz, J = 13.8 Hz, allylic coupling J = 2 Hz, 1 H, 5-CH), 1.55, 0.97 (2 s, 2.8 H each, Me), 1.48, 1.18 (2 s, 0.2 H each, Me); ^{13}C NMR (values in parentheses refer to signals of the minor isomer) δ 171.7, 51.6 (52.0) (s, q, CO_2Me), 148.7, 127.7, 126.3, 124.9 (s, 3 d, Ph), 134.0, 118.0 (d, t, CH=CH_2), 84.5, 82.7 (2 s, C-2, C-5), 53.9 (52.6) (d, C-3), 49.4 (48.3) (t, C-4), 39.5 (t, 5-CH_2), 28.7, 24.3 (29.7, 25.5) (2 q, Me); IR 3080, 3030, 2980-2890 (C-H), 1740 (CO_2Me), 1640 (C=C). Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.41; H, 8.08. Found C, 74.32; H, 7.97.

Methyl *trans*-5-Allenyl-5-*tert*-butyl-2,2-diphenyltetrahydrofuran-3-carboxylate (27). According to procedure C (16 h at room temperature), **26**[9] (0.129 g, 0.36 mmol) and propargyltrimethylsilane (0.112 g, 1.00 mmol) provided 0.141 g of crude product. Filtration through a short pad of Al_2O_3 (eluation with pentane/dichloromethane) and concentration at 0.02 mm gave 0.106 g (78%) of **27** as a colorless very viscous oil which was pure according to ^{1}H NMR spectroscopy: ^{1}H NMR δ 7.9-7.6, 7.5-7.0 (2 m, 2 H and 8 H, Ph), 4.92 (br dt, J = 1.5 Hz, $J \approx$ 6.5 Hz, 1 H, C=CH), 4.55, 4.48 (AB part of an ABX system, J_{AB} = 10.8 Hz, J_{AX} = 7.2 Hz, J_{BX} = 6.0 Hz, 2 H, H_2C=C), 4.11 (dd, J = 11 Hz, J = 8.1 Hz, 1 H, 3-H), 3.31 (s, 3 H, CO_2Me), 2.71 (dt, J = 1.5 Hz, $J \approx$ 11.5 Hz, 1 H, 4-H), 2.26 (dd, J = 8.1 Hz, J = 11 Hz, 1 H, 4-H), 1.18 (s, 9 H, CMe_3); IR (film) 3100-2820 (C-H), 1950 (C=C=C), 1740 (CO_2Me), 1600 (Ph). Anal. Calcd for $C_{25}H_{28}O_3$: C, 79.75; H, 7.50. Found: C, 80.02; H, 7.91.

Acknowledgment. We thank the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the Universitätsbund Würzburg, and the Karl-Winnacker-Stiftung (Hoechst AG) for generous support as well as Miss Brigitte Suchland (TH Darmstadt) for some supplementary experiments.

Registry No. **1a**, 77903-45-8; **1b**, 82884-41-1; **1c**, 77903-44-7; **1d**, 79646-62-1; **2**, 101960-05-8; **3**, 101960-08-1; **4**, 114057-48-6; **5**, 114057-49-7; **6**, 101960-07-0; **7**, 101960-11-6; *trans*-**8**, 101960-21-8; *cis*-**8**, 101960-09-2; *trans*-**9**, 101960-22-9; *cis*-**9**, 101960-10-5; **10** (isomer 1), 114057-50-0; **10** (isomer 2), 114057-51-1; **10** (isomer 3), 114057-52-2; **10** (isomer 4), 114057-53-3; *trans*-**11**, 114057-54-4; *cis*-**11**, 114057-55-5; *trans*-**12**, 101960-20-7; *cis*-**12**, 101960-19-4; **13**, 114057-56-6; **14a**, 101960-04-7; **14b**, 102536-69-6; *trans*-**15a**, 102536-75-4; *cis*-**15a**, 102536-76-5; *trans*-**15b**, 114057-57-7; *cis*-**15b**, 114057-58-8; *trans*-**16a**, 102536-73-2; *cis*-**16a**, 102536-74-3; *trans*-**16b**, 102536-71-0; *cis*-**16b**, 102536-72-1; *trans*-**17a**, 114057-59-9; *trans*-**17b**, 114057-60-2; *trans*-**18a**, 114057-61-3; *cis*-**18a**, 114057-62-4; **19**, 114057-63-5; **20**, 102536-88-9; **21**, 102536-85-6; **22**, 114057-64-6; **23**, 114057-65-7; **24**, 114057-66-8; **25**, 114057-67-9; **26**, 103619-89-2; *trans*-**27**, 114057-68-0; Et_3SiH, 617-86-7; *t*-$BuMe_2SiCN$, 56522-24-8; Me_3SiCN, 7677-24-9; allyltrimethylsilane, 762-72-1; bis(trimethylsilyl)acetylene, 14630-40-1; propargyltrimethylsilane, 13361-64-3.

Enantioselective Birch Reduction and Reductive Alkylations of Chiral 2-Phenylbenzoic Acid Derivatives. Application to the Synthesis of Hydrofluoren-9-ones, Hydrophenanthren-9-ones, and (-)-(1*R*,2*R*)-2-Phenylcyclohexanamine

Arthur G. Schultz,* Mark Macielag, David E. Podhorez, and Joseph C. Suhadolnik

Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12180-3590

Rudolph K. Kullnig

Sterling-Winthrop Research Institute, Rensselaer, New York 12144

Received June 15, 1987

Reductive alkylations of the chiral 2-phenylbenzoic acid amide **1** give 3-alkyl-4-phenylcyclohex-1-ene-3-carboxylic acid derivatives **2a-d** with high diastereoselectivities. The chiral auxiliary can be removed by reaction with methyllithium to give enantiomerically pure methyl ketones **3a** and **3b**. Birch reduction of **4** in the presence of varying amounts of alcohol additives gives primarily either **5a** or **6b**. Acid-catalyzed hydrolytic removal of the chiral auxiliary from **6a** and **6b** provides both enantiomers of *cis*-2-phenylcyclohexanecarboxylic acid, e.g., **8** and **9**. Carboxylic acid **9** is converted to (-)-(1*R*,2*R*)-2-phenylcyclohexanamine (**10b**) via isocyanate **10a**. Isocyanate **10a** undergoes cyclization to tricyclic lactam **11** on treatment with $AlCl_3$ in CH_2Cl_2. Syntheses of examples of the hydrofluoren-9-one and hydrophenanthren-9-one ring systems also are reported.

Enantioselective reductive alkylations have been performed with 2-hydroxy-, 2-amino-, and 2-alkylbenzoic acid derivatives.[1] We now describe the application of this process to the 2-phenylbenzoic acid analogue, e.g., **1**.[2] This is the first report of reductive alkylations of a biaryl-carboxylic acid derivative.[3,4] In the reduction step, two of the three double bonds of the carbonyl-substituted aromatic ring are saturated, and one new chiral center is generated at the phenyl-substituted carbon atom; a second chiral center is produced in the alkylation step with excellent overall stereocontrol. The process should be useful

(1) (a) Schultz, A. G.; Sundararaman, P. *Tetrahedron Lett.* **1984**, *25*, 4591. (b) Schultz, A. G.; Puig, S. *J. Org. Chem.* **1985**, *50*, 915. (c) Schultz, A. G.; Sundararaman, P.; Macielag, M.; Lavieri, F. P.; Welch, M. *Tetrahedron Lett.* **1985**, *26*, 4575. (d) McCloskey, P. J.; Schultz, A. G. *Heterocycles* **1987**, *25*, 437. (e) Schultz, A. G.; McCloskey, P. J.; Court, J. J. *J. Am. Chem. Soc.* **1987**, *109*, 6493.

(2) Prior presentation at the 193rd American Chemical Society National Meeting, April 5-10, 1987, Denver, CO, ORGN 102.

(3) For reports of the Birch reduction of 2- and 4-biphenylcarboxylic acids to give dihydrobenzoic acids, see: (a) Franks, D.; Grossel, M. C.; Hayward, R. C.; Knutsen, L. J. S. *J. Chem. Soc., Chem. Commun.* **1978**, 941. (b) Rabideau, P. W.; Nyikos, S. J.; Huser, D. L.; Burkholder, E. G. *J. Chem. Soc., Chem. Commun.* **1980**, 210.

(4) Hook, J. M.; Mander, L. N. *Nat. Prod. Rep.* **1986**, *3*, 35.

0022-3263/88/1953-2456$01.50/0