Stereoselective Synthesis of Highly Substituted γ-Lactones by Diastereoselective Alkylation of α-(Benzenesulfonyl) Derivatives with Unusual Facial Selectivity

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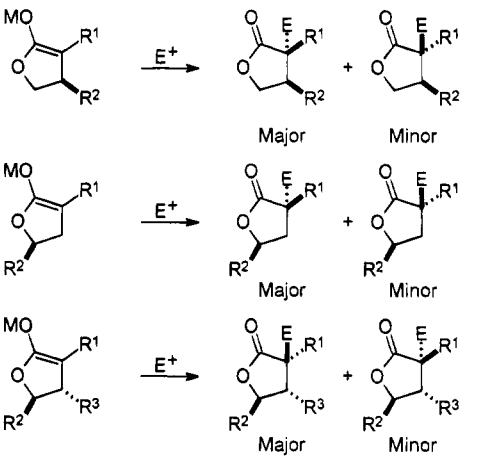
The oxidation of α-(phenylthio) γ-lactones obtained by the base-induced cyclization of enantiomerically enriched γ-[(phenylthio)acyl]-α,β-unsaturated esters to sulfones in those cases where the α-carbon has an available proton and further basic alkylation led to an unexpected facial selectivity. The reaction proceeded smoothly with alkylating agents and unsaturated carbonyl compounds, but was unsuccessful when an addition to carbonyl derivatives was attempted. The alkylation reaction was performed over a wide range of substituted substrates in order to investigate the scope and limitations of the method and to have information about the possible origin of the selectivity. The application of the alkylation reaction was extended to the synthesis of bicyclic systems, including a cyclobutane with total stereochemical control. The presence of the α-(benzenesulfonyl) group is shown to be essential to achieve the facial selection. In order to rationalize the stereochemical results, extensive semiempirical calculations were performed. The use of MNDO and AM1 permits rationalization of the fact that the α-(benzenesulfonyl) group encumbers a diastereoface of the enolate generated in the ring, leading to the observed stereochemistry.

Introduction

γ-Lactone chemistry plays a very important role in the synthesis of biologically active natural products[1] including nucleosides and related bioactive compounds.[2] Numerous examples of stereoselective alkylation reactions of butyrolactone-derived enolates may be found in studies directed at natural product total syntheses.[3] The diastereoselective alkylation of endocyclic five-membered enolates exhibits good levels of both 1,2- and 1,3-asymmetric induction, the π-facial selection being dictated by resident allylic or homoallylic substituents that sterically encumber electrophilic attack from the π-face in the enolate system.[3,4] Alkylation of nonfused β,γ-disubstituted γ-lactone ring systems is directed to the π-face of the enolate *anti* to the β-substituent (Scheme 1).[5]

In connection with our program dealing with the chemistry of such units and considering our recently obtained results in the stereoselective synthesis α-(phenylthio) γ-lactones obtained by the base-induced cyclization of enantiomerically enriched γ-[(phenylthio)acyl]-α,β-unsaturated esters[6] we were very interested in exploring the alkylation of such molecules in order to extend the stereochemical control of the final γ-lactones. In this paper we report on our studies directed to the synthesis of highly alkylated systems by diastereoselective alkylation of the α-(benzenesulfonyl) γ-lactone in which an unusual stereochemical course of the reaction nicely complements the results obtained in the intramolecular cyclization (Scheme 2).[7]

Scheme 1



Results and Discussion

Diastereoselective Alkylation of α-(Benzenesulfonyl) γ-Lactones. Having obtained excellent stereocontrol in the created stereocenters by the intramolecular Michael addition of the (phenylthio)acyl derivatives of γ-hydroxy-α,β-unsaturated esters,[6] we focused our attention on alkylation α to the carbonyl substituent. Treatment with the appropriate electrophile of the carbanion generated from **4** might provide an alternative to the synthesis of the sulfone **6** (Scheme 3).[5]

To our surpise, when the lactone **4** was treated with sodium hydride and methyl iodide the diastereoisomer **7** of **6** was obtained as the sole stereoisomer. This result represents a highly stereoselective formal electrophilic substitution of the hydrogen vicinal to the carbonyl lactone.[8]

[⊗] Abstract published in *Advance ACS Abstracts,* December 1, 1994.

(1) Corey, E. J.; Cheng, X. M. In *The Logic of Chemical Synthesis*; John Wiley & Sons, Inc.: New York, 1989.

(2) Dueholm, K. L.; Pedersen, I. B. *Synthesis* **1992**, 1.

(3) Evans, D. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985, Vol. 4, pp 2–110 and references cited therein.

(4) (a) Larcheveque, M.; Henrot, S. *Tetrahedron* **1987**, *43*, 2303. (b) Tomioka, K.; Cho, Y.-S.; Sato, F.; Koga, K. *J. Org. Chem.* **1988**, *53*, 4094.

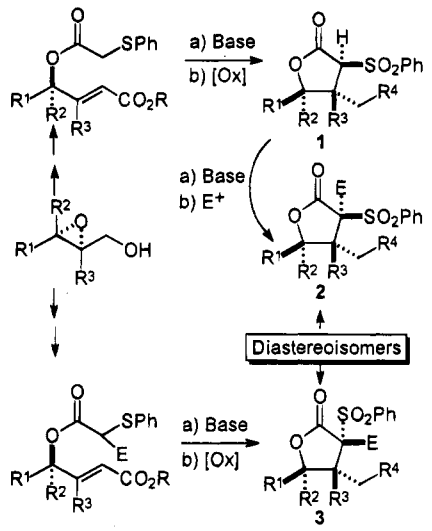
(5) (a) Hanessian, S.; Murray, P. J. *J. Org. Chem.* **1987**, *52*, 1171. (b) Boeckman, R. K., Jr.; Heckendorn, D. K.; Chinn, R. L. *Tetrahedron Lett.* **1987**, *28*, 3551.

(6) (a) Rodríguez, C. M.; Martín, V. S. *Tetrahedron Lett.* **1991**, *32*, 2165. (b) Rodríguez, C. M.; Martín, T.; Ramírez, M. A.; Martín, V. S. *J. Org. Chem.* **1994**, *59*, 4461.

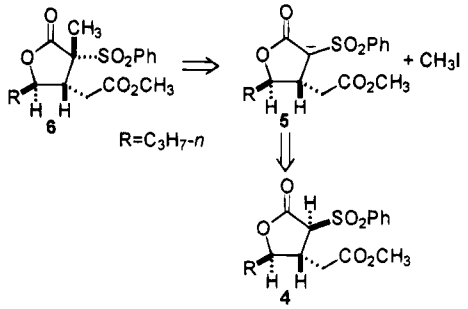
(7) For a preliminary account see: Rodríguez, C. M.; Ramirez, M. A.; Martín, V. S. *Tetrahedron Lett.* **1992**, *33*, 3039.

0022-3263/94/1959-8081$04.50/0

Scheme 2



Scheme 3



In order to investigate the scope and limitations of the method, various electrophiles were used (Table 1). With all the alkylating reagents assayed the carbon–carbon bonds were formed in excellent yields, as a single detectable stereoisomer (^{1}H-NMR 400 MHz) (entries 1–4, Table 1), by simply mixing the original lactone, NaH, and the alkylating agent, in DMF, at 0 °C. These reaction conditions were not effective when an intermolecular Michael addition was attempted with methyl acrylate and methyl propiolate. Fortunately, smooth reactions were produced when the sulfone **4** was treated with lithium bis(trimethylsilyl)amide, in THF–HMPA (1:1) at −78 °C, and the unsaturated carbonyl compounds were added, letting the system reach room temperature. In the methyl propiolate case a 5:1 mixture of the *E*:*Z* products (determined by NMR) was obtained (entry 5, Table 1). The addition of methyl acrylate at −78 °C, keeping the reaction at this temperature for 4 h, yielded the Michael addition product **12**. However, when the reaction was allowed to reach room temperature the cyclic enol **13** was the only observed product as the result of concomitant Michael addition and Dieckmann condensation (entry 7, Table 1). Surprisingly, any attempt to attain an addition reaction with a carbonyl compound proved fruitless (entry 8, Table 1).

The presence of the sulfone group is essential to achieve such a high degree of stereoselectivity.[9] Thus, when the carbanion was generated from the sulfide **16** and treated with allyl bromide, a 45:55 mixture of **17** and **18** was obtained (Scheme 4).

The complete stereoselection and the isolation of the cyclic product **13** suggested to us that intramolecular alkylation may be an optimal way to achieve the stereoselective synthesis of substituted cyclic compounds. To test this idea the stereoselective synthesis of the γ-lactone **19** was achieved in a straightforward manner.[6] Further alkaline treatment and sulfide oxidation[10] afforded the carboxylic acid **21** which after diborane reduction yielded the hydroxy sulfone **14** (Scheme 5).[11] This alcohol was selectively monomesylated to **22** using an equivalent amount of methanesulfonyl chloride. When excess of mesyl chloride was used the dimesylate **24** was the obtained product. On the other hand, when the hydroxyl protection of **14** as a benzilic ether was attempted, the product **15**, resulting from the carbon–carbon bond was isolated, when 1 equiv of benzyl bromide was used, clearly illustrating the high nucleophilicity toward alkylating agents (entry 9, Table 1). This tendency was manifested also in the intramolecular alkylation of the anion generated from the mesylate **22** since the substitute cyclobutane **23** was the only observed product.[12,13]

With the discussed results in our hands we were intrigued about the origin of the stereoselection in the alkylation reaction. Thus, in order to establish which substituents of the γ-lactone are responsible for the selectivity we synthesized the less functionalized lactones **26** and **32** and submitted them to alkylation under our standard conditions. The lactone **26** was synthesized from the sulfide **25** obtained from glutamic acid by known methodology.[14] The synthesis of racemic **32** was achieved from glycerol dimethyl acetal using our general methodology previously described (Scheme 6).[6]

The alkylation with methyl iodide of **26** yielded the γ-lactone **27**.[14c] The π-facial selection is dictated by the γ-substituent that sterically encumbers the electrophile attack from the *syn* π-face in the enolate system.

When the same reaction was performed with **32** the stereoisomer **33** was the only detected diastereoisomer. The same stereochemical course was also obtained with other electrophiles although in some cases a poorer selectivity was found (Table 2).

The β-substituent directs the alkylation to the *syn*-face. Obviously, in this case, a simple steric effect of such a substituent on the planar enolate is not in agreement with the stereochemical results obtained (Figure 1). Although the β-substituent effect on the stereochemistry is not obvious in the alkylation reaction, it can be concluded that in a highly substituted system such as **4**,

(8) For other examples of generation of α-hetero-substituted carbanions with retention of configuration see: Pearson, W. H.; Lindbeck, A. C. *J. Am. Chem. Soc.* **1991**, *113*, 8546 and references cited therein. See also: Seebach, D.; Boes, M.; Naef, R.; Schweizer, W. B. *J. Am. Chem. Soc.* **1983**, *105*, 5390.

(9) To the best of our knowledge the only reported case found in the literature in which the alkylation of γ-lactones followed a stereochemical course similar to the one presented in this paper is in *trans*-α,β-dibenzyl-γ-butyrolactones. See: Moritani, Y.; Ukita, T.; Nishitani, T.; Seki, M.; Iwasaki, T. *Tetrahedron Lett.* **1990**, *31*, 3615.

(10) Rodríguez, C. M.; Ode, J. M.; Palazón, J. M.; Martín, V. S. *Tetrahedron* **1992**, *48*, 3571.

(11) Yoou, N. M.; Pak, C. S.; Brown, H. C.; Kvishnamurthy, S.; Stocky, T. P. *J. Org. Chem.* **1973**, *38*, 2786.

(12) For the synthesis of optically active cyclobutanes see: Narasaka, K.; Hayashi, Y.; Shimadzu, H.; Niihata, S. *J. Am. Chem. Soc.* **1992**, *114*, 8869 and references cited therein.

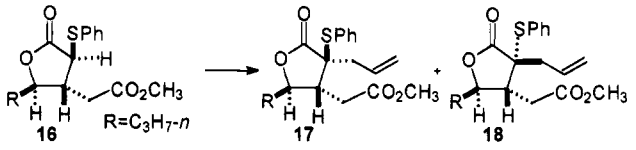
(13) The synthesis of (1*R*,2*S*)-(+)-grandisol (Tumlinson, J. H.; Gueldner, R. C.; Hardee, D. D.; Thompson, A. C.; Hedin, P. A.; Minyard, J. P. *J. Org. Chem.* **1971**, *36*, 2616), a component of the boll weevil pheromone, has been performed using as the main step the described methodology and will be published elsewhere: Martin, T.; Rodríguez, C. M.; Martín, V. S. Unpublished results.

(14) (a) Taniguchi, M.; Koga, K.; Yamada, S. *Tetrahedron* **1974**, *30*, 3547. (b) Ravid, U.; Silverstein, R. M.; Smith, L. R. *Tetrahedron* **1978**, *34*, 1449. (c) Wilson, L. J.; Liotta, D. C. *J. Org. Chem.* **1992**, *57*, 1948 and references cited therein.

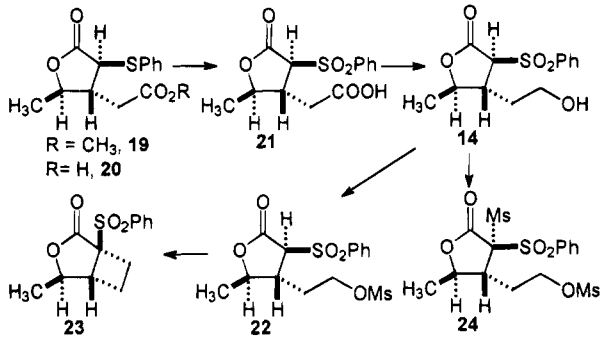
Table 1. Substitution of Hydrogen by Electrophiles in α-(Benzenesulfonyl) γ-Lactones 1

entry	substrate	electrophile	product 2	yield (%)
1	4	CH_3I	$R^1 = C_3H_7$-*n*, $R^2 = R^3 = H$, $R^4 = CO_2CH_3$, E = CH_3, **7**	88
2		CH_2=$CHCH_2Br$	$R^1 = C_3H_7$-*n*, $R^2 = R^3 = H$, $R^4 = CO_2CH_3$, E = CH_2CH=CH_2, **8**	97
3		$PhCH_2Br$	$R^1 = C_3H_7$-*n*, $R^2 = R^3 = H$, $R^4 = CO_2CH_3$, E = CH_2Ph, **9**	94
4		*n*-C_4H_9Br	$R^1 = C_3H_7$-*n*, $R^2 = R^3 = H$, $R^4 = CO_2CH_3$, E = C_4H_9-*n*, **10**	83
5		$HC{\equiv}CCO_2CH_3$	$R^1 = C_3H_7$-*n*, $R^2 = R^3 = H$, $R^4 = CO_2CH_3$, E = CH=$CHCO_2CH_3$ (*E*:*Z*, 5:1 mixture), **11**	78
6		CH_2=$CHCO_2CH_3$	$R^1 = C_3H_7$-*n*, $R^2 = R^3 = H$, $R^4 = CO_2CH_3$, E = $CH_2CH_2CO_2CH_3$ **12**	85
7		CH_2=$CHCO_2CH_3$	$R^1 = C_3H_7$-*n*, $R^2 = R^3 = H$, R^4 = C(O), E = CH_2C=$C(OH)OCH_3$, (*E*)-**13**	88
8		PhCHO		
9	$R^1 = C_3H_7$-*n*, $R^2 = R^3 = H$, $R^4 = CH_2OH$, **14**	$PhCH_2Br$	$R^1 = C_3H_7$-*n*, $R^2 = R^3 = H$, $R^4 = CH_2OH$, E = CH_2Ph, **15**	92

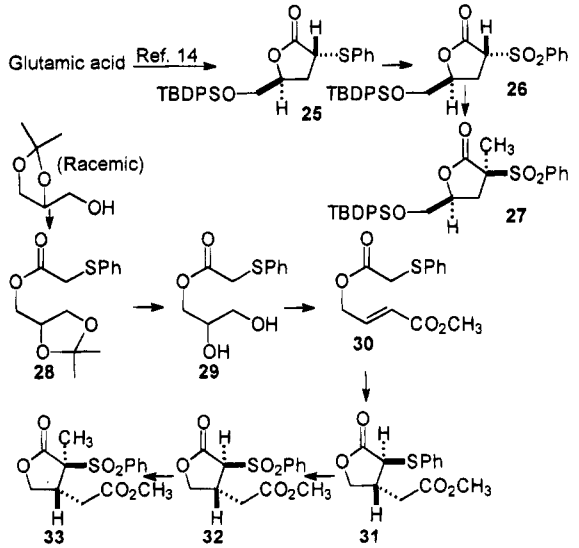
Scheme 4



Scheme 5



Scheme 6



both β- and γ-substituents relative to the carbonyl lactone are co-operative in their stereochemical effects on the alkylation reaction, leading to the observed stereochemistry.

Finally, it should be pointed out that the stereochemistry in the alkylation reaction was not affected when an additional substituent was introduced in the β- or γ-position. Thus, the oxidation of the mixture of sulfides **39** and **40** afforded the diastereoisomeric lactones **41** (*RRS*:*RRR*, 2.5:1), which after alkylation with methyl iodide, in DMF, yielded the product **42** as the only cyclic product, contaminated with an equal amount of **43** (Scheme 7). Such an opened product is generated by some excess of sodium hydride which produces a retro-Michael reaction in the alkylated product leading to the stable trisubstituted olefin. Thus, when the amount of base was better controlled using lithium bis(trimethylsilyl)amide, the side reaction was strongly minimized, producing a ratio of 13:1 of cyclic vs opened products. On the other hand any attempt to perform the cyclization on **43** under the reaction conditions was fruitless.

In a similar manner, when the sulfone **45**, obtained from **44**,[6] was treated with different alkylating agents the product **46** was obtained as the major or sole stereoisomer (Table 3). In this case, the stereochemical result is dependent on the nature of the alkylating agent. Thus, for very reactive reagents, in which the case the reaction times are shorter, only **46** was observed, but in the sluggish cases the alternative stereoisomer **47** appears.

The stereochemistry in all the alkylated products has also been determined by ROESY[15] and/or NOEDIFF[16] experiments (Figure 2).

Discussion of the Stereochemical Results. In order to rationalize the stereochemical behavior of the α-alkylation on the highly substituted γ-lactones obtained by the intramolecular Michael addition we considered the use of semiempirical calculations. We also considered the possibility of finding a model which would explain why the reaction is strongly stereoselective with the α-(benzenesulfonyl) lactones, but not stereoselective with the phenylthio analogs.

It is well known that the generation of α-sulfonyl anions from acyclic sulfones occurs with retention of configuration.[17] Two possible explanations have been postulated to rationalize such a stereochemical result: (a) a pyramidal configuration of the carbanionic center and (b) a hindrance to the free rotation of the Cα−S bond in

(15) Bax, A.; Davis, D. G. *J. Magn. Reson.* **1985**, *63*, 207.
(16) (a) Noggle, J. H.; Schimer, R. E. In *The Nuclear Overhauser Effect, Chemical Applications*; Academic Press: New York, 1971. (b) Jeener, J.; Meier, B. H.; Bachman, P.; Ernst, R. R. *J. Chem. Phys.* **1979**, *71*, 4546.
(17) (a) Aggarwal, V. K. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 175 and references cited therein. (b) Simpkins, N. S. *Sulphones in Organic Synthesis*; Tetrahedron Organic Chemistry Series; Pergamon Press: New York, 1993; Vol. 10 and references cited therein.

Table 2. Alkylation of α-(benzenesulfonyl)-β-substituted γ-Lactones 32

entry	electrophile	products (2:3)		yield (%)
1	CH_3I	**33**		90
2	CH_2=$CHCH_2Br$	$R^1 = R^2 = R^3 = H$, $R^4 = CO_2CH_3$, $E = CH_2CH$=CH_2, **34**	$R^1 = R^2 = R^3 = H$, $R^4 = CO_2CH_3$, $E = CH_2CH$=CH_2, **35**	72:13
3	$PhCH_2Br$	$R^1 = R^2 = R^3 = H$, $R^4 = CO_2CH_3$, $E = CH_2Ph$, **36**	$R^1 = R^2 = R^3 = H$, $R^4 = CO_2CH_3$, $E = CH_2Ph$, **37**	64:21
4	$BrCH_2CO_2CH_3$	$R^1 = R^2 = R^3 = H$, $R^4 = CO_2CH_3$, $E = CH_2CO_2CH_3$, **38**		88

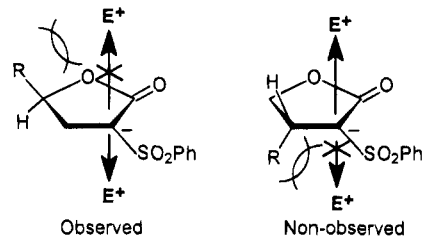
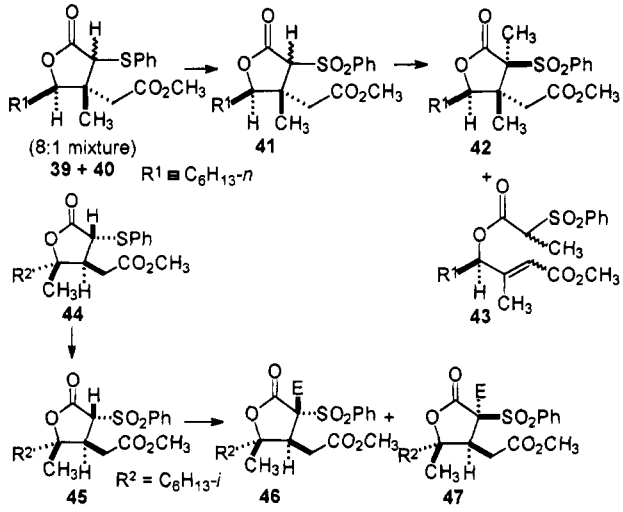


Figure 1.

Scheme 7



a planar anion.[17] In our case, the first option is highly unlikely because an additional carbonyl group vicinal to the carbanion should lead to a planar enolate in order to achieve the highest degree of stabilization of the negative species.

In order to obtain a model for our chemical results we performed an analysis of the anions for both free and associated metal species, using AM1, PM3, and MNDO Hamiltonians. The use of MNDO is essential if a parametrization of an associated cation (Li^+) is desired since this is the only alkaline metal cation fully parametrized.[18] The calculation employing one or two molecules of dimethylether as solvent was also possible using the MNDO–Li system. Because sodium parametrization is not available, a "sparkles" entity was used instead, considering its definition as a simplified atom of nuclear charge of +1, ionic radius of 0.7 Å, and zero heat of formation, no orbitals, and no ionization potential.[18] The analysis of rotamers through the sulfur–carbanion bond showed, in all cases, the presence of two energetic minima in which the phenyl group is oriented either to one or the other diastereoface of the enolate in the γ-lactone ring (Table 4).

The study showed that for carbanions derived from the α-(benzenesulfonyl) γ-lactones the rotamer with less energy consistently corresponds to that oriented *anti* relative to the β-substituent (the (methoxycarbonyl)-methylene group) (Figure 3) independent of the Hamiltonian used and even performing the study on cation-free species. When cation-associated species were used the cation is coordinated to both the carbonyl group of the γ-lactone and one oxygen of the sulfone group forming a relatively planar six-membered ring. Such coordination forces the benzene ring to be located over the lactone ring. This geometry is even observed when the calculations are performed on the free enolate. Also, the use of one or two molecules of dimethyl ether coordinated to the metal led to comparable geometries and energetic differences between the two rotamers. The interconversion barrier in all cases is in between 8–9 kcal/mol.

Although the anion geometry is essentially planar, the *anti*-π-face of the enolate relative to the β-substituent is encumbered by the phenyl group of the benzenesulfone, hindering attack by electrophiles. The overall stereochemical result is the electrophilic substitution of a hydrogen in an α-(benzenesulfonyl) γ-lactone with a formal retention of configuration (Scheme 8).

When the calculations were performed on the anion derived from the sulfide **16** a substantial difference was obtained depending on whether the metal cation was considered as "sparkles" (AM1 and MNDO) or Li^+ using the parametrization of MNDO. The geometry of the two conformers of the anion were similar to those obtained for the α-(benzenesulfonyl) anion when the first option was used (Figure 4). However, when Li^+ was used the system becomes highly planar, changing the coordinate from the sulfur to the phenyl group with a similar distance between the cation and all the carbons of the aromatic ring. In this case the two conformers found showed almost identical energies (Figure 4). The coordination between the Li^+ and the phenyl is so strong that all attempts to associate two molecules of solvent proved fruitless. The use of one molecule of dimethyl ether substantially does not affect either geometries or relative energies.

The obtained results using MNDO with the parametrization of Li^+ are in concordance with the experimental results. The two conformers with minor energy are almost isoenergetic, and hence, diastereoselection in the alkylation of the enolate should be absent. Although the coordination of Li^+ with aromatic rings is a commonly accepted feature,[19] the tendency of MNDO to overestimate the C–Li bond energies[20] is well known, and thus, a more accurate representation may be "something" intermediate between the extreme geometries of this

(18) Stewart, J. J. P. *MOPAC Manual* **1990**.

(19) (a) *Comprehensive Organometallic Chemistry*; Wilkinson, S. W., Ed.; Pergamon Press: New York, 1982; Vol. 1, p 23 and references cited therein. (b) Eiermann, M.; Hafner, K. *J. Am. Chem. Soc.* **1992**, *114*, 135.

(20) Sethson, I.; Johnels, D.; Lejon, T.; Edlund, U.; Wind, B.; Sygula, A.; Rabideau, P. W. *J. Am. Chem. Soc.* **1992**, *114*, 953.

Table 3. Influence of the Alkylating Agent over the Stereochemical Course in α-(Benzenesulfonyl)-β,γ,γ'-tetrasubstituted γ-Lactones 45

entry	electrophile	product (46:47)		yield (%)
1	CH_3I	E = CH_3, **48**		98
2	CH_2=$CHCH_2Cl$	E = CH_2CH=CH_2, **49**	E = CH_2CH=CH_2, **50**	72:13
3	$PhCH_2Br$	E = CH_2Ph, **51**	E = CH_2Ph, **52**	60:20
4	$BrCH_2CO_2CH_3$	E = $CH_2CO_2CH_3$, **53**		83

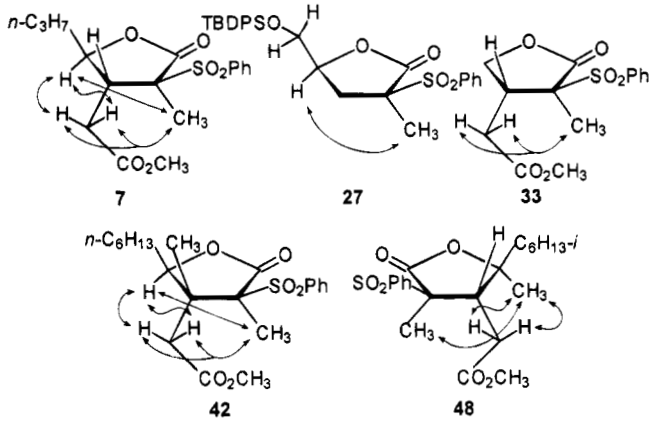


Figure 2. Representative NOE-interactions in alkylated γ-lactones.

planar model [options c and d in Figure 4] and the bent one [options a and b in Figure 4].

Conclusions

The alkylation of the anion generated α to the lactone carbonyl of α-(benzenesulfonyl) γ-lactones proceeded with excellent diasteroselection. The presence of the α-(benzenesulfonyl) group was essential to achieve such a degree of stereoselectivity, as was the presence of an alkyl group in the β-position of the γ-lactone ring. The application of the alkylation reaction was extended to the synthesis of bicyclic systems, including a cyclobutane with total stereochemical control.

In order to rationalize the stereochemical course of such a process extensive semiempirical calculations were performed. The π-facial selectivity for alkylation of the anion of the α-(benzenesulfonyl) γ-lactone was rationalized by studying the stability of the enolates. The coordination of the cation with one oxygen of the sulfone group and the oxygen of the enolate causes the *anti*-π-face of the enolate relative to the β-substituent to be encumbered by the phenyl group of the phenylsulfone, directing electrophiles to the *syn* face. When the sulfur is not oxidized, the two major conformers are found to be essentially isoenergetic, accounting for the poor diastereofacial selection observed.

Experimental Section

Materials, Methods, and Computational Methods. Essentially similar to those used in ref 6b.

General Procedure for the Alkylation of α-(Benzenesulfonyl) γ-Lactones. Preparation of Methyl (2*R*,3*R*,4*S*)-[4-(Benzenesulfonyl)-4-methyl-5-oxo-2-propyltetrahydrofuran-3-yl]acetate (7). To a suspension of NaH (10.6 mg, 0.35 mmol, 80% in mineral oil) in dry DMF (1 mL) under argon was added dropwise the lactone **4**[6] (100 mg, 0.29 mmol) in dry DMF (0.5 mL) at 0 °C. The reaction mixture was stirred for 15 min, after which time CH_3I (22 μL, 0.35 mmol) was added. The reaction was allowed to warm to rt and stirred for 8 h. After this period TLC showed complete conversion. Then to the reaction mixture was added AcOH (30 μL) and H_2O (10 mL), and it was extracted with ether (3 × 3 mL). The combined organic phases were washed with a saturated aqueous solution of $NaHCO_3$ (10 mL) and brine (10 mL), dried over $MgSO_4$, concentrated and purified by column chromatography, yielding **7** (91.6 mg, 88% yield) as an oil: $[\alpha]^{25}_D$ +22.1° (*c* 1.79, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.90 (t, *J* = 7.1 Hz, 3 H), 1.26 (s, 3 H), 1.53 (m, 4 H), 2.39 (dd, *J* = 15.7, 8.7 Hz, 1 H), 2.87 (dd, *J* = 15.7, 4.3 Hz, 1 H), 3.44 (ddd, *J* = 8.7, 8.7, 4.3 Hz, 1 H), 3.75 (s, 3 H), 4.09 (ddd, *J* = 8.4, 8.4, 3.2 Hz, 1 H), 7.63 (m, 3 H), 7.99 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 13.7 (q), 14.3 (q), 18.3 (t), 33.1 (t), 35.5 (t), 40.6 (d), 52.2 (q), 70.6 (s), 82.3 (d), 128.8 (d), 131.4 (d), 134.1 (s), 134.7 (d), 171.1 (s), 171.6 (s); IR ($CHCl_3$) (cm^{-1}): 2928, 1774, 1738, 1311, 1154, 1085; MS *m/z* (relative intensity) 355 (M + 1)$^+$ (32), 323 (11), 281 (13), 213 (100), 141 (50); HRMS calcd for $C_{17}H_{22}O_6S$ (M)$^+$ 354, 1137, found 354.1139.

Preparation of Methyl (2*R*,3*R*,4*S*)-[4-Allyl-4-(benzenesulfonyl)-5-oxo-2-propyltetrahydrofuran-3-yl]acetate (8). The general allylation procedure was applied to **4**[6] on a 100 mg (0.29 mmol) scale using allyl bromide (31 μL, 0.35 mmol) for 4 h, yielding **8** (108.4 mg, 97% yield) as an oil: $[\alpha]^{25}_D$ +24.6° (*c* 1.85, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.83 (t, *J* = 6.9 Hz, 3 H), 1.33 (m, 2 H), 1.58 (m, 2 H), 2.50 (dd, *J* = 15.8, 8.8 Hz, 1 H), 2.79 (dd, *J* = 15.8, 8.7 Hz, 1 H), 2.95 (d, *J* = 12.5 Hz, 2 H), 3.49 (ddd, *J* = 9.1, 9.1, 3.7 Hz, 1 H), 3.74 (s, 3 H), 4.02 (ddd, *J* = 8.8, 8.8, 2.8 Hz, 1 H), 5.24 (m, 2 H), 5.56 (m, 1 H), 7.65 (m, 3 H), 7.98 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 14.1 (q), 18.3 (t), 32.6 (t), 33.8 (t), 35.9 (t), 41.1 (d), 52.6 (q), 73.7 (s), 83.3 (d), 122.9 (t), 129.4 (d), 130.1 (d), 131.8 (d), 134.6 (s), 135.2 (d), 170.5 (s), 171.7 (s); IR ($CHCl_3$) (cm^{-1}) 2960, 1772, 1738, 1312, 1153, 1082; MS *m/z* (relative intensity) 349 (M − OCH_3)$^+$ (11), 265 (8), 239 (88), 141 (17), 125 (36); HRMS calcd for $C_{18}H_{21}O_5S$ (M − OCH_3)$^+$ 349.1109, found 349.1095.

Preparation of Methyl (2*R*,3*R*,4*S*)-[4-(Benzenesulfonyl)-4-benzyl-5-oxo-2-propyltetrahydrofuran-3-yl]acetate (9). The general alkylation procedure was applied to **4**[6] on a 100 mg (0.29 mmol) scale using benzyl bromide (42 μL, 0.35 mmol) for 4 h, yielding **9** (118.9 mg, 94% yield) as an oil: $[\alpha]^{25}_D$ +34.6° (*c* 2.08, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.67 (t, *J* = 7.1 Hz, 3 H), 1.21 (m, 2 H), 1.35 (m, 2 H), 2.38 (dd, *J* = 16.4, 8.5 Hz, 1 H), 2.98 (ddd, *J* = 8.5, 8.5, 2.9 Hz, 1 H), 3.12 (dd, *J* = 16.4, 2.9 Hz, 1 H), 3.30 (d, *J* = 14.1 Hz, 1 H), 3.52 (ddd, *J* = 8.9, 8.9, 2.6 Hz, 1 H), 3.63 (d, *J* = 14.1 Hz, 1 H), 3.73 (s, 3 H), 7.27 (m, 5 H), 7.65 (m, 3 H), 8.05 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 13.9 (q), 18.0 (t), 32.3 (t), 34.8 (t), 35.2 (t), 41.3 (d), 52.7 (q), 75.4 (s), 83.0 (d), 128.6 (d), 129.3 (d), 129.5 (d), 130.5 (d), 133.3 (d), 134.6 (s), 135.0 (s), 135.2 (d), 171.4 (s), 171.8 (s); IR ($CHCl_3$) (cm^{-1}) 2990, 1770, 1740, 1315, 1155, 1085; MS *m/z* (relative intensity) 430 (M)$^+$ (12), 399 (M − OCH_3)$^+$ (2), 398 (7), 288 (100), 91 (46); HRMS calcd for $C_{22}H_{23}O_5S$ (M − OCH_3)$^+$ 399.1266, found 399.1254.

Preparation of Methyl (2*R*,3*R*,4*S*)-[4-(Benzenesulfonyl)-4-butyl-5-oxo-2-propyltetrahydrofuran-3-yl]acetate (10). The general alkylation procedure was applied to **4**[6] on a 100 mg (0.29 mmol) scale using *n*-butyl bromide (38 μL, 0.35 mmol) for 6 h, yielding **10** (96.7 mg, 83% yield) as an oil: $[\alpha]^{25}_D$ +30.5° (*c* 1.66, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.89 (t, *J* = 7.2 Hz, 3 H), 0.93 (t, *J* = 7.2 Hz, 3 H), 1.34 (m, 6 H), 1.64 (m, 2 H), 2.02 (m, 1 H), 2.16 (m, 1 H), 2.41 (dd, *J* = 15.7, 8.8 Hz, 1 H), 2.91 (dd, *J* = 15.7, 3.9 Hz, 1 H), 3.48 (ddd, *J* = 8.8, 8.8, 3.9 Hz, 1 H), 3.75 (s, 3 H), 4.05 (ddd, *J* = 8.4, 8.4, 2.6 Hz, 1 H), 7.65 (m, 3 H); 7.98 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 13.5 (q), 13.7 (q), 17.9 (t), 22.9 (t) 27.3 (t), 28.5 (t), 32.4 (t), 35.9 (t), 44.6 (d), 52.2 (q), 73.6 (s), 83.1 (d), 128.9 (d), 131.4 (d), 134.6 (d), 134.6 (s), 170.5 (s), 171.7 (s); IR ($CHCl_3$) (cm^{-1}) 2961, 1771, 1738, 1311, 1151, 1082; MS *m/z* (relative intensity) 397 (M + 1)$^+$ (37), 365 (10), 279 (23), 255 (100), 149 (86); HRMS calcd for $C_{20}H_{29}O_6S$ (M + 1)$^+$ 397.1685, found 397.1665.

Table 4. Energetic Study of the α-Carbanion of Substituted γ-Lactones with α-(Benzenesulfonyl) or α-(Phenylthio) Groups

lactone	associated cation	Hamiltonian used	dihedral Ph−S−C4−C3 (deg)[a]	ΔH (kcal/mol)	ΔE[b] (kcal/mol)
4	Na[c]	AM1	−84.10	−342.47	1.22
			100.42	−341.25	
		AM1	−106.50	−279.75	0.35
			117.67	−279.40	
	Na[c]	PM3	−73.27	−332.72	1.32
			89.40	−331.40	
	Na[c]	MNDO	−51.78	−199.54	1.38
			85.87	−198.16	
	Li	MNDO	−59.10	−126.66	1.51
			81.34	−125.15	
	Li + 1 ether[d]	MNDO	−60.40	−192.95	1.41
			82.70	−191.54	
	Li + 2 ether[d]	MNDO	−58.33	−251.57	1.54
			82.24	−250.03	
41	Na[c]	AM1	−94.20	−361.48	0.78
			99.61	−360.70	
		AM1	−108.88	−299.18	0.39
			118.40	−298.79	
		MNDO	−129.44	−141.18	0.25
			135.33	−140.93	
	Li	MNDO	−78.00	−129.81	0.57
			81.86	−129.24	
	Li + 1 ether[d]	MNDO	−79.96	−196.14	0.57
			83.39	−195.57	
	Li + 2 ether[d]	MNDO	−79.23	−254.61	0.55
			82.53	−254.06	
16	Na[c]	AM1	−89.19	−258.65	0.48
			96.64	−258.17	
		AM1	−87.15	−200.49	0.26
			94.47	−200.23	
	Na[c]	PM3	−83.87	−253.31	0.76
			94.28	−252.45	
	Na[c]	MNDO	−84.22	−249.69	1.04
			96.89	−248.65	
	Li	MNDO	−148.50	−187.31	−0.17
			154.06	−187.48	
	Li + 1 ether[d]	MNDO	−147.21	−250.62	−0.15
			152.97	−250.77	
	Li + 2 ether[d]	MNDO	−147.19	−302.51	−0.15
			152.94	−302.66	

[a] Dihedral angles for rotamers with less energetic values. [b] Energetic difference between the two less energetic rotamers. [c] "Sparkles". [d] One or two molecules of dimethyl ether are coordinated to the metal.

Preparation of Methyl (3*S*,4*R*,5*R*)-3-[3-(Benzenesulfonyl)-4-[(methoxycarbonyl)methyl]-2-oxo-5-propyltetrahydrofuran-3-yl]acrylate (11). The general alkylation procedure was applied to **4**[6] on a 100 mg (0.29 mmol) scale in a 1:1 THF:HMPA mixture (3 mL) using lithium bis(trimethylsilyl)-amide 1 M in THF (320 μL, 0.32 mmol) as base, and methyl propiolate (30 μL, 0.44 mmol), for 2 h at −78 °C, yielding the unseparable *E*:*Z* mixture **11** (97.3 mg, 78% yield, ratio *E*:*Z*, 5:1, determined by NMR) as an oil. Data for the major isomer (*E*)-**11**: ^{1}H-NMR ($CDCl_3$) δ 0.94 (t, *J* = 6.5 Hz, 3 H), 1.67 (m, 4 H), 2.45 (dd, *J* = 15.9, 8.7 Hz, 1 H), 3.01 (dd, *J* = 15.9, 4.1 Hz, 1 H), 3.67 (m, 1 H), 3.74 (s, 3 H), 3.76 (s, 3 H), 4.10 (ddd, *J* = 5.8, 2.9, 2.9 Hz, 1 H), 5.89 (d, *J* = 16.0 Hz, 1 H), 6.97 (d, *J* = 16.0 Hz, 1 H), 7.62 (m, 3 H), 7.89 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 13.6 (q), 18.5 (t), 33.4 (t), 35.2 (t), 42.5 (d), 52.2 (q), 52.3 (q), 67.5 (s), 82.3 (d), 128.7 (d), 129.6 (d), 130.9 (s), 131.4 (d), 133.8 (d), 135.2 (d), 164.5 (s), 167.6 (s), 170.6 (s); IR ($CHCl_3$) (cm^{-1}) 2954, 1773, 1732, 1650, 1325, 1219, 1151; MS *m*/*z* (relative intensity) 425 $(M + 1)^+$ (53), 424 $(M)^+$, (20), 393 (30), 293 (45), 251 (96), 141 (32), 77 (100).

Preparation of Methyl (3*S*,4*R*,5*R*)-3-[3-(Benzenesulfonyl)-4-[(methoxycarbonyl)methyl]-2-oxo-5-propyltetrahydrofuran-3-yl]propionate (12). The general alkylation procedure was applied to **4**[6] on a 100 mg (0.29 mmol) scale on a 1:1 THF:HMPA mixture (3 mL) using lithium bis(trimethylsilyl)amide 1 M in THF (323 μL, 0.32 mmol) as base and methyl acrylate (40 μL, 0.44 mmol), for 4 h at −78 °C, yielding **12** (100.5 mg, 85% yield) as an oil: $[\alpha]^{25}_D$ +21.1° (*c*, 1.93, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.84 (t, *J* = 6.9 Hz, 3 H), 1.32 (m, 2 H), 1.6 (m, 2 H), 2.29 (m, 1 H), 2.36 (dd, *J* = 16.1, 8.8 Hz, 1 H), 2.52 (m, 1 H), 2.62 (m, 2 H), 2.94 (dd, *J* = 16.1, 3.2 Hz, 1 H), 3.36 (ddd, *J* = 8.8, 8.8, 3.2 Hz, 1 H), 3.67 (s, 3 H), 3.76 (s, 3 H), 4.12 (ddd, *J* = 8.6, 8.6, 2.8 Hz, 1 H), 7.66 (m, 3 H), 8.01 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 13.6 (q), 17.8 (t), 22.6 (t), 29.1 (t), 31.6 (t), 34.9 (t), 42.1 (d), 52.0 (q), 52.3 (q), 71.4 (s), 82.2 (d), 129.1 (d), 131.4 (d), 134.4 (s), 134.9 (d), 169.4 (s), 171.2 (s), 172.4 (s); IR ($CHCl_3$) (cm^{-1}) 3019, 1772, 1735, 1438, 1210, 1046; MS *m*/*z* (relative intensity): 396 $(M + 1 - OCH_3)^+$ (1), 395 $(M - OCH_3)^+$ (6), 285 (11), 253 (48), 77 (100); HRMS calcd for $C_{19}H_{24}O_7S$ $(M + 1 - OCH_3)$ 396.1243, found 396.1247.

Preparation of (3*R*,3a*R*,7a*S*)-7a-(Benzenesulfonyl)-6-(hydroxymethoxymethylene)-3-propyltetrahydroisobenzofuran-1,5-dione (13). The procedure was performed as described above for **12**, but the reaction was allowed to warm until rt was reached and stirred for 1 h until TLC showed that it was completed. Then it was diluted with ether (5 mL) and washed with saturated aqueous solution of NH_4Cl (5 mL). The aqueous phase was extracted with ether (2 × 5 mL). The combined organic phases were dried over $MgSO_4$, concentrated, and purified, yielding **13** (102 mg, 88% yield) as an oil: $[\alpha]^{25}_D$ −36.0° (*c* 1.5, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.94 (t, *J* = 7.3 Hz, 3 H), 1.61 (m, 4 H), 2.40 (dd, *J* = 15.7, 2.1 Hz, 1 H), 2.66 (d, *J* = 14.3 Hz, 1 H), 2.7 (dd, *J* = 15.7, 6.0 Hz, 1 H), 2.94 (d, *J* = 14.3 Hz, 1 H), 3.42 (ddd, *J* = 6.0, 6.0, 2.1 Hz, 1 H), 3.67 (s, 3 H), 3.88 (m, 1 H), 7.68 (m, 3 H), 7.93 (m, 2 H), 12.1 (br s, 1 H); ^{13}C-NMR ($CDCl_3$) δ 14.1 (q), 19.1 (t), 26.1 (t), 32.2 (t), 37.3 (t), 41.7 (d), 52.3 (q), 73.4 (s), 83.5 (d), 94.1 (s), 129.4 (d), 131.5 (d), 134.7 (s), 135.3 (d), 170.8 (s), 171.8 (s), 172.8 (s); IR ($CHCl_3$)

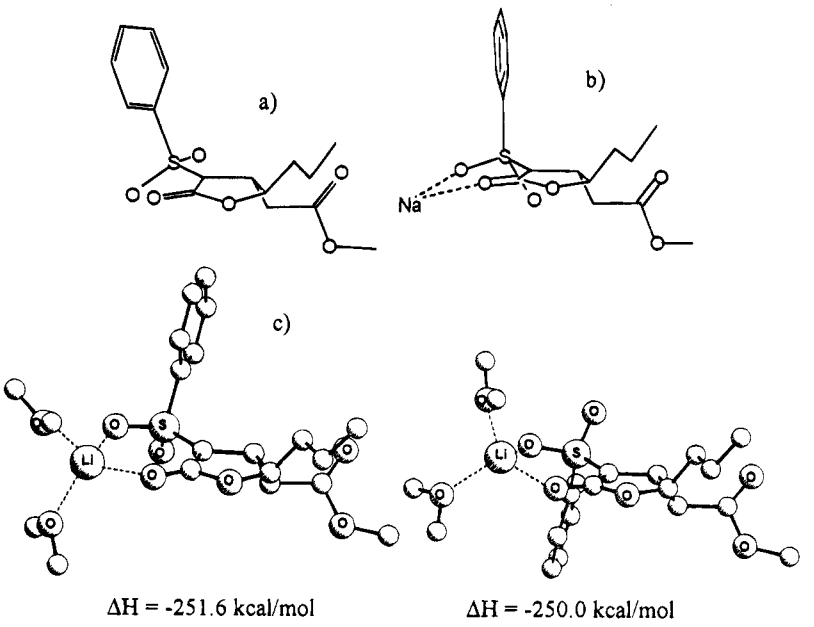
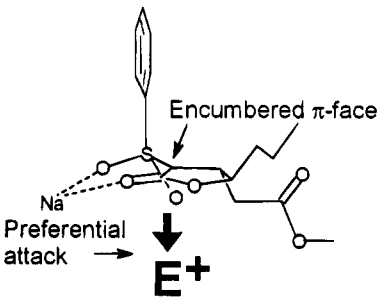


Figure 3. Conformers of lower energy for the anion of the γ-lactone **4** using (a) free anion (MOPAC/AM1); (b) anion−Na^+ sparkles (MOPAC/AM1); (c) the two less energetic conformers for the anion−Li^+−two molecules of ether (MOPAC/MNDO).

Scheme 8



(cm^{-1}) 3302, 2991, 1769, 1661, 1621, 1310, 1149, 1098; MS *m/z* (relative intensity) 395 $(M + 1)^+$ (32), 363 (39), 330 (4), 252 (100), 190 (85); HRMS calcd for $C_{19}H_{22}O_7S$ $(M)^+$ 394.1086, found 394.1096.

Preparation of (3*S*,4*R*,5*R*)-3-(Benzenesulfonyl)-3-benzyl-4-(2-hydroxyethyl)-5-methyldihydrofuran-2-one (15). To a suspension of NaH (79.2 mg, 2.64 mmol, 80% in mineral oil) in dry CH_2Cl_2 (5.87 mL) under argon was added dropwise the alcohol−lactone **14** (500 mg, 1.76 mmol) at 0 °C. The reaction mixture was stirred for 15 min, and benzyl bromide (250 μL, 2.11 mmol) was added. Then it was allowed to warm to rt and additionally stirred for 8 h. The mixture was extracted with CH_2Cl_2 (3 × 5 mL), and the organic phase was washed with saturated aqueous solution of NH_4Cl (7 mL), dried over $MgSO_4$, concentrated, and purified by silica gel column chromatography, yielding **15** (606 mg, 92% yield) as an oil: $[\alpha]^{25}_D$ +27.9° (*c* 2.08, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 1.28 (d, *J* = 5.8 Hz, 3 H), 1.72 (m, 1 H), 2.33 (m, 1 H), 2.62 (br s, 1 H), 3.16 (m, 1 H), 3.29 (m, 1 H), 3.41 (s, 2 H), 3.75 (m, 1 H), 3.88 (m, 1 H), 7.28 (m, 5 H), 7.73 (m, 3 H), 8.08 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 19.8 (q), 30.4 (t), 35.3 (t), 43.8 (d), 60.82 (t), 76.8 (s), 79.9 (d), 127.9 (d), 128.8 (d), 128.9 (d), 130.1 (d), 131.7 (d), 133.2 (s), 134.6 (d), 171.5 (s); IR ($CHCl_3$) (cm^{-1}) 3531, 2937, 1769, 1448, 1309, 1148, 1081; MS *m/z* (relative intensity) 375 $(M + 1)^+$ (1), 233 (30), 215 (28), 187 (9), 143 (21), 91 (100); HRMS calcd for $C_{20}H_{23}O_5S$ $(M + 1)^+$ 375.1266, found 375.1230.

Preparation of Methyl (4*S*)- and (4*R*)-(2*R*,3*R*)-[4-Allyl-5-oxo-4-(phenylthio)-2-propyltetrahydrofuran-3-yl]acetates 17 and 18. The general alkylation procedure was applied to **16**[6] on a 100 mg (0.32 mmol) scale using allyl bromide (42 μL, 0.49 mmol) for 4 h, yielding **17** (59 mg, 52% yield) and **18** (48 mg, 43% yield), both as an oil: Compound **17**: $[\alpha]^{25}_D$ +21.1° (*c* 2.14, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.96 (t, *J* = 7.0 Hz, 3 H), 1.53 (m, 2 H), 1.63 (m, 2 H), 2.48 (m, 2 H), 2.58 (m, 1 H), 2.95 (m, 2 H), 3.78 (s, 3 H), 4.20 (m, 1 H), 5.21 (m, 2 H), 5.70 (m, 1 H), 7.40 (m, 3 H), 7.57 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 13.7 (q), 18.8 (t), 31.4 (t), 35.14 (t), 38.2 (t), 43.9 (d), 52.0 (q), 57.9 (s), 81.4 (d), 120.8 (t), 128.9 (d), 129.1 (s), 130.1 (d), 131.7 (d), 137.4 (d), 171.6 (s), 173.5 (s); IR ($CHCl_3$) (cm^{-1}) 2990, 1764, 1738, 1314, 1125, 997; MS *m/z* (relative intensity) 348 $(M)^+$ (77), 289 (12), 239 (100), 197 (63), 110 (52); HRMS calcd for $C_{19}H_{24}O_4S$ $(M)^+$ 348.1395, found 348.1399. Compound **18**: $[\alpha]^{25}_D$ +14.5° (*c*, 2.57, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.083 (t, *J* = 7.0 Hz, 3 H), 1.24 (m, 4 H), 2.40 (dd, *J* = 14.6, 8.2 Hz, 1 H), 2.58 (d, *J* = 7.2 Hz, 2 H), 2.69 (m, 1 H), 2.77 (dd, *J* = 14.6, 5.2 Hz, 1 H), 3.77 (s, 3 H), 4.08 (m, 1 H), 5.27 (m, 2 H), 5.90 (m, 1 H), 7.39 (m, 3 H), 7.61 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 13.7 (q), 17.8 (t), 31.3 (t), 35.5 (t), 37.0 (t), 43.8 (d), 51.9 (q), 59.3 (s), 81.5 (d), 120.3 (t), 129.0 (d), 129.3 (s), 129.9 (d), 131.4 (d), 137.2 (d), 171.6 (s), 174.5 (s).

Preparation of (2*R*,3*R*,4*S*)-[4-(Benzenesulfonyl)-2-methyl-5-oxotetrahydrofuran-3-yl]acetic Acid (20). To a stirred solution of lactone **19**[6] (2.21 g, 7.89 mmol) in THF:H_2O (4:1, 39.5 mL) was added NaOH (3.15 g, 78.9 mmol). The reaction was stirred for 1 h, until starting material was not detected by TLC. Then concentrated HCl was added at 0 °C until pH ≈ 1 was reached and extracted in AcOEt (2 × 30 mL). The combined organic phases were washed with 50 mL of a saturated solution of brine, dried over $MgSO_4$, evaporated in vacuo, and purified by column chromatography to give **20** (1.93 g, 92% yield) as an oil: $[\alpha]^{25}_D$ +22.2° (*c* 2.48, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 1.26 (d, *J* = 6.2 Hz, 3 H), 2.31 (m, 1 H), 2.62 (dd, *J* = 16.3, 7.0 Hz, 1 H), 2.71 (dd, *J* = 16.3, 5.1 Hz, 1 H), 3.8 (d, *J* = 10.7 Hz, 1 H), 4.33 (m, 1 H), 7.29 (m, 3 H), 7.54 (m, 2 H), 10.98 (br s, 1 H); ^{13}C-NMR ($CDCl_3$) δ 20.0 (q), 34.5 (t), 45.1 (d), 52.0 (d), 79.7 (d), 129.3 (d), 129.7 (d), 131.5 (s), 134.5 (d), 174.6 (s), 176.3 (s); IR ($CHCl_3$) (cm^{-1}) 3399, 2983, 1774, 1714, 1440, 1388, 1298, 1174, 1059; MS *m/z* (relative intensity) 266 $(M)^+$ (100), 221 (13), 207 (10), 110 (68), 77 (22); HRMS calcd for $C_{13}H_{14}O_4S$ $(M)^+$ 266.0612, found 266.0603.

Preparation of (2*R*,3*R*,4*S*)-[4-(Benzenesulfonyl)-2-methyl-5-oxotetrahydrofuran-3-yl]acetic Acid (21). To a stirred solution of lactone **20** (2 g, 7.52 mmol) in a biphasic solvent system (0.33 mL of CH_3CN−0.33 mL of CCl_4−0.5 mL of H_2O/mmol of compound) was added periodic acid as the stoichiometric oxidant (3.6 g, 15.8 mmol) and $RuCl_3 x H_2O$ (31.2 mg, 0.15 mmol) at rt. The reaction mixture was vigorously stirred for 2 h, and then ether (50 mL) was added and the stirring was continued for 10 min. After that time, $MgSO_4$ was added and the mixture was filtered through Whatman paper no. 2

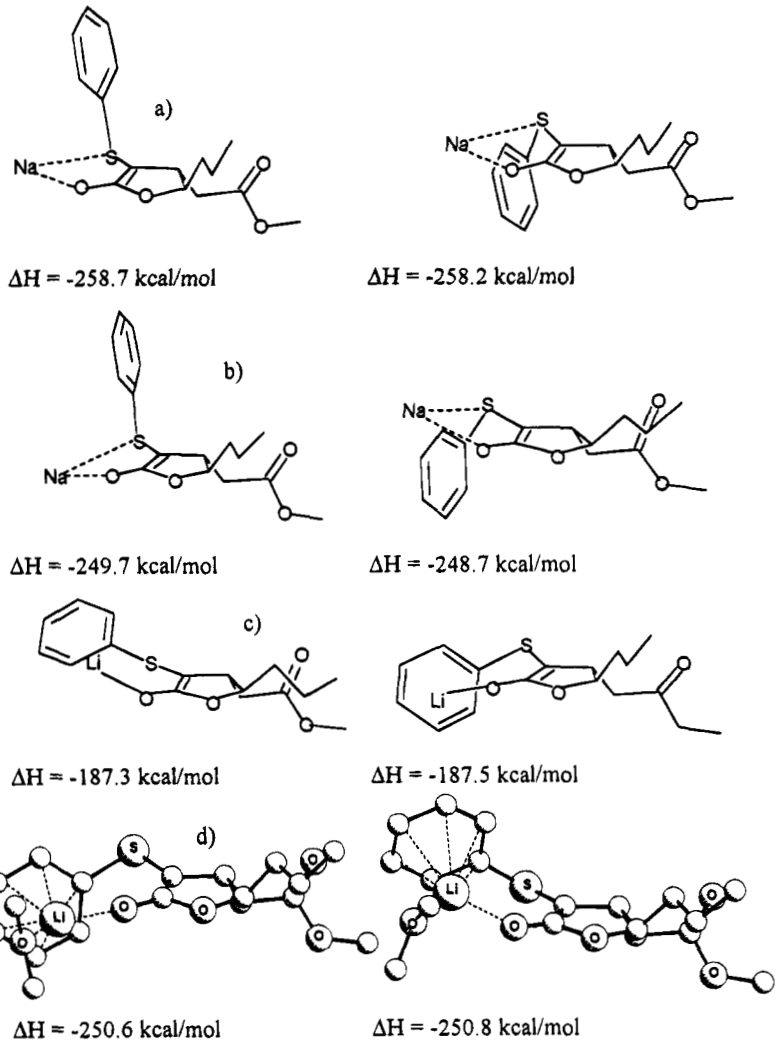


Figure 4. *Lower energy conformers for the anion of the γ-lactone* **16** using (a) anion–Na^+ sparkles (MOPAC/AM1); (b) anion-Na^+ sparkles (MOPAC/MNDO); (c) anion-Li^+ (MOPAC/MNDO); (d) anion–Li^+–one molecule of ether (MOPAC/MNDO).

and washed with ether (3 × 15 mL). The combined organic phases were concentrated, and the residue obtained was purified by flash chromatography to yield **21** as a white solid, mp 102–104 °C (2.04 g, 91% yield): $[\alpha]^{25}_D$ +24.6° (*c* 1.29, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 1.53 (d, *J* = 6.2 Hz, 3 H), 2.87 (dd, *J* = 17.4, 4.4 Hz, 1 H), 2.99 (dd, *J* = 17.4, 6.2 Hz, 1 H), 3.13 (m, 1 H), 4.41 (d, *J* = 8.6 Hz, 1 H), 4.47 (m, 1 H), 5.09 (br s, 1 H), 7.71 (m, 3 H), 7.97 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 20.0 (q), 34.6 (t), 39.7 (d), 67.7 (d), 79.0 (d), 129.2 (d), 129.4 (s), 129.7 (d), 134.8 (d), 174.6 (s), 177.0 (s); IR ($CHCl_3$) (cm^{-1}) 3399, 3018, 1776, 1716, 1360, 1323, 1151, 1024; MS *m/z* (relative intensity) 239 $(M - C_2H_3O_2)^+$ (2), 157 (5), 141 (19), 77 (100); HRMS calcd for $C_{11}H_{11}O_4S$ $(M - C_2H_3O_2)^+$ 239.0378, found 239.0377.

Preparation of (3*S*,4*R*,5*R*)-3-(Benzenesulfonyl)-4-(2-hydroxyethyl)-5-methyldihydrofuran-2-one (14). To a stirred solution of crystalline solid **21** (2 g, 6.71 mmol) in dry THF (33.5 mL, 0.2 M) under argon was added dropwise the complex BH_3–Me_2S 1.2 M in THF (5.59 mL, 6.71 mmol) at −10 °C. The mixture was allowed to warm slowly to rt and stirred additionally for 6–8 h until TLC showed the end of the reaction. Then the mixture was cooled to 0 °C and poured into the same volume of cold H_2O (33.5 mL). The aqueous phase was saturated with solid K_2CO_3 and extracted with ether (3 × 10 mL). The combined ether extracts were washed with 30 mL of a saturated solution of brine, dried over $MgSO_4$, evaporated in vacuo, and purified by column chromatography to give the crystalline alcohol **14** (1.68 g, 88% yield): mp 72–74 °C; $[\alpha]^{25}_D$ +25.1° (*c* 1.89, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 1.48 (d, *J* = 6.3 Hz, 3 H), 1.86 (m, 2 H), 2.35 (br s, 1 H), 2.99 (m, 1 H), 3.87 (t, *J* = 5.6 Hz, 2 H), 4.21 (d, *J* = 7.3 Hz, 1 H), 4.36 (m, 1 H), 7.65 (m, 3 H), 7.98 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 20.5 (q), 35.1 (t), 40.9 (d), 59.5 (t), 69.5 (d), 80.5 (d), 129.2 (d), 129.5 (d), 134.6 (t), 136.9 (s), 167.5 (s); IR ($CHCl_3$) (cm^{-1}) 3547, 2936, 1772, 1354, 1321, 1149, 1084; MS *m/z* (relative intensity) 285 $(M + 1)^+$ (3), 267 (2), 254 (2), 239 (2), 141 (17), 77 (100); HRMS calcd for $C_{13}H_{17}O_5S$ $(M + 1)^+$ 285.0797, found 285.0814.

Preparation of 2-[(2*R*,3*R*,4*S*)-4-(Benzenesulfonyl)-2-methyl-5-oxotetrahydrofuran-3-yl]ethyl Methanesulfonate (22). To a stirred solution of **14** (500 mg, 1.76 mmol) in dry CH_2Cl_2 (17.6 mL, 0.1 M) under argon was slowly added Et_3N (290 μL, 2.11 mmol) at −20 °C. After 15 min of vigorous stirring, methanesulfonyl chloride was added (170 μL, 1.76 mmol) and stirring continued for 15 min. Then the reaction mixture was poured into ice and extracted with ether (3 × 5 mL), and the organic layer was washed with H_2O (5 mL) and brine (5 mL), dried over $MgSO_4$, concentrated, and purified by silica gel column chromatography, yielding **22** (612 mg, 96% yield): $[\alpha]^{25}_D$ +19.2° (*c* 1.37, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 1.43 (d, *J* = 6.2 Hz, 3 H), 2.14 (m, 2 H), 2.87 (m, 1 H), 3.06 (s, 3 H), 4.09 (d, *J* = 7.6 Hz, 1 H), 4.31 (m, 1 H), 4.38 (t, *J* = 5.9 Hz, 2 H), 7.63 (m, 3 H), 7.93 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 20.3 (q), 32.4 (t), 37.1 (q), 40.6 (d), 67.1 (t), 69.6 (d), 80.0 (d), 129.3 (d), 129.6 (d), 134.8 (d), 136.7 (s), 166.9 (s); IR ($CHCl_3$) (cm^{-1}) 2933, 1772, 1375, 1320, 1175, 1084; MS *m/z* (relative intensity) 298 (15), 239 (9), 141 (45), 77 (100); HRMS calcd for $C_{14}H_{18}O_5S$ 298.0875, found 298.0877.

Preparation of (1*S*,4*R*,5*R*)-1-(Benzenesulfonyl)-4-methyl-3-oxa-bicyclo[3.2.0]heptan-2-one (23). Compound **22** (500 mg, 1.38 mmol) was dissolved in dry DMF (13.8 mL, 0.1 M) under argon, and NaH (49.7 mg, 1.66 mmol, 80% in mineral oil) was added at 0 °C, with stirring. The reaction was allowed to warm to rt and monitored for TLC until complete conversion

(4 h). Then it was quenched with AcOH (100 μL), extracted with ether (2 × 20 mL), and washed with H_2O (20 mL) and brine (20 mL). The crude obtained was purified by flash chromatography, yielding **23** (316 mg, 86% yield) as an oil: $[\alpha]^{25}_D$ +26.9° (*c* 1.06, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 1.35 (d, *J* = 6.4 Hz, 3 H), 1.95 (m, 1 H), 2.08 (m, 1 H), 2.40 (m, 1 H), 2.79 (m, 1 H), 3.44 (m, 1 H), 4.48 (q, *J* = 6.4 Hz, 1 H), 7.57 (m, 3 H), 7.86 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 20.9 (q), 21.2 (t), 25.5 (t), 30.1 (s), 43.2 (d), 81.9 (d), 129.4 (d), 130.6 (d), 135.0 (d), 135.6 (s), 171.7 (s); IR ($CHCl_3$) (cm^{-1}) 3019, 1770, 1634, 1311, 1153, 1086; MS *m/z* (relative intensity) 267 $(M + 1)^+$ (19), 239 (1), 223 (1), 167 (9), 125 (100), 77 (33); HRMS calcd for $C_{13}H_{15}O_4S$ $(M + 1)^+$ 267.0691, found 267.0692.

Preparation of 2-[(2*R*,3*R*,4*S*)-4-(Benzenesulfonyl)-2-methyl-4-(methylsulfonyl)-5-oxotetrahydrofuran-3-yl]-ethyl Methanesulfonate (24). To a stirred solution of **14** (200 mg, 0.7 mmol) in dry CH_2Cl_2 (7 mL) under argon was added dropwise Et_3N (216 μL, 1.55 mmol) at room temperature. After 15 min, to the vigorously stirred solution was added methanesulfonyl chloride (138 μL, 1.41 mmol) and the mixture was monitored by TLC (1 h). The reaction mixture was poured into ice and extracted with ether (3 × 5 mL), and the combined organic phases were washed with H_2O (5 mL) and brine (5 mL), dried over $MgSO_4$, and concentrated. The crude obtained was purified by silica gel column chromatography, yielding **24** (282 mg, 91% yield) as an oil: $[\alpha]^{25}_D$ +22.3° (*c* 2.23, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 1.25 (d, *J* = 6.2 Hz, 1 H), 2.34 (m, 2 H), 2.76 (m, 1 H), 3.07 (s, 3 H), 3.13 (s, 3 H), 4.35 (m, 1 H), 4.5 (t, *J* = 5.9 Hz, 2 H), 7.68 (m, 3 H), 8.07 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 19.6 (q), 26.3 (t), 31.5 (s), 37.3 (q), 43.8 (q), 46.7 (d), 67.7 (t), 80.3 (d), 129.6 (d), 130.8 (s), 131.9 (d), 136.0 (d), 166.7 (s); IR ($CHCl_3$) (cm^{-1}) 3029, 1767, 1331, 1175, 1081; MS *m/z* (relative intensity) 345 $(M - OMs)^+$ (2), 299 (1), 253 (2), 204 (7), 149 (78), 141 (30), 77 (100); HRMS calcd for $C_{14}H_{17}O_6S_2$ $(M - OMs)^+$ 345.0388, found 345.0405.

Preparation of (3*R*,5*S*)-3-(Benzenesulfonyl)-5-[[(*tert*-butyldiphenylsilyl)oxy]methyl]dihydrofuran-2-one (26). The RuO_4 oxidation described above used to obtain **21** was applied to **25**[14] on a 100 mg (0.22 mmol) scale for 2 h, yielding **26** (97.3 mg, 91% yield) as an oil: $[\alpha]^{25}_D$ +14.6° (*c* 2.31, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 1.02 (s, 9 H), 2.74 (m, 1 H), 3.01 (m, 1 H), 3.68 (dd, *J* = 11.7, 2.5 Hz, 1 H), 3.94 (dd, *J* = 11.7, 2.6 Hz, 1 H), 4.33 (dd, *J* = 10.1, 6.4 Hz, 1 H), 4.74 (m, 1 H), 7.39 (m, 8 H), 7.62 (m, 5 H), 7.96 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 19.1 (s), 26.7 (q), 31.6 (t), 45.3 (d), 65.1 (t), 77.9 (d), 127.8 (d), 128.4 (d), 129.2 (d), 129.9 (d), 132.2 (s), 132.6 (s), 133.2 (d), 135.4 (d), 135.5 (d), 175.0 (s); IR ($CHCl_3$) (cm^{-1}) 2961, 1781, 1325, 1152, 1112, 1085; MS *m/z* (relative intensity) 437 $(M - Bu\text{-}t)^+$ (45), 359 (19), 295 (31), 199 (85), 77 (100); HRMS calcd for $C_{23}H_{21}O_5SiS$ $(M - Bu\text{-}t)^+$ 437.0879, found 437.0883.

Preparation of (3*S*,5*S*)-3-Methyl-3-(benzenesulfonyl)-5-[[(*tert*-butyldiphenylsilyl)oxy]methyl]dihydrofuran-2-one (27). The general alkylation procedure was applied to **26** on a 90 mg (0.18 mmol) scale using CH_3I (14 μL, 0.22 mmol) for 2 h at rt, yielding **27** (62.9 mg, 68% yield) as an oil: $[\alpha]^{25}_D$ +14.3° (*c* 2.20, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 1.08 (s, 9 H), 1.61 (s, 3 H), 2.30 (dd, *J* = 14.1, 7.1 Hz, 1 H), 3.14 (dd, *J* = 14.1, 8.2 Hz, 1 H), 3.84 (d, *J* = 5.0 Hz, 2 H), 4.54 (m, 1 H), 7.42 (m, 6 H), 7.54 (t, *J* = 7.7 Hz, 2 H), 7.67 (m, 5 H), 7.95 (d, *J* = 7.2 Hz, 2 H); ^{13}C-NMR ($CDCl_3$) δ 19.2 (s), 20.0 (q), 26.7 (q), 32.1 (t), 64.3 (t), 68.0 (s), 76.5 (d), 127.8 (d), 128.7 (d), 129.9 (d), 131.1 (d), 132.7 (s), 132.8 (s), 134.2 (s), 134.5 (d), 135.5 (d), 135.6 (d), 171.4 (s); IR ($CHCl_3$) (cm^{-1}) 2935, 1777, 1310, 1154, 1112; MS *m/z* (relative intensity) 508 $(M)^+$ (4), 451 $(M - Bu\text{-}t)^+$ (52), 163 (93), 141 (100), 125 (95); HRMS calcd for $C_{24}H_{23}O_5SiS$ $(M - Bu\text{-}t)^+$ 451.1036, found 451.1021.

Preparation of (2,2-Dimethyl[1,3]dioxolan-4-yl)methyl (Phenylthio)acetate (28). To a stirred solution of (phenylthio)acetic acid (3.06 g, 18.2 mmol) in dry CH_2Cl_2 (75.7 mL) under argon were sequentially added with stirring DMAP (92.5 mg, 0.75 mmol) and (2,2-dimethyl[1,3]dioxolan-4-yl)methanol (2 g, 15.15 mmol) at 0 °C. The mixture was stirred for 15 min, after which time was added DCC (2.18 g, 10.6 mmol). Then it was allowed to warm to rt and stirred until TLC showed the end of the reaction (≈3 h). The mixture was diluted in CH_2Cl_2 (100 mL), filtered through a pad of Celite, washed with HCl (5‰ w/v) aqueous solution (2 × 100 mL), saturated aqueous solution of $NaHCO_3$ (100 mL), and brine (100 mL), dried over $MgSO_4$, concentrated, and purified in silica gel column chromatography, yielding **28** (4.1 g, 96% yield) as an oil: ^{1}H-NMR ($CDCl_3$) δ 1.35 (s, 3 H), 1.41 (s, 3 H), 3.65 (dd, *J* = 8.5, 6.0 Hz, 1 H), 3.67 (s, 2 H), 3.99 (dd, *J* = 8.5, 6.4 Hz, 1 H), 4.14 (m, 2 H), 4.23 (m, 1 H), 7.26 (m, 3 H), 7.41 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 25.3 (q), 26.6 (q), 36.4 (t), 65.5 (t), 66.1 (t), 73.2 (d), 109.8 (s), 127.0 (d), 129.0 (d), 130.0 (d), 134.7 (s), 169.4 (s); IR ($CHCl_3$) (cm^{-1}) 3018, 1735, 1380, 1154, 1084; MS *m/z* (relative intensity) 282 $(M)^+$ (36), 267 (72), 168 (26), 123 (100), 101 (71), 59 (71); HRMS calcd for $C_{14}H_{18}O_4S$ $(M)^+$ 282.0926, found 282.0922.

Preparation of 2,3-Dihydroxypropyl (Phenylthio)acetate (29). To a stirred solution of **28** (3 g, 0.011 mol) in THF (112 mL, 0.1 M) was added concd HCl (10% mol) at rt. When TLC showed no starting material, the reaction was quenched with Et_3N until neutral pH was reached and extracted with ether (150 mL). The organic phase was washed with brine (150 mL), dried over $MgSO_4$, and concentrated, yielding after flash chromatography **29** (2.32 g, 90% yield) as an oil: ^{1}H-NMR ($CDCl_3$) δ 2.62 (br s, 1 H), 3.20 (br s, 1 H), 3.49 (dd, *J* = 11.5, 5.9 Hz, 1 H), 3.58 (dd, *J* = 11.5, 3.1 Hz, 1 H), 3.66 (s, 2 H), 3.83 (m, 1 H), 4.14 (m, 2 H), 7.25 (m, 3 H), 7.38 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 36.9 (t), 63.6 (t), 66.5 (t), 70.3 (d), 127.6 (d), 129.6 (d), 130.4 (d), 135.0 (s), 170.5 (s); IR ($CHCl_3$) (cm^{-1}): 3599, 3023, 1734, 1442, 1277, 1131; MS *m/z* (relative intensity) 242 $(M)^+$ (21), 168 (24), 123 (100), 101 (63), 57 (83); HRMS calcd for $C_{11}H_{14}O_4S$ $(M)^+$ 242.0613, found 242.0622.

Preparation of Methyl 4-[(Phenylthio)acetoxy]but-2(*E*)-enoate (30). To a stirred solution of **29** (2 g, 8.26 mmol) in C_6H_6 (82.6 mL) was added $Pb(OAc)_4$ (4.66 g, 10.5 mmol) at 0 °C under argon. The reaction mixture was allowed to warm to rt, and the solution was stirred for 1 h. Then it was poured into AcOEt (100 mL) and filtered through a pad of Celite. The resulting solution was treated with solid $NaHCO_3$ and filtered. The solvent was evaporated "in vacuo", and the resulting crude aldehyde was used without purification.

To a stirred solution of crude aldehyde in dry C_6H_6 (82.6 mL, 0.1 M) was added methyl (triphenylphosphoranylidene)-acetate (5.86 g, 17.5 mmol) at 0 °C under argon. The mixture was stirred for 2 h at rt and then extracted in ether (100 mL). The organic phase was washed with brine (50 mL), dried over $MgSO_4$, and concentrated, yielding after flash chromatography **30** (1.83 g, 83% yield, ratio *E*:*Z*, 12:1) as an oil: ^{1}H-NMR ($CDCl_3$) δ 3.67 (s, 2 H), 3.73 (s, 3 H), 4.73 (d, *J* = 4.5 Hz, 2 H), 5.96 (d, *J* = 15.7 Hz, 1 H), 6.85 (ddd, *J* = 15.7, 4.5, 4.5 Hz, 1 H), 7.24 (m, 3 H), 7.40 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 37.0 (t), 52.1 (q), 63.7 (t), 122.5 (d), 127.7 (d), 129.5 (d), 130.7 (d), 134.9 (s), 141.1 (d), 166.5 (s), 169.5 (s); IR ($CHCl_3$) (cm^{-1}) 3027, 1728, 1719, 1227, 1132; MS *m/z* (relative intensity) 266 $(M)^+$ (14), 150 (33), 123 (100), 85 (53), 77 (32); HRMS calcd for $C_{13}H_{14}O_4S$ $(M)^+$ 266.0613, found 266.0619.

Preparation of Methyl (3*R*,4*S*)- and (3*S*,4*R*)-[5-Oxo-4-(phenylthio)tetrahydrofuran-3-yl]acetate (31). To a suspension of NaH (140 mg, 4.1 mmol, 80% in mineral oil) in dry DMF (15 mL) under argon at −50 °C was added dropwise the unsaturated ester **30** (1 g, 3.76 mmol) in dry DMF (15 mL). The reaction mixture was stirred for 2 h, after which time TLC showed complete conversion into the lactone. The reaction was quenched with AcOH (0.4 mL) and extracted with ether (2 × 20 mL). The combined organic phases were washed with a saturated aqueous solution of $NaHCO_3$ (10 mL) and brine (10 mL), dried, and concentrated. Purification by column chromatography gave the lactone **31** (700 mg, 70%) yield as an oil: ^{1}H-NMR ($CDCl_3$) δ 2.49 (dd, *J* = 17.4, 10.2 Hz, 1 H), 2.73 (ddddd, *J* = 10.2, 8.4, 7.6, 7.2, 5.6 Hz, 1 H), 2.74 (dd, *J* = 17.4, 5.6 Hz, 1 H), 3.54 (d, *J* = 8.4 Hz, 1 H), 3.68 (s, 3 H), 3.95 (dd, *J* = 9.2, 7.6 Hz, 1 H), 4.43 (dd, *J* = 9.2, 7.2 Hz, 1 H), 7.32 (m, 3 H), 7.56 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 35.9 (t), 38.6 (d), 50.7 (d), 52.5 (q), 71.2 (t), 129.4 (d), 129.7 (d), 131.4 (s), 134.6 (d), 171.5 (s), 174.4 (s); IR ($CHCl_3$) (cm^{-1}) 3027, 1778, 1737, 1439, 1209, 1155, 1019; MS *m/z* (relative intensity) 266 $(M)^+$ (100), 147 (80), 109 (84), 71 (49), 65 (56), 59 (62); HRMS calcd for $C_{13}H_{14}O_4S$ $(M)^+$ 266.0613, found 266.0609.

Preparation of Methyl (3*R*,4*S*)- and (3*S*,4*R*)-[4-(Benzenesulfonyl)-5-oxotetrahydrofuran-3-yl]acetate (32). To a stirred solution of the lactone **31** (500 mg, 1.88 mmol) in MeOH (6.3 mL, 0.3 M) was added $KHSO_5$ (1.73 g, 2.82 mmol) in H_2O (5.64 mL) at 0 °C. The mixture was vigorously stirred for 5 h, until TLC showed completion. Then it was diluted with AcOEt (5 mL), and the organic phase was washed with H_2O (5 mL) and brine (5 mL), dried over $MgSO_4$, concentrated, and purified, giving **32** (532 mg, 95% yield) as an oil: ^{1}H-NMR ($CDCl_3$) δ 2.01 (dd, J = 16.8, 8.2 Hz, 1 H), 2.35 (dd, J = 16.8, 5.1 Hz, 1 H), 3.25 (s, 3 H), 3.32 (dd, J = 8.9, 6.0 Hz, 1 H), 3.40 (ddddd, J = 8.2, 7.8, 6.8, 6.0, 5.1 Hz, 1 H), 3.61 (d, J = 6.8 Hz, 1 H), 4.15 (dd, J = 8.9, 7.8 Hz, 1 H), 6.99 (m, 3 H), 7.99 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 33.8 (d), 36.8 (t), 52.6 (q), 67.8 (d), 71.5 (t), 129.7 (d), 129.9 (d), 135.2 (d), 136.9 (s), 167.8 (s), 171.2 (s); IR ($CHCl_3$) (cm^{-1}) 3027, 1782, 1737, 1326, 1168, 1082; MS *m/z* (relative intensity) 299 $(M + 1)^+$ (1), 267 $(M - OCH_3)^+$ (15), 234 (38), 157 (99), 141 (94), 77 (100); HRMS calcd for $C_{13}H_{15}O_6S$ $(M + 1)^+$ 299.0589, found 299.0594.

Preparation of Methyl (3*R*,4*S*)- and (3*S*,4*R*)-[4-(Benzenesulfonyl)-4-methyl-5-oxotetrahydrofuran-3-yl]acetate (33). The general alkylation procedure was applied to **32** on a 100 mg (0.34 mmol) scale using CH_3I (33 μL, 0.5 mmol) for 1 h at −30 °C, yielding **33** (98.8 mg, 90% yield), as a solid: mp 76−78 °C; ^{1}H-NMR ($CDCl_3$) δ 1.45 (s, 3 H), 2.44 (dd, J = 16.7, 11.1 Hz, 1 H), 2.90 (dd, J = 16.7, 3.7 Hz, 1 H), 3.74 (s, 3 H), 3.80 (dddd, J = 11.1, 7.9, 6.7, 3.7 Hz, 1 H), 3.96 (dd, J = 9.2, 6.7 Hz, 1 H), 4.77 (dd, J = 9.2, 7.9 Hz, 1 H), 7.60 (m, 2 H), 7.73 (m, 1 H), 7.94 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 14.9 (q), 34.2 (t), 36.0 (d), 52.7 (q), 69.4 (s), 71.1 (t), 129.4 (d), 131.6 (d), 134.4 (s), 135.3 (d), 171.4 (s), 172.1 (s); IR ($CHCl_3$) (cm^{-1}) 3018, 1778, 1737, 1448, 1312, 1227, 1150; MS *m/z* (relative intensity) 312 $(M)^+$ (1), 281 $(M - OCH_3)^+$ (7), 207 (46), 171 (100), 77 (45), 55 (83); HRMS calcd for $C_{14}H_{16}O_6S$ $(M)^+$ 312.0668, found 312.0681.

Preparation of Methyl (3*R,4*S**)- and (3*R**,4*R**)-[4-Allyl-4-(benzenesulfonyl)-5-oxotetrahydrofuran-3-yl]acetate (34, 35).** The general alkylation procedure was applied to **32** on a 100 mg (0.34 mmol) scale using allyl bromide (46 μL, 0.53 mmol) for 5 h at −30 °C, yielding **34** (82 mg, 72% yield) and **35** (14.7 mg, 13% yield) both as an solid: Compound **34**: mp 85−87 °C; ^{1}H-NMR (C_6D_6) δ 2.33 (dd, J = 16.2, 11.4 Hz, 1 H), 2.58 (dd, J = 14.4, 8.5 Hz, 1 H), 2.78 (dd, J = 14.4, 5.8 Hz, 1 H), 3.04 (dd, J = 16.2, 3.2 Hz, 1 H), 3.32 (s, 3 H), 3.42 (dd, J = 8.9, 8.9 Hz, 1 H), 4.06 (dddd, J = 11.4, 8.9, 8.9, 3.2 Hz, 1 H), 4.38 (dd, J = 8.9, 8.9 Hz, 1 H), 4.77 (dd, J = 10.1, 2.8 Hz, 1 H), 4.85 (dd, J = 16.9, 2.8 Hz, 1 H), 5.34 (dddd, J = 16.9, 10.1, 8.5, 5.8 Hz, 1 H), 7.01 (m, 3 H), 8.05 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 32.2 (t), 33.8 (t), 35.7 (d), 52.1 (q), 70.6 (t), 71.6 (s), 122.3 (t), 128.9 (d), 129.6 (d), 131.3 (d), 134.0 (s), 134.8 (d), 170.6 (s), 171.1 (s); IR ($CHCl_3$) (cm^{-1}): 3027, 1782, 1738, 1440, 1312, 1223; MS *m/z* (relative intensity) 339 $(M + 1)^+$ (4), 307 $(M - OCH_3)^+$ (20), 197 (100), 165 (72), 137 (76), 77 (100); HRMS calcd for $C_{16}H_{19}O_6S$ $(M + 1)^+$ 339.0902, found 339.0901. Compound **35**: mp 110−111 °C; ^{1}H-NMR ($CDCl_3$) δ 2.58 (dd, J = 13.6, 5.7 Hz, 1 H), 2.79 (dd, J = 13.6, 8.8 Hz, 1 H), 3.06 (dd, J = 17.6, 9.8 Hz, 1 H), 3.33 (dd, J = 17.6, 5.1 Hz, 1 H), 3.46 (dddd, J = 10.8, 9.8, 8.4, 5.1 Hz, 1 H), 3.76 (s, 3 H), 4.47 (dd, J = 10.8, 8.4 Hz, 1 H), 4.59 (dd, J = 8.4, 8.4 Hz, 1 H), 5.26 (dd, J = 11.9, 2.8 Hz, 1 H), 5.27 (dd, J = 14.7, 2.8 Hz, 1 H), 5.53 (dddd, J = 14.7, 11.9, 8.8, 5.7 Hz, 1 H), 7.58 (m, 2 H), 7.73 (m, 1 H), 7.83 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 31.95 (t), 35.68 (t), 38.02 (d), 52.53 (q), 71.63 (t), 72.65 (s), 123.12 (d), 129.15 (d), 130.01 (d), 131.28 (d), 135.35 (d), 135.39 (d), 171.15 (s), 172.01 (s); IR ($CHCl_3$) (cm^{-1}) 3034, 1769, 1735, 1309, 1205, 1148.

Preparation of Methyl (3*R,4*S**)- and (3*R**,4*R**)-[4-(Benzenesulfonyl)-4-benzyl-5-oxotetrahydrofuran-3-yl]-acetate (36, 37).** The general alkylation procedure was applied to **32** on a 100 mg (0.34 mmol) scale using benzyl bromide (63 μL, 0.53 mmol) for 10 h at −30 °C, yielding **36** (83.3 mg, 64% yield) and **37** (27 mg, 21% yield) both as an solid: Compound **36**: mp 108−110 °C; ^{1}H-NMR ($CDCl_3$) δ 2.68 (dd, J = 16.8, 11.3 Hz, 1 H), 2.88 (dd, J = 10.1, 8.8 Hz, 1 H), 3.19 (dd, J = 16.8, 2.6 Hz, 1 H), 3.27 (d, J = 14.1 Hz, 1 H), 3.50 (d, J = 14.1 Hz, 1 H), 3.70 (s, 3 H), 3.87 (dddd, J = 11.3, 10.1, 8.8, 2.6 Hz, 1 H), 4.42 (dd, J = 8.8, 8.8 Hz, 1 H), 7.27 (m, 5 H), 7.62 (m, 2 H), 7.74 (m, 1 H), 8.05 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 32.4 (t), 35.5 (t), 36.7 (d), 52.6 (q), 70.8 (t), 73.5 (s), 128.6 (d), 129.4 (d), 129.6 (d), 130.3 (d), 132.1 (d), 133.2 (s), 134.6 (s), 135.3 (d), 171.6 (s), 172.2 (s); IR ($CHCl_3$) (cm^{-1}) 3038, 1777, 1735, 1309, 1214, 1151; MS *m/z* (relative intensity) 389 $(M + 1)^+$ (4), 357 $(M - OCH_3)^+$ (4), 247 (100), 143 (45), 141 (95), 129 (100), 91 (100), 77 (100); HRMS calcd for $C_{20}H_{21}O_6S$ $(M + 1)^+$ 389.1059, found 389.1076. Compound **37**: mp 172−174 °C; ^{1}H-NMR (C_6D_6) δ 2.75 (dd, J = 17.5, 8.5 Hz, 1 H), 3.30 (dddd, J = 10.7, 8.5, 8.3, 6.5 Hz, 1 H), 3.36 (d, J = 13.2 Hz, 1 H), 3.40 (s, 3 H); 3.51 (dd, J = 17.5, 6.5 Hz, 1 H), 3.56 (d, J = 13.2 Hz, 1 H), 3.75 (dd, J = 8.3, 8.3 Hz, 1 H), 4.19 (dd, J = 10.7, 8.3 Hz, 1 H), 6.94 (m, 2 H), 7.00 (m, 2 H), 7.04 (m, 2 H), 7.36 (m, 2 H), 7.86 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 31.6 (t), 36.2 (t), 36.9 (d), 52.1 (q), 71.2 (t), 74.5 (s), 127.9 (d), 128.8 (d), 129.0 (d), 130.5 (d), 131.0 (d), 134.0 (s), 134.9 (d), 136.2 (s), 171.3 (s), 171.5 (s); IR ($CHCl_3$) (cm^{-1}) 2957, 1773, 1735, 1309, 1249, 1180.

Preparation of Methyl (3*R*,4*S*)- and (3*S*,4*R*)-[4-(Benzenesulfonyl)-4-[(methoxycarbonyl)methyl]-5-oxotetrahydrofuran-3-yl]acetate (38). The general alkylation procedure was applied to **32** on a 100 mg (0.34 mmol) scale using methyl bromoacetate (50 μL, 0.53 mmol) for 1 h at −30 °C yielding **38** (114.6 mg, 88% yield) as a solid: mp 102−104 °C; ^{1}H-NMR ($CDCl_3$) δ 2.44 (dd, J = 16.4, 11.6 Hz, 1 H), 2.75 (dd, J = 16.4, 3.6 Hz, 1 H), 3.01 (d, J = 17.6 Hz, 1 H), 3.18 (d, J = 17.6 Hz, 1 H), 3.68 (s, 3 H), 3.72 (s, 3 H), 3.93 (dddd, J = 11.6, 8.7, 8.7, 3.6 Hz, 1 H), 4.12 (dd, J = 8.7, 8.7 Hz, 1 H), 4.72 (dd, J = 8.7, 8.7 Hz, 1 H), 7.61 (m, 2 H), 7.74 (m, 1 H), 7.91 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 34.3 (t), 34.5 (d), 34.8 (t), 52.7 (q), 53.3 (q), 70.6 (s), 72.0 (t), 129.6 (d), 131.8 (d), 133.7 (s), 135.6 (d), 170.2 (s), 171.2 (s); IR ($CHCl_3$) (cm^{-1}) 3029, 1772, 1740, 1736, 1439, 1325, 1202, 1149; MS *m/z* (relative intensity) 371 $(M + 1)^+$ (26), 339 $(M - OCH_3)^+$ (18), 229 (46), 197 (100), 165 (56), 125 (63), 77 (67); HRMS calcd for $C_{16}H_{19}O_8S$ $(M + 1)^+$ 371.0801, found 371.0784.

Preparation of Methyl (4*S*)- and (4*R*)-(2*R*,3*R*)-[4-(Benzenesulfonyl)-2-hexyl-3-methyl-5-oxotetrahydrofuran-3-yl]acetate (41). To a stirred solution of lactones **39** and **40**[6] (8:1) (200 mg, 0.55 mmol) in MeOH (1.8 mL) was added $KHSO_5$ (506.7 mg, 0.82 mmol) in H_2O (1.65 mL) at 0 °C. The mixture was vigorously stirred for 5 h, until TLC showed the end of the reaction. Then it was diluted with AcOEt (5 mL) and washed with H_2O and saturated brine. The organic phase was dried over $MgSO_4$, concentrated, and purified, giving **41a** (2*R*,3*R*,4*S*) and **41b** (2*R*,3*R*,4*R*) as an irresolvable epimeric mixture in C_4, in a ratio of 2.5:1 (by NMR) (206.7 mg, 95% yield) as an oil: Compound **41a**: ^{1}H-NMR ($CDCl_3$) δ 0.87 (t, J = 6.2 Hz, 3 H), 1.30 (m, 8 H), 1.46 (s, 3 H), 1.56 (m, 2 H), 2.50 (d, J = 16.4 Hz, 1 H), 3.27 (d, J = 16.4 Hz, 1 H), 3.73 (s, 3 H), 4.15 (dd, J = 10.0, 2.0 Hz, 1 H), 5.30 (s, 1 H), 7.57 (m, 2 H), 7.68 (m, 1 H), 8.08 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 13.9 (q), 17.1 (q), 22.4 (t), 26.3 (t), 27.8 (t), 28.8 (t), 31.4 (t), 37.6 (t), 46.5 (s), 51.9 (q), 67.5 (d), 83.1 (d), 128.9 (d), 129.1 (d), 134.1 (d), 139.7 (s), 166.8 (s), 171.5 (s). Compound **41b** ^{1}H-NMR ($CDCl_3$) δ: 0.87 (t, J = 6.2 Hz, 3 H), 1.30 (m, 8 H), 1.46 (s, 3 H), 1.56 (m, 2 H), 2.63 (d, J = 17.6 Hz, 1 H), 3.37 (d, J = 17.6 Hz, 1 H), 3.76 (s, 3 H), 4.03 (s, 1 H), 4.80 (dd, J = 9.2, 2.6 Hz, 1 H), 7.57 (m, 2 H), 7.68 (m, 1 H), 7.90 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 13.9 (q), 20.5 (q), 22.4 (t), 26.5 (t), 28.8 (t), 28.9 (t), 31.5 (t), 36.9 (t), 46.1 (s), 51.7 (q), 72.6 (d), 86.9 (d), 128.9 (d), 129.1 (d), 134.5 (d), 138.1 (s), 167.8 (s), 170.6 (s).

Preparation of Methyl (2*R*,3*R*,4*S*)-[4-(Benzenesulfonyl)-2-hexyl-3,4-dimethyl-5-oxotetrahydrofuran-3-yl]acetate (42). The general alkylation procedure was applied to the mixture of sulfones **41** on a 90 mg (0.23 mmol) scale in a 1:1 THF:HMPA mixture (3 mL) using lithium bis(trimethylsilyl)amide 1 M in THF (250 μL, 0.25 mmol) as base and CH_3I (20 μL, 0.34 mmol), for 4 h at −78 °C, yielding **42** (82 mg, 88% yield) as an oil: $[\alpha]^{25}_D$ +65.5° (c 2.47, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.89 (t, J = 6.6 Hz, 3 H), 1.31 (m, 8 H), 1.40 (s, 3 H), 1.62 (m, 2 H), 1.68 (s, 3 H), 2.64 (d, J = 13.6 Hz, 1 H), 2.87 (d, J = 13.6 Hz, 1 H), 3.73 (s, 3 H), 4.34 (dd, J = 8.8, 2.0 Hz, 1 H), 7.57 (m, 2 H), 7.67 (m, 1 H), 8.12 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 14.4 (q), 17.8 (q), 18.4 (q), 22.9 (t), 27.3 (t), 29.4 (t), 29.7 (t), 32.0 (t), 39.4 (t), 49.1 (s), 52.4 (q), 74.4 (s), 85.5 (d), 129.0 (d),

131.7 (d), 134.6 (d), 137.9 (s), 171.3 (s), 171.6 (s); IR ($CHCl_3$) (cm^{-1}) 2930, 1776, 1737, 1449, 1311, 1240, 1152; MS *m/z* (relative intensity) 412 $(M + 2)^+$ (1), 411 $(M + 1)^+$ (4), 410 $(M)^+$ (1), 337 (53), 269 (75), 195 (92), 155 (100), 127 (76), 113 (69), 77 (75); HRMS calcd for $C_{21}H_{31}O_6S$ $(M + 1)^+$ 411.1841, found 411.1852.

Preparation of Methyl (2*S*,3*S*,4*R*)-[4-(Benzenesulfonyl)-2-(4-methylpentyl)-5-oxotetrahydrofuran-3-yl]acetate (45). The RuO_4 oxidation of sulfides used above to obtain **21** was applied to **44**[6] on a 600 mg (1.65 mmol) scale for 4 h at 0 °C, yielding **45** (627 mg, 96% yield) as a solid: mp 80–82 °C; $[\alpha]^{25}_D$ +13.8° (*c* 1.47, Et_2O); ^{1}H-NMR ($CDCl_3$) δ 0.85 (d, *J* = 6.5 Hz, 6 H), 1.11 (m, 2 H), 1.19 (m, 1 H), 1.25 (s, 3 H), 1.30 (m, 1 H), 1.47 (m, 1 H), 1.58 (m, 1 H), 1.70 (m, 1 H), 2.69 (dd, *J* = 16.1, 8.6 Hz, 1 H), 2.96 (dd, *J* = 16.1, 4.6 Hz, 1 H), 3.39 (ddd, *J* = 10.9, 8.6, 4.6 Hz, 1 H), 3.75 (s, 3 H), 4.28 (d, *J* = 10.9 Hz, 1 H), 7.61 (m, 2 H), 7.71 (m, 1 H), 8.02 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 21.1 (t), 22.4 (q), 22.9 (q), 28.2 (d), 34.6 (t), 39.1 (t), 40.6 (t), 40.8 (d), 52.6 (q), 67.9 (d), 87.5 (s), 129.6 (d), 130.4 (d), 135.1 (d), 137.1 (s), 166.4 (s), 171.7 (s); IR ($CHCl_3$) (cm^{-1}) 2979, 1770, 1738, 1449, 1327, 1227, 1046; MS *m/z* (relative intensity) 365 $(M - OCH_3)^+$ (2), 311 (3), 293 (14), 239 (34), 169 (62), 127 (58), 77 (100); HRMS calcd for $C_{19}H_{25}O_5S$ $(M - OCH_3)^+$ 365.1423, found 365.1449.

Preparation of Methyl (2*S*,3*S*,4*R*)-[4-(Benzenesulfonyl)-2,4-dimethyl-2-(4-methylpentyl)-5-oxotetrahydrofuran-3-yl]acetate (48). The general alkylation procedure was applied to **45** on a 100 mg (0.25 mmol) scale using CH_3I (24 μL, 0.38 mmol) for 1 h at −30 °C, yielding **48** (101.7 mg, 98% yield) as an oil: $[\alpha]^{25}_D$ −18.4° (*c* 1.84, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.83 (m, 6 H), 1.05 (m, 3 H), 1.22 (m, 1 H), 1.29 (s, 3 H), 1.45 (m, 2 H), 1.58 (m, 1 H), 1.63 (s, 3 H), 2.48 (dd, *J* = 15.5, 10.1 Hz, 1 H), 2.82 (dd, *J* = 15.5, 4.4 Hz, 1 H), 3.66 (dd, *J* = 10.1, 4.4 Hz, 1 H), 3.74 (s, 3 H), 7.59 (m, 2 H), 7.70 (m, 1 H), 7.97 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 16.2 (q), 20.8 (t), 22.9 (q), 23.0 (q), 23.6 (q), 28.0 (d), 32.3 (t), 39.2 (t), 41.3 (t), 41.8 (d), 52.6 (q), 70.5 (s), 87.2 (s), 129.3 (d), 131.2 (d), 134.6 (s), 135.1 (d), 171.1 (s), 171.6 (s); IR ($CHCl_3$) (cm^{-1}): 3027, 2952, 1765, 1740, 1438, 1309, 1149; MS *m/z* (relative intensity) 410 $(M)^+$ (6), 379 $(M - OCH_3)^+$ (12), 346 (40), 269 (100), 183 (89), 141 (96), 77 (72); HRMS calcd for $C_{21}H_{30}O_6S$ $(M)^+$ 410.1763, found 410.1768.

Preparation of Methyl (2*S*,3*S*,4*R*)- and Methyl (2*S*,3*S*,4*S*)-[4-Allyl-4-(benzenesulfonyl)-2-methyl-2-(4-methylpentyl)-5-oxotetrahydrofuran-3-yl]acetate (49 and 50). The general alkylation procedure was applied to **45** on a 100 mg (0.25 mmol) scale using allyl bromide (33 μL, 0.38 mmol) for 2 h at 0 °C, yielding **49** (79.3 mg, 72% yield) and **50** (18.7 mg, 13% yield) both as an oil: Compound **49**: $[\alpha]^{25}_D$ −12.8° (*c* 2.98, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.84 (m, 6 H), 1.05 (m, 2 H), 1.19 (m, 1 H), 1.27 (s, 3 H), 1.32 (m, 2 H), 1.42 (m, 1 H), 1.64 (m, 1 H), 2.66 (dd, *J* = 15.6, 10.2 Hz, 1 H), 2.77 (dd, *J* = 14.5, 9.3 Hz, 1 H), 2.81 (dd, *J* = 15.6, 4.5 Hz, 1 H), 2.99 (dd, *J* = 14.5, 4.3 Hz, 1 H), 3.72 (dd, *J* = 10.2, 4.5 Hz, 1 H), 3.75 (s, 3 H), 5.25 (dd, *J* = 11.2, 1.1 Hz, 1 H), 5.30 (dd, *J* = 16.9, 1.1 Hz, 1 H), 5.65 (dddd, *J* = 16.9, 11.2, 9.3, 4.3 Hz, 1 H), 7.61 (m, 2 H), 7.71 (m, 1 H), 7.97 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 21.2 (t), 22.5 (q), 22.9 (q), 22.9 (q), 28.0 (d), 32.1 (t), 34.5 (t), 39.2 (t), 42.7 (t), 43.5 (d), 52.6 (q), 74.5 (s), 87.6 (s), 121.7 (t), 129.4 (d), 131.8 (d), 131.9 (d), 134.6 (s), 125.1 (d), 169.8 (s), 171.8 (s); IR ($CHCl_3$) (cm^{-1}) 2953, 1760, 1738, 1309, 1220, 1148; MS *m/z* (relative intensity) 437 $(M + 1)^+$ (1), 405 $(M - OCH_3)^+$ (13), 372 (28), 333 (31), 295 (100), 277 (61), 135 (67), 77 (78); HRMS calcd for $C_{23}H_{33}O_6S$ $(M + 1)^+$ 437.1998, found 437.2004. Compound **50**: $[\alpha]^{25}_D$ −4.1° (*c* 0.63, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.87 (d, *J* = 6.6 Hz, 6 H), 1.15 (m, 2 H), 1.34 (m, 1 H), 1.42 (m, 1 H), 1.54 (m, 2 H), 1.62 (s, 3 H), 1.67 (m, 1 H), 2.57 (dd, *J* = 12.9, 4.9 Hz, 1 H), 2.65 (dd, *J* = 12.5, 9.3 Hz, 1 H), 2.96 (dd, *J* = 12.9, 8.8 Hz, 1 H), 3.49 (dd, *J* = 10.9, 9.3 Hz, 1 H), 3.51 (dd, *J* = 12.5, 10.5 Hz, 1 H), 3.79 (s, 3 H), 5.31 (dd, *J* = 9.4, 0.8 Hz, 1 H), 5.43 (dd, *J* = 16.4, 0.8 Hz, 1 H), 5.50 (dddd, *J* = 16.4, 9.4, 8.8, 4.9 Hz, 1 H), 7.56 (m, 2 H), 7.71 (m, 1 H), 7.84 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 21.5 (q), 21.6 (t), 22.4 (q), 22.6 (q), 27.9 (d), 31.6 (t), 38.2 (t), 38.9 (t), 42.6 (t), 43.5 (d), 52.0 (q), 74.5 (s), 86.9 (s), 123.2 (t), 128.4 (d), 130.2 (d), 131.4 (d), 134.6 (d), 135.5 (s), 169.7 (s), 171.9 (s); IR ($CHCl_3$) (cm^{-1}) 3023, 1757, 1740, 1312, 1220, 1144.

Preparation of Methyl (2*S*,3*S*,4*R*)- and Methyl (2*S*,3*S*,4*S*)-[4-Benzyl-4(benzenesulfonyl)-2-methyl-2-(4-methylpentyl)-5-oxotetrahydrofuran-3-yl]acetate (51 and 52). The general alkylation procedure was applied to **45** on a 100 mg (0.25 mmol) scale using benzyl bromide (30 μL, 0.38 mmol) for 16 h at −30 °C, yielding **51** (73.6 mg, 60% yield) and **52** (24.5 mg, 20% yield) both as an oil: Compound **51**: $[\alpha]^{25}_D$ −12.9° (*c* 2.48, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.30 (s, 3 H), 0.81 (m, 6 H), 1.02 (m, 2 H), 1.14 (m, 1 H), 1.29 (m, 2 H), 1.41 (m, 1 H), 1.55 (m, 1 H), 2.59 (dd, *J* = 15.4, 9.9 Hz, 1 H), 2.92 (dd, *J* = 15.5, 4.3 Hz, 1 H), 3.26 (d, *J* = 14.1 Hz, 1 H), 3.63 (d, *J* = 14.1 Hz, 1 H), 3.75 (s, 3 H), 3.81 (dd, *J* = 9.9, 4.3 Hz, 1 H), 7.27 (s, 4 H), 7.38 (m, 1 H), 7.62 (m, 2 H), 7.72 (m, 1 H), 8.02 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 21.0 (q), 21.2 (t), 22.9 (q), 22.9 (q), 27.9 (d), 32.3 (t), 35.4 (t), 39.2 (t), 42.8 (t), 43.7 (d), 52.6 (q), 76.9 (s), 87.8 (s), 128.5 (d), 129.4 (d), 129.5 (d), 131.2 (d), 132.2 (d), 134.1 (s), 134.7 (s), 135.1 (d), 170.8 (s), 171.8 (s); IR ($CHCl_3$) (cm^{-1}) 2954, 1755, 1738, 1438, 1311, 1222, 1147; MS *m/z* (relative intensity) 455 $(M - OCH_3)^+$ (2), 345 (78), 327 (74), 259 (31), 129 (91), 91 (100), 77 (99); HRMS calcd for $C_{27}H_{35}O_6S$ $(M + 1)^+$ 487.2154, found 487.2141. Compound **52**: $[\alpha]^{25}_D$ −5.5° (*c* 1.65, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.74 (m, 6 H), 0.79 (m, 4 H), 1.10 (m, 1 H), 1.25 (m, 2 H), 1.52 (s, 3 H), 2.60 (dd, *J* = 17.2, 4.8 Hz, 1 H), 3.20 (d, *J* = 12.6 Hz, 1 H), 3.41 (dd, *J* = 10.5, 4.8 Hz, 1 H), 3.48 (d, *J* = 12.6 Hz, 1 H), 3.55 (dd, *J* = 17.2, 10.5 Hz, 1 H), 3.83 (s, 3 H), 7.27 (m, 3 H), 7.36 (m, 2 H), 7.59 (m, 2 H), 7.73 (m, 1 H), 7.93 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 20.2 (t), 22.0 (q), 22.4 (q), 22.6 (q), 27.2 (d), 31.9 (t), 38.8 (t), 39.1 (t), 41.8 (t), 42.1 (d), 52.0 (q), 76.4 (s), 86.7 (s), 127.9 (d), 128.5 (d), 128.7 (d), 131.3 (d), 131.6 (d), 133.5 (s), 134.6 (d), 135.7 (s), 170.0 (s), 172.2 (s); IR ($CHCl_3$) (cm^{-1}) 2952, 1756, 1737, 1438, 1310, 1220, 1147.

Preparation of Methyl (2*S*,3*S*,4*R*)-[4-(Benzenesulfonyl)-2-methyl-4-[(methoxycarbonyl)methyl]-2-(4-methylpentyl)-5-oxotetrahydrofuran-3-yl]acetate (53). The general alkylation procedure was applied to **45** on a 100 mg (0.25 mmol) scale using methyl bromoacetate (36 μL, 0.38 mmol) for 2 h at −30 °C, yielding **53** (100.5 mg, 85% yield) as an oil: $[\alpha]^{25}_D$ −21.9° (c 2.94, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.87 (d, *J* = 6.8 Hz, 6 H), 1.12 (m, 2 H), 1.37 (s, 3 H), 1.40 (m, 2 H), 1.51 (m, 1 H), 1.60 (m, 1 H), 1.75 (m, 1 H), 2.47 (dd, *J* = 15.7, 5.2 Hz, 1 H), 2.59 (dd, *J* = 15.7, 9.8 Hz, 1 H), 3.04 (d, *J* = 17.2 Hz, 1 H), 3.19 (d, *J* = 17.2 Hz, 1 H), 3.68 (s, 3 H), 3.72 (dd, *J* = 9.8, 5.2 Hz, 1 H), 3.75 (s, 3 H), 7.60 (m, 2 H), 7.73 (m, 1 H), 7.92 (m, 2 H); ^{13}C-NMR ($CDCl_3$) δ 20.0 (q), 21.8 (t), 22.9 (q), 23.0 (q), 28.2 (d), 33.2 (t), 34.9 (t), 39.3 (t), 43.3 (t), 43.4 (d), 52.7 (q), 53.1 (q), 73.6 (s), 88.8 (s), 129.5 (d), 132.0 (d), 133.8 (s), 135.5 (d), 169.7 (s), 170.0 (s), 171.6 (s); IR ($CHCl_3$) (cm^{-1}) 2952, 1757, 1743, 1438, 1311, 1208, 1150; MS *m/z* (relative intensity) 469 $(M + 1)^+$ (1), 437 $(M - OCH_3)^+$ (2), 404 (12), 295 (24), 241 (100), 209 (74), 139 (62), 77 (100); HRMS calcd for $C_{23}H_{33}O_8S$ $(M + 1)^+$ 469.1896, found 469.1893.

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Supplementary Material Available: Full geometries and energies of the anions of Table 4, copies of ^{13}C-NMR spectra for the new compounds, and NOE experiments for compounds **6** and **7** (67 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.