One-Step Palladium-Catalyzed Synthesis of Substituted Dihydrofurans from the Carbonate Derivatives of γ-Hydroxy-α,β-unsaturated Sulfones

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Received July 17, 1998

The palladium-catalyzed nucleophilic allylic substitution of the carbonate derivatives of γ-hydroxy-α,β-unsaturated sulfones (**2**) with soft carbon nucleophiles such as malonates, β-keto esters, 1,3-diketones, and α-sulfonyl ketones took place cleanly and with full regiocontrol (γ-substitution). Typical optimized conditions are $Pd_2(dba)_3$ (5 mol %), dppe (20 mol %), molecular sieves, in toluene−THF at 100 °C. Unexpectedly, when β-keto esters, 1,3-diketones, and α-sulfonyl ketones were used as nucleophiles a cascade process occurred, via initial γ-regioselective allylic substitution and further intramolecular conjugate addition of the enol moiety to the α,β-unsaturated sulfone, to give 2,3,4,5-tetrasubstituted dihydrofurans (**13**−**25**) in moderate to good yields. Moreover, the cyclization step is highly stereoselective giving predominantly or exclusively the 4,5-dihydrofuran of *trans* configuration. From readily available enantiopure (*S*)-**2**, this one-step procedure of synthesis of substituted dihydrofurans has been applied to the synthesis of enantiomerically pure tetrasubstituted tetrahydrofurans.

Introduction

During the last two decades, the palladium-catalyzed nucleophilic substitution of allylic oxygenated compounds, mainly esters, carbonates, and epoxides, has become a crucial method for the formation of carbon−carbon and carbon−heteroatom bonds.[1] The impressive range of allylic systems and nucleophile partners that can be used, as well as the high levels of chemo- and stereoselectivity usually attained in this kind of process, explains its widespread use in modern organic synthesis.

Despite the huge literature on allylic metal-catalyzed nucleophilic substitutions, it is worth noting that unlike allylic systems substituted with alkyl, aryl, or electron-donating substituents, those substituted with electron-withdrawing groups at the double bond such as ester, carbonyl, or cyano groups, have been much less studied.[2] This is due to their usually lower reactivity toward the Pd(0) catalysts, their tendency to undergo conjugate addition of the nucleophile, and the easier deprotonation of the π-allylpalladium intermediate (β-elimination) to give 1,3-dienes. On the other hand, it is known that in these cases when the allylic substitution occurs, the nucleophile attack takes place exclusively at the terminus of the allyl unit not bearing the electron-withdrawing group.[2] This regiochemical outcome has been usually explained in terms of electronic (attack to the most electron deficient position) rather than steric reasons.

γ-Oxygenated-α,β-unsaturated sulfones are interesting and readily available starting compounds for stereoselective synthesis mainly due to their excellent properties as Michael acceptors,[3] which allows an efficient functionalization at the β position and subsequently at the α position by treatment of its α-sulfonyl carbanion with electrophiles. From a synthetic point of view, this type of compound would even be more versatile in organic synthesis if it was possible to substitute the oxygenated function at the γ position by a wide variety of nucleophiles, to afford a new vinyl sulfone suitable for further functionalization at β and α positions. In a preliminary communication we reported that the carbonate derivatives of γ-hydroxy-α,β-unsaturated sulfones undergo a regioselective allylic substitution at the γ position under appropriate palladium-catalyzed conditions.[4] We now give a full account of this work, reporting additional examples as well as the scope and limitations of the process and its application to the synthesis of enantiomerically pure tetrahydrofurans.

It is interesting to point out that to the best of our knowledge the only previous studies on metal-promoted allylic substitutions in γ-oxygenated-α,β-unsaturated sulfones dealt with the stoichiometric reaction of their

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(2) For palladium-catalyzed allylic substitutions in γ-oxygenated-α,β-unsaturated esters, see: (a) Suzuki, T.; Sato, T.; Hirama, M. *Tetrahedron Lett.* **1990**, *31*, 4747. (b) Tanikaga, R.; Jun, T. X.; Kaji, A. *J. Chem. Soc., Perkin Trans 1* **1990**, 1185. (c) Tsuda, T.; Horii, Y.; Nakagawa, Y.; Ishida, T.; Saegusa, T. *J. Org. Chem.* **1989**, *54*, 977. (d) Tanikaga, R.; Takeuchi, J.; Takyu, M.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1987**, 386. (e) Tsuji, J.; Ueno, H.; Kobayashi, Y.; Okumoto, H. *Tetrahedron Lett.* **1981**, *22*, 2573. For substitutions on π-allylpalladium complexes substituted with carbonyl or cyano groups, see for instance: (f) Sugiura, M.; Yagi, Y.; Wei, S.-Y.; Nukai, T. *Tetrahedron Lett.* **1998**, *39*, 4351. (g) Hunt, D. A.; Quante, J. M.; Tyson, R. L.; Dasher, L. W. *J. Org. Chem.* **1984**, *49*, 5262. (h) Tsuji, J.; Ueno, H.; Kobayashi, Y.; Okumoto, H. *Tetrahedron Lett.* **1981**, *22*, 2573. (i) Jackson, W. R.; Strauss, J. U. *Aust. J. Chem.* **1977**, *30*, 553.

(3) (a) Isobe, M. *Perspectives in the Organic Chemistry of Sulfur*; Zwanenburg, B., Klunder, A. J. H., Eds.; Elsevier: New York, 1987; pp 209−229. (b) Fuchs, P. L.; Braish, T. F. *Chem. Rev.* **1986**, *86*, 903. See also: (c) Carretero, J. C.; Gómez Arrayás, R.; Storch de Gracia, I. *Tetrahedron Lett.* **1996**, *37*, 3379. (d) Carretero, J. C.; Gómez Arrayás, R. *J. Org. Chem.* **1995**, *60*, 6000. (e) De Blas, J.; Carretero, J. C.; Domínguez, E. *Tetrahedron Lett.* **1994**, *35*, 4603. (f) Domínguez, E.; Carretero, J. C. *Tetrahedron* **1994**, *50*, 7557. (g) Domínguez, E.; Carretero, J. C. *Tetrahedron Lett.* **1993**, *34*, 5803.

(4) Alonso, I.; Carretero, J. C.; Garrido, J. L.; Magro, V.; Pedregal, C. *J. Org. Chem.* **1997**, *62*, 5682.

10.1021/jo981391r CCC: $15.00
Published on Web 11/19/1998

cationic tetracarbonyl(η_3-allyl)iron derivatives with nucleophiles.[5] Also, as a related precedent in this field, the formation and isolation of π-allyl palladium chloride dimers substituted at α-position with a sulfonyl group, by stoichiometric reaction of allyl sulfones with palladium dichloride, have been described.[6]

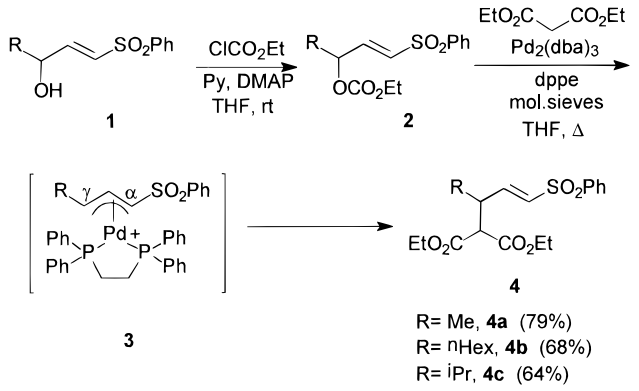
Results and Discussion

The starting γ-hydroxy vinyl sulfones **1** were readily prepared following the reported one-step procedure based on the piperidine-catalyzed condensation of phenylsulfonyl arylsulfinyl methanes with aldehydes.[7] First we studied the reaction of their acetates with sodium dimethyl malonate (1.1 equiv) in the presence of catalytic amounts of $Pd_2(dba)_3$ (3−6 mol %) and phosphine ligands (6−20 mol %). However, it was observed that, regardless of the solvent (THF, toluene or DMF), temperature (from −30 °C to 68 °C), and ligand [PPh_3, $P(OEt)_3$, dppe, dppp] used, the main or sole product was the Michael adduct instead of the desired γ-substituted product. In an attempt to increase the rate of formation of the π-allylpalladium complex by increasing the reactivity of the leaving group, the corresponding chloroacetates were studied. In fact, it has been previously described that the palladium-catalyzed allylic substitution in γ-oxygenated-α,β-unsaturated esters occurred satisfactorily from their chloroacetates but not from the corresponding acetates.[2b] Disappointingly, in our case the chloroacetates evolved in a manner similar to that of the acetates, giving again predominantly the Michael adduct.

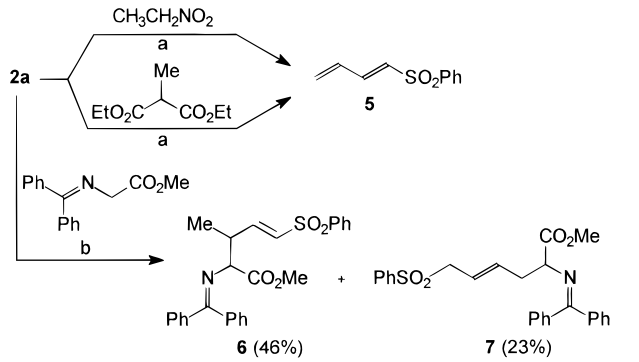
These results showed that the conjugate addition of the malonate anion was a much faster process than the allylic substitution and, consequently, the impossibility of generating the π-allylpalladium intermediate under these conditions. Trying to avoid this competitive conjugate addition we turned our attention to the carbonate derivatives **2** (Tsuji's method),[8] which were readily prepared in high yield by reaction of **1** with ethyl chloroformate (pyridine, DMAP, THF, rt). These substrates allow the reaction to be carried out in the presence of diethyl malonate instead of its anion, generating in situ the required nucleophile only after formation of the π-allylpalladium complex and subsequent release of the alkoxide, which would deprotonate the malonate. Now, if the attack of the malonate anion to the π-allylpalladium intermediate was faster than the conjugate addition to **2**, the desired allyl-substituted product would be the main product of the reaction.

We were pleased to find that the reaction of **2a** (R = Me) with diethyl malonate in the presence of $Pd_2(dba)_3$ (5 mol %) and PPh_3 (20 mol %) in THF at reflux afforded a mixture of three products in which the Michael adduct was not detected. The major product was the desired γ-substituted product **4a**, and the other minor products

Scheme 1



Scheme 2



(a) $Pd_2(dba)_3$ (5 mol %), dppe (20 mol %), mol.sieves, THF-toluene, 100ºC.
(b) $Pd_2(dba)_3$ (5 mol %), dppe (20 mol %), mol.sieves, THF, reflux.

were 1-(phenylsulfonyl)-1,3-butadiene (**5**),[9] likely formed by β-elimination on the π-allylpalladium intermediate, and the starting alcohol **1a**, presumably formed as a result of the hydrolysis of the carbonate **2a**. Interestingly, **2a** was cleanly converted into the allylic product **4a** (79% yield) when the reaction was carried out in the presence of powdered molecular sieves (4 Å) and dppe as phosphine ligand. Likely the bidentate phosphine ligand increases the stability of the π-allylpalladium complex (**3**), while the molecular sieves prevent the hydrolysis of the carbonate. Under these conditions, the reaction worked well also for other γ-substituted carbonates such as **2b** (R = ^{n}Hex) and **2c** (R = ^{i}Pr), affording with complete regiocontrol the corresponding γ-substituted products **4b** and **4c** (68% and 64% yields, respectively) regardless of the size of the substitution at γ-position (Scheme 1).

On the contrary, unsatisfactory results were obtained when **2a** was treated with other stabilized nucleophiles usually used in palladium-catalyzed allylic substitutions (Schemes 2 and 3). Thus, the reactions with methyl diethylmalonate[10] and nitroethane[11] led mainly to the elimination product **5**, probably due to the poorer nucleophilic character of their anions compared to the malonate anion. In the case of the reaction with diphenylglycine imine[12] a mixture of the desired γ-substituted product **6** (46% as a 1:1 mixture of stereoisomers)

(5) (a) Enders, D.; Jandeleit, B.; Raabe, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1949. (b) Enders, D.; Von Berg, S.; Jandeleit, B. *Synlett* **1996**, 18.

(6) Ogura, K.; Shibuya, N.; Takahashi, K.; Iida, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 1092. See also: Muzart, J.; Pale, P,; Pete, J. *Tetrahedron Lett.* **1983**, *24*, 4567.

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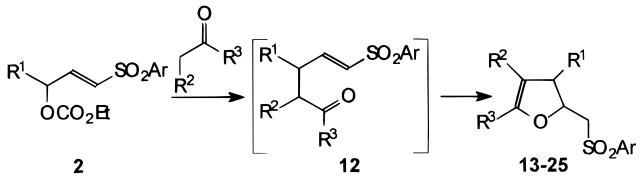
(8) (a) Tsuji, J.; Shimizu, I.; Minami, I.; Ohashi, Y.; Sugiura, T.; Takahashi, K. *J. Org. Chem.* **1985**, *50*, 1523. (b) Tsuji, J.; Shimizu, I.; Minami, I.; Ohashi, Y. *Tetrahedron Lett.* **1982**, *23*, 4809. Reviews: (c) Tsuji, J.; Minami, I. *Acc. Chem. Res.* **1987**, *20*, 140. (d) Tsuji, J. *Tetrahedron* **1986**, *42*, 4361.

(9) (a) Eisch, J. J.; Galle, J. E.; Hallenbeck, L. E. *J. Org. Chem.* **1982**, *47*, 1608. (b) Crumbie, R. L.; Ridley, D. D. *Aust. J. Chem.* **1981**, *34*, 1017.

(10) See, for instance: Vicart, N.; Cazes, B.; Goré, J. *Tetrahedron Lett.* **1995**, *36*, 535.

(11) See, for instance: (a) Genet, J. P.; Ferroud, D. *Tetrahedron Lett.* **1984**, *25*, 3579. (b) Wase, P. A.; Morrow, S. D.; Hardinger, S. A. *J. Org. Chem.* **1982**, *47*, 365.

Table 1. Palladium-Catalyzed Reaction of Carbonates 2 with Acid Ketones[a]

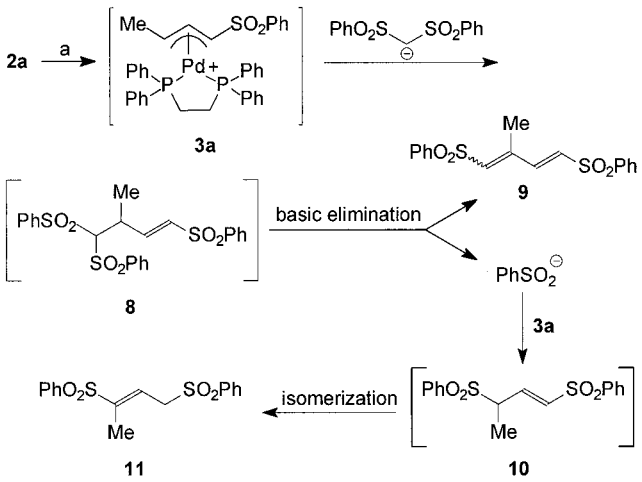


2 **12** **13-25**

	substrate			nucleophile			product	
entry	**2**	Ar	R^1	R^2	R^3		*trans*/*cis*[b]	yld[c]
1	**2a**	Ph	Me	CO_2Et	Me	**13**	78/22	76[d]
2	**2a**	Ph	Me	CO_2Et	Ph	**14**	83/17	63[d]
3[d]	**2a**	Ph	Me	COMe	Me	**15**	75/25	79[d]
4	**2a**	Ph	Me	-CO−$(CH_2)_3$-		**16**	80/20	89[d]
5[e]	**2a**	Ph	Me	$PhSO_2$	Me	**17**	75/25	80[d]
6	**2b**	Ph	^{n}Hex	CO_2Et	Me	**18**	>98/<2	79
7	**2b**	Ph	^{n}Hex	CO_2Et	Ph	**19**	>98/<2	57
8	**2b**	Ph	^{n}Hex	COMe	Me	**20**	>98/<2	67
9[f]	**2c**	Ph	^{i}Pr	CO_2Et	Me	**21**	>98/<2	38
10	**2c**	Ph	^{i}Pr	CO_2Et	Ph	**22**	>98/<2	14
11	**2c**	Ph	^{i}Pr	COMe	Me	**23**	>98/<2	14
12[g]	**2d**[h]	*p*-Tol	H	CO_2Et	Me	**24**	−	41
13[g]	**2d**[h]	*p*-Tol	H	-CO−$(CH_2)_3$-		**25**	−	42

[a] Reaction conditions: **2**, $R_2CH_2COR_3$ (4 equiv), $Pd_2(dba)_3$ (5 mol %), dppe (20 mol %), powdered molecular sieves 4 Å in 1:1 mixture of THF−toluene (0.1 M solution of **2**) at 100 °C. [b] Determined by ^{1}H NMR on the crude mixtures. [c] In pure product after silica gel chromatography. [d] The *cis*+*trans* mixture could not be separated by chromatography. [e] dppf was used as ligand instead of dppe.[17] [f] Reaction carried out in THF at reflux. [g] 10 mol % of dppe was used.[18] [h] The precursor alcohol **1d** was prepared according to a reported procedure.[19]

Scheme 3



(a) $CH_2(SO_2Ph)_2$ (4 equiv), $Pd_2(dba)_3$ (5 mol %), dppe (20 mol %), mol. sieves, THF-toluene, 100°C.

along with the unexpected δ-substituted regioisomer **7** (23% yield) was obtained. Compound **7** would likely be the result of the nucleophilic addition of the diphenylglycine imine anion to C-4 of the intermediate diene **5** (Scheme 2).

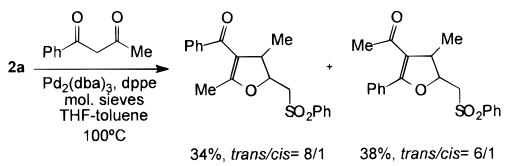
On the other hand, the reaction of **2a** with bis(phenylsulfonyl)methane[13] led to a mixture of the 1,4-disulfone **9** and the 1,3-disulfone **11** (ratio **9:11** = 48:52 determined by ^{1}H NMR on the crude mixture) (Scheme 3). This result might be explained by initial attack of the bis(phenylsulfonyl)methane anion to the γ-position of the π-allylpalladium complex **3a** to give the expected trisulfone **8**, that would be unstable under the reaction conditions, eliminating phenylsulfinate to afford diene **9**. Furthermore, addition of phenylsulfinate anion to complex **3a** would lead to the disulfone **10**, which would isomerize to the most substituted olefin **11**.

Much more synthetically useful results were obtained in the case of the palladium-catalyzed reaction of carbonates **2** with acid ketones such as β-keto esters, 1,3-diketones,[14] and α-sulfonyl ketones (Table 1). Unexpectedly, with all these nucleophiles, tetrasubstituted dihydrofurans **13**−**25** were obtained as the major products when the reactions were performed at 100 °C in a 1:1 mixture of toluene:THF. These results show that a tandem process, based on an initial γ-allylic substitution leading to intermediates **12**, followed by their cyclization via intramolecular conjugate addition of the enolate to the vinyl sulfone moiety had taken place.[15] The participation of intermediates **12** in this cascade process was unambiguously proved by isolation of **12a** (R^1 = Me, R^2 = CO_2Et, R^3 = Me). Thus, by performing the palladium-catalyzed reaction of **2a** with ethyl acetoacetate under milder conditions (26 h at room temperature), we isolated

(12) See, for instance: (a) Genet, J. P.; Juge, S.; Besnier, I.; Uziel, J.; Ferroud, D.; Kardos, N.; Achi, S.; Ruiz-Montes, J.; Thorimbert, S. *Bull. Soc. Chim. Fr.* **1990**, *127*, 781. (b) Ferroud, D.; Genet, J. P.; Kiolle, R. *Tetrahedron Lett.* **1986**, *27*, 23.

(13) See, for instance: Trost, B. M.; Varhoeven, T. R.; Fortunak, J. M. *Tetrahedron Lett.* **1979**, 2301.

(14) As it is shown below, the cyclization step is hardly regioselective from non symmetrically substituted 1,3-diketones (like benzoylacetone).



34%, *trans*/*cis*= 8/1 38%, *trans*/*cis*= 6/1

(15) For other recent synthesis of dihydrofurans based on tandem processes, see: (a) Lee, Y. R.; Kim, B. S. *Tetrahedron Lett.* **1997**, *38*, 2095. (b) Hagiwara, H.; Sato, K.; Suzuki, T.; Ando, M. *Tetrahedron Lett.* **1997**, *38*, 2103. (c) Hayashi, T.; Yamane, M.; Ohno, A. *J. Org. Chem.* **1997**, *62*, 204. (d) Hayashi, T.; Ohno, A.; Lu, S.-J.; Matsumoto, Y.; Fukuyo, E.; Yanagi, K. *J. Am. Chem. Soc.* **1994**, *116*, 4221. For a iodine-catalyzed cyclization of unsaturated 1,3-diketones, see: Antonioletti, R.; Cecchine, C.; Ciani, B; Magnanti, S. *Tetrahedron Lett.* **1995**, *36*, 9019.

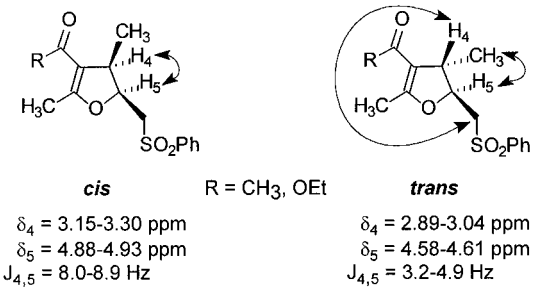


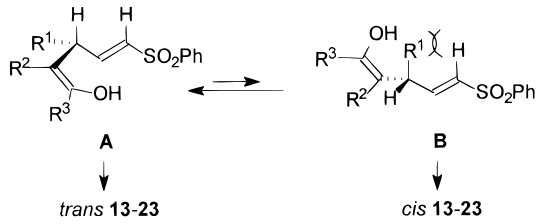
Figure 1. Significant chemical shifts ($CDCl_3$) and NOESY correlations of *cis* and *trans* dihydrofurans **13**−**23**.

a mixture of the dihydrofuran **13** and its intermediate **12a**[16] which were readily separated by chromatography (25% and 43% yields, respectively). Dihydrofurans **13**−**25** were isolated after chromatographic purification in moderate to good yields (41−89%), excepting in the case of the substrate with the bulkiest alkyl chain at γ-position, **2c** (R = ^{i}Pr), which afforded much lower yields (14−38%, entries 9−11) due to the major formation of 4-methyl-1-(phenylsulfonyl)-1,3-pentadiene (24−37%) as a result of the competitive β-elimination process on its sterically more demanding π-allylpalladium intermediate.

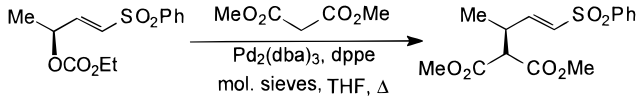
Concerning the stereoselectivity of the cyclization, it should be pointed out that this occurred in all cases with a remarkable *trans*-stereoselectivity. The stereocontrol was nearly complete from substrates **2b** and **2c** (R^1 = ^{n}Hex and ^{i}Pr respectively, de > 98%), although significantly lower from the less sterically demanding substrate **2a** (R^1 = Me, de = 50−66%). The *cis*/*trans* configuration of dihydrofurans **13**−**23** has been established by NMR. Particularly useful diagnostic criteria are the chemical shifts of H_4 and H_5 and the coupling constants between them which are much higher in the *cis* isomers than in the *trans* ones, and the strong NOESY cross-peaks observed between H_4 and H_5 in the *cis* isomers and its absence in the case of the *trans* ones. In the latter case, the *trans* stereoselectivity was also confirmed by the presence of significant NOE correlations between H_4 and the sulfonylmethyl group and between H_5 and the alkyl chain at C-4 (Figure 1).

This high *trans*-stereoselectivity might be explained on the basis of the ground state conformers of the acyclic intermediates **12** (Scheme 4). Thus conformer **A**, which leads to the *trans* isomer, should be the most stable because minimizes the allylic 1,3-strain between α and γ positions[20] whereas the cyclization of the less stable conformer **B**, having a R^1/Hα 1,3-allylic interaction, would lead to the minor *cis* dihydrofuran. On the other hand, taking into account that the relative thermodynamic unstability of conformer **B** with respect to **A** would increase with the steric size of the R^1 alkyl chain, this model could also explain the higher *trans*-stereoselectivity observed from **2b** and **2c** compared with **2a**.

Scheme 4



Scheme 5



As enantiomerically pure γ-hydroxyvinyl sulfones **1** can be readily prepared by enzymatic enantioselective acetylation of racemic **1** in the presence of Lipase-PS,[21] the results shown in Table 1 should represent a new access into enantiomerically pure substituted dihydrofurans and their corresponding tetrahydrofurans[22] after further C=C reduction.

First, we proved that as expected the palladium-catalyzed allylic substitution of substrates **2** took place with complete retention of configuration. Thus, reaction of *(S)*-**2a** with dimethyl malonate under the usual palladium-catalyzed conditions [$Pd_2(dba)_3$ (5 mol %), dppe (20 mol %), molecular sieves, THF, 68 °C] afforded the known compound (*R*)-**26**[23] [ee > 96%, determined by ^{1}H NMR with $Pr(hfc)_3$] (Scheme 5).

As an example of the straightforward application of the cyclization procedure to the enantioselective synthesis of tetrasubstituted tetrahydrofurans, the palladium-catalyzed reaction of (*S*)-**2b** with ethyl acetylacetate afforded (4*R*,5*R*)-**18** (79% yield) which was transformed in 70% yield into a 86:14 mixture of enantiomerically pure tetrahydrofurans **27**:**28** by reduction with Et_3SiH in TFA at 60 °C[24] (Scheme 6). The stereochemical assignments of **27** and **28** were established by ^{1}H NMR, particularly by NOESY experiments (Figure 2). Thus, in the case of the major adduct **27** the strong NOE correlations H_3/H_5 and H_3/Me(C-2) define their corresponding *syn* relation-

(16) **13** was quantitatively formed when **12a** was treated with a catalytic amount of NaH (5 mol %, THF, reflux), showing that the cyclization is a base-catalyzed process that takes place via the enolate of **12a**. On the other hand, in the absence of added base, **12a** also cyclized cleanly into **13** in the presence of both dppe and $Pd_2(dba)_3$ in THF at reflux, but not in the absence of either the phosphine or the palladium catalyst (no conversion was observed after 24 h in THF at 68 °C). It seems plausible that in the presence of the palladium catalyst the phosphine might undergo the conjugate addition to the α,β-unsaturated sulfone to form a zwitterionic intermediate, which would act as a base converting **12a** into its enolate. For metal-promoted Michael reactions requiring the presence of free phosphine, see: Gómez-Bengoa, E.; Cuerva, J. M.; Mateo, C.; Echavarren, A. M. *J. Am. Chem. Soc.* **1996**, *118*, 8553. For other phosphine-catalyzed nucleophile additions, see: (a) Zhang, C.; Lu, X. *Synlett*. **1995**, 645. (b) Trost, B. M.; Li, C.-J. *J. Am. Chem. Soc.* **1994**, *116*, 10819. (c) Kim, B.; Kodomari, M.; Regen, S. L. *J. Org. Chem*. **1984**, *49*, 3233. (d) Baraldi, P. TG.; Guarneri, M.; Pollini, G. P.; Simoni, D.; Barcon, A.; Benetti, S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2501. (e) White, D. A.; Baizer, M. M. *Tetrahedron Lett*. **1973**, 3597.

(17) In the reaction of **2a** with (phenylsulfonyl)acetone in the presence of $Pd_2(dba)_3$ (5 mol %) and dppe as ligand (20 mol %), besides the dihydrofuran **17** (25% yield) significant amounts of disulfone **11** (40%) and 4-methyl-6-(phenylsulfonyl)hex-3,5-dien-2-one (12%) were detected. These side products would be likely the result of the competitive sulfonyl elimination on the π-allylpalladium intermediate.

(18) Under the usual conditions (20 mol % of dppe) the yield in dihydrofurans **24** and **25** is lower due to the formation of an important amount of ethyl (*E*)-3-(*p*-tolylsulfonyl)-1-propen-1-yl carbonate.

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(22) For a review on the synthesis of substituted tetrahydrofurans, see: Bolvin, T. L. B. *Tetrahedron* **1987**, *43*, 3309.

(23) Jandeleit, B. Ph.D. Dissertation, Aachen (Germany), 1995 (see also ref 5a).

(24) Baldwin, J. E.; Bamford, S. J.; Fryer, A. M.; Rudolph, M. P. W.; Wood, M. E. *Tetrahedron* **1997**, *53*, 5255.

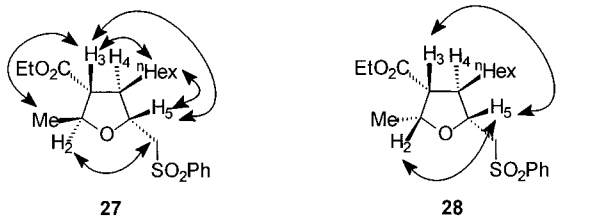
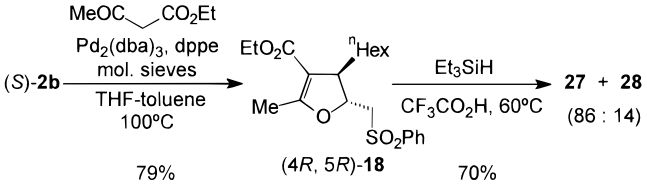


Figure 2. Significant NOESY correlations ($CDCl_3$ and C_6D_6) of compounds **27** and **28**.

Scheme 6



ships. This assignment is also supported by the presence of significant NOE correlations H_2/CH_2SO_2Ph, H_3/CH_2-(C-4) and H_5/CH_2(C-4). On the other hand, the stereochemistry of the minor isomer **28** (epimer of **27** at C-2) was tentatively assigned taking into account the strong NOESY cross-peaks H_2/H_5 and H_3/H_5.

Conclusions

In summary, it has been demonstrated that under appropriate conditions the carbonate derivatives of the readily available γ-hydroxy-α,β-unsaturated sulfones (**1**) can be used as efficient substrates in Pd(0)-catalyzed regioselective γ-allylic substitutions with soft carbon nucleophiles. Interestingly, a cascade process occurred when β-keto esters, 1,3-diketones, and α-sulfonyl ketones were used as nucleophiles, leading directly to tetrasubstituted dihydrofurans in a highly stereoselective manner. Likely, this process takes place by initial γ-allylic substitution and further cyclization by conjugate addition of the enol moiety to the α,β-unsaturated sulfone.

Taking into account that sulfones **1** can be readily prepared in enantiomerically pure form and that the palladium-catalyzed γ-allylic substitution takes place with complete retention of configuration, the procedure described here constitutes a new, short, and efficient approach to the enantioselective synthesis of substituted dihydrofurans and, hence, to the synthesis of substituted tetrahydrofurans after C−C double bond reduction.

Experimental Section

^{1}H NMR (200 or 300 MHz) and ^{13}C NMR (50 or 75 MHz) spectra were recorded in $CDCl_3$ or C_6D_6. Both chemical shifts (ppm downfield from internal tetramethylsilane) and coupling constants (Hz) were obtained by first-order analysis of spin patterns. Mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded by using FAB technique. Mass data are reported in mass units (m/z), and values in brackets show the relative intensity from the base peak (as 100%). Analytical thin-layer chromatography was performed on DC-Alufolien 0.2 mm silica gel 60-F plates (Merck). Visualization was accomplished with UV light and ethanolic phosphomolybdic acid solution followed by heating. Flash chromatography was performed on silica gel Merck-60 (230−400 mesh). All solvents were dried before use. THF was distilled from sodium−benzophenone under argon. Toluene was distilled from P_2O_5 and stored over sodium. Carbonates **2** were prepared by straightforward reaction of alcohols **1** with ethyl chloroformate,[2b] pyridine, and DMAP. *N*-(Diphenylmethylene)glycine methyl ester was prepared according to a previously reported procedure.[25]

Ethyl (*E*)-1-(Phenylsulfonyl)-1-buten-3-yl Carbonate (2a). Eluent: ethyl acetate−hexane (1:4), R_f = 0.11. Yield: 95%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.84−7.70 (m, 2 H), 7.51−7.32 (m, 3 H), 6.75 (dd, 1 H, J = 4.0 and 15.4 Hz), 6.39 (dd, 1 H, J = 2.0 and 15.4 Hz), 5.23−5.17 (m, 1 H), 3.97 (q, 2 H, J = 7.3 Hz), 1.24 (d, 3 H, J = 6.9 Hz), 1.21 (t, 3 H, J = 7.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 153.5, 143.3, 139.5, 133.4, 129.4, 129.1 127.4, 71.2, 64.0, 19.1, 13.8. Anal. Calcd for $C_{13}H_{16}O_5S$: C, 54.91; H, 5.67; S, 11.28. Found: C, 55.32; H, 5.23; S, 11.60. [(*S*)-**2a**, $[\alpha]^{25}_D$ = −4.9 (c = 0.92, $CHCl_3$) (prepared from (*S*)-**1a**[21])].

Ethyl (*E*)-1-(Phenylsulfonyl)-1-nonen-3-yl Carbonate (2b). Eluent: ethyl acetate−hexane (1:4), R_f = 0.25. Yield: 89%. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.90−7.84 (m, 2 H), 7.66−7.49 (m, 3 H), 6.92 (dd, 1 H, J = 4.4 and 15.1 Hz), 6.51 (dd, 1 H, J = 1.6 and 15.1 Hz), 5.34−5.25 (m, 1 H), 4.16 (q, 2 H, J = 7.1 Hz), 1.75−1.65 (m, 2 H), 1.38−1.23 (m, 8 H), 1.27 (t, 3 H, J = 7.0 Hz), 0.88−0.82 (m, 3 H). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 153.8, 142.8, 139.7, 133.3, 130.8, 129.1, 127.4, 74.8, 64.1, 33.3, 31.2, 28.5, 24.2, 22.2, 13.9, 13.8. MS: 355 (2, M^+ + 1), 265 (100, M^+ + 1 − CO_2 − EtOH). HRMS: exact mass calcd for $C_{18}H_{27}O_5S$ (M^+ + 1) 355.1579, found 355.1565. [(*S*)-**2b**, $[\alpha]^{25}_D$ = +6.3 (c = 1.13, $CHCl_3$) (prepared from (*S*)-**1b**[21])].

Ethyl (*E*)-4-Methyl-1-(phenylsulfonyl)-1-penten-3-yl Carbonate (2c). Eluent: ethyl acetate−hexane (1:5), R_f = 0.18. Yield: 90%. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.88−7.84 (m, 2 H), 7.66−7.48 (m, 3 H), 6.91 (dd, 1 H, J = 4.7 and 15.2 Hz), 6.51 (dd, 1 H, J = 1.6 and 15.1 Hz), 5.15 (ddd, 1 H, J = 1.6, 1.6 and 4.7 Hz), 4.15 (q, 2 H, J = 7.1 Hz), 2.10−1.94 (m, 1 H), 1.26 (t, 3 H, J = 7.0 Hz), 0.93 (d, 3 H, J = 6.9 Hz), 0.92 (d, 3 H, J = 6.9 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 154.2, 141.6, 139.7, 133.4, 131.6, 129.1, 127.4, 79.1, 64.2, 31.9, 17.6, 17.3, 13.9. Anal. Calcd for $C_{15}H_{20}O_5S$: C, 57.67; H, 6.45; S, 10.26. Found: C, 58.16; H, 6.50; S, 10.80.

Ethyl (*E*)-1-(*p*-Tolylsulfonyl)-1-propen-3-yl Carbonate (2d). Eluent: ethyl acetate−hexane (1:3), R_f = 0.6 in ethyl acetate−hexane (1:1). Yield: 98%. Mp: 39−41 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.76 (d, 2 H, J = 8.3 Hz), 7.34 (d, 2 H, J = 8.1 Hz), 6.94 (dt, 1 H, J = 3.8 and 15.2 Hz), 6.60 (dt, 1 H, J = 2.0 and 15.2 Hz), 4.82 (dd, 2 H, J = 2.0 and 3.8 Hz), 4.20 (q, 2 H, J = 7.2 Hz), 2.44 (s, 3 H), 1.30 (t, 3 H, J = 7.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 154.3, 144.7, 138.0, 136.8, 131.8, 130.0, 127.9, 64.8, 64.5, 21.6, 14.2. Anal. Calcd for $C_{13}H_{16}O_5S$: C, 54.92; H, 5.68; S, 11.25. Found: C, 55.07; H, 5.81; S, 11.58.

General Procedure for the Palladium-Catalyzed Reaction of Carbonates 2 with Nucleophiles. A solution of 0.18 mmol of carbonate **2** and the corresponding nucleophile (4 equiv) in THF (1.5 mL) or in a mixture of THF (0.5 mL) and toluene (1 mL) was added to a stirred suspension of $Pd_2(dba)_3$ (5 mol %), dppe (20 mol %), and powdered molecular sieves 4 Å (40 mg) in THF (0.5 mL). The reaction was immediately heated at reflux or 100 °C [depending on the solvent used: THF or THF−toluene (1:1), respectively] under argon atmosphere until the carbonate disappeared by TLC (2−24 h). Then, the reaction mixture was diluted with ethyl acetate and filtered through a Florisil column. The solvent was concentrated, and the residue was purified by flash chromatography.

Diethyl 2-[(*E*)-1-Methyl-3-(phenylsulfonyl)-2-propen-1-yl]malonate (4a). Carbonate: **2a**. Nucleophile: diethyl malonate. Solvent: THF. Reaction time: 4 h. Eluent: ethyl acetate−hexane [1:5 and 1:3 (R_f = 0.25)]. Yield: 79%. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.87−7.83 (m, 2 H), 7.64−7.47 (m, 3 H), 6.96 (dd, 1 H, J = 7.9 and 15.1 Hz), 6.35 (dd, 1 H, J = 0.8 and 15.1 Hz), 4.15 (q, 2 H, J = 7.1 Hz), 4.06 (q, 2 H, J = 7.2 Hz), 3.34 (d, 1 H, J = 8.2 Hz), 3.21−3.04 (m, 1 H), 1.21 (t, 3 H, J = 7.1 Hz), 1.17 (t, 3 H, J = 7.1 Hz), 1.15 (d, 3 H, J = 6.9 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 167.4, 147.0, 140.2, 133.3, 131.2, 129.2, 127.5, 61.6, 56.4, 35.6, 16.9, 13.9. MS: 355 (100, M^+ +

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1), 195 (13, $M^+ + 1 - EtCO_2CH_2CO_2Et$). HRMS: exact mass calcd for $C_{17}H_{23}O_6S$ ($M^+ + 1$) 355.1215, found 355.1220.

Diethyl 2-[(*E*)-1-Hexyl-3-(phenylsulfonyl)-2-propen-1-yl]malonate (4b). Carbonate: **2b**. Nucleophile: diethyl malonate. Solvent: THF. Reaction time: 4.5 h. Eluent: ethyl acetate−hexane [1:6 and 1:3 (R_f = 0.15)]. Yield: 68%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.86−7.83 (m, 2 H), 7.61−7.48 (m, 3 H), 6.85 (dd, 1 H, J = 9.7 and 15.0 Hz), 6.35 (d, 1 H, J = 15.4 Hz), 4.11 (q, 2 H, J = 7.1 Hz), 4.01 (dq, 2 H, J = 1.3 and 7.2 Hz), 3.39 (d, 1 H, J = 8.3 Hz), 2.99−2.88 (m, 1 H), 1.58−1.34 (m, 2 H), 1.21−1.12 (m, 8 H), 1.18 (t, 3 H, J = 7.2 Hz), 1.15 (t, 3 H, J = 7.1 Hz), 0.85−0.80 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 167.4, 167.2, 146, 140.4, 133.2, 132.5, 129.1, 127.5, 61.6, 61.5, 55.6, 41.4, 31.7, 30.8, 28.7, 26.8, 22.4, 13.9. MS: 425 (100, M^+ + 1), 265 (30, $M^+ + 1 - EtCO_2CH_2CO_2Et$). HRMS: exact mass calcd for $C_{22}H_{33}O_6S$ ($M^+ + 1$) 425.1998, found 425.1989.

Diethyl 2-[(*E*)-1-Isopropyl-3-(phenylsulfonyl)-2-propen-1-yl]malonate (4c). Carbonate: **2c**. Nucleophile: diethyl malonate. Solvent: THF. Reaction time: 4 h. Eluent: ethyl acetate−hexane [1:10 and 1:8 (R_f = 0.05)]. Yield: 64%. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.83−7.77 (m, 2 H), 7.58−7.41 (m, 3 H), 6.90 (dd, 1 H, J = 10.6 and 15.1 Hz), 6.30 (d, 1 H, J = 15.1 Hz), 4.01 (q, 2 H, J = 6.9 Hz), 3.96 (q, 2 H, J = 7.2 Hz), 3.53 (d, 1 H, J = 8.7 Hz), 2.74 (ddd, 1 H, J = 5.7, 8.7, and 10.5 Hz), 1.89−1.72 (m, 1 H), 1.12 (t, 3 H, J = 7.1 Hz), 1.11 (t, 3 H, J = 7.0 Hz), 0.85 (d, 3 H, J = 6.2 Hz), 0.81 (d, 3 H, J = 6.2 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 167.5, 167.1, 143.7, 140.3, 133.3, 133.1, 129.0, 127.4, 61.5, 61.4, 53.8, 47.4, 29.2, 20.9, 18.0, 13.8. MS: 383 (100, M^+ + 1), 223 (23, $M^+ + 1 - EtCO_2CH_2CO_2Et$). HRMS: exact mass calcd for $C_{19}H_{27}O_6S$ (M^+ + 1) 383.1528, found 383.1536.

Methyl (*E*)-2-[*N*-(Diphenylmethylene)amino]-3-methyl-5-(phenylsulfonyl)-4-pentenoate (6). Carbonate: **2a**. Nucleophile: *N*-(Diphenylmethylene)glycine methyl ester. Solvent: THF−toluene (1:1). Reaction time: 4.5 h. Eluent: ethyl acetate−hexane (1:7, 1:5 and 1:3), R_f = 0.36 in ethyl acetate−hexane (1:2). Yield: 46%. Diastereoisomer ratio **6A/6B** = 56:44. Diastereoisomer **6A**: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.87−7.82 (m, 2 H), 7.60−7.26 (m, 11 H), 7.11−7.07 (m, 2 H), 7.08 (dd, 1 H, J = 8.0 and 15.0 Hz), 6.39 (dd, 1 H, J = 1.2 and 15.1 Hz), 4.04 (d, 1 H, J = 5.6 Hz), 3.61 (s, 3 H), 3.22−3.07 (m, 1 H), 1.01 (d, 3 H, J = 6.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.8, 170.9, 148.2, 140.4, 138.9, 135.8, 133.1, 130.6, 129.1, 128.8, 128.7, 128.6, 128.1, 127.7, 127.6, 127.5, 69.4, 52.1, 39.7, 16.2. Diastereoisomer **6B**: ^{1}H NMR (300 MHz, $CDCl_3$) (significant signals) δ: 6.85 (dd, 1 H, J = 7.4 and 15.1 Hz), 6.32 (dd, 1 H, J = 1.2 and 15.1 Hz), 4.10 (d, 1 H, J = 5.5 Hz), 1.19 (d, 3 H, J = 6.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) (significant signals) δ: 172.0, 170.8, 140.6, 139.0, 135.9, 133.2, 130.9, 130.8, 68.4, 39.8, 14.7. MS (mixture **6A**+**6B**): 448 (100, M^+ + 1). HRMS (mixture **6A**+**6B**): exact mass calcd for $C_{26}H_{26}NO_4S$ (M^+ + 1) 448.1582, found 448.1583.

Methyl (*E*)-2-[*N*-(Diphenylmethylene)amino]-6-(phenylsulfonyl)-4-hexenoate (7). Carbonate: **2a**. Nucleophile: *N*-(Diphenylmethylene)glycine methyl ester. Solvent: THF−toluene (1:1). Reaction time: 4.5 h. Eluent: ethyl acetate−hexane (1:7, 1:5, and 1:3), R_f = 0.28 in ethyl acetate−hexane (1:2). Yield: 23%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.78−7.74 (m, 2 H), 7.63−7.29 (m, 11 H), 7.16−7.11 (m, 2 H), 5.55−5.38 (m, 2 H), 4.08 (dd, 1 H, J = 5.6 and 7.3 Hz), 3.71 (bd, 2 H, J = 6.5 Hz), 2.69−2.51 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.8, 171.0, 138.3, 136.8, 136.1, 133.5, 130.5, 129.0, 128.9, 128.8, 128.6, 128.4, 128.1, 127.7, 119.0, 64.7, 59.9, 52.2, 36.8. MS: 448 (73, M^+ + 1), 306 (13, $M^+ + 1 - PhSO_2H$).

1,4-Bis(phenylsulfonyl)-2-methyl-1,3-butadiene (9). Carbonate: **2a**. Nucleophile: bis(phenylsulfonyl)methane. Solvent: THF−toluene (1:1). Reaction time: 3 h. Eluent: ethyl acetate−hexane (2:7), R_f = 0.1. Isomer ratio (1*E*,3*E*)-**9**/(1*Z*,3*E*)-**9** = 75:25. Yield: 30%. Isomer (1*E*,3*E*)-**9**: ^{1}H NMR (significant signals) (200 MHz, $CDCl_3$) δ: 7.13 (d, 1H, J = 15.1 Hz), 6.69 (d, 1 H, J = 15.1 Hz), 6.61 (bs, 1H) and 2.23 (d, 3 H, J = 1.1 Hz). Isomer (1*Z*,3*E*)-**9**: Yield: 7% (in pure product after chromatography). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.54 (bd, 1 H, J = 15.1 Hz), 7.98−7.89 (m, 4 H), 7.69−7.53 (m, 6 H), 6.65 (d, 1 H, J = 15.6 Hz), 6.46 (bs, 1 H) and 1.97 (d, 3 H, J = 1.1 Hz). MS: 349 (61, M^+ + 1), 207 (8, $M^+ + 1 - PhSO_2H$). HRMS: exact mass calcd for $C_{17}H_{17}O_4S_2$ (M^+ + 1) 349.0568, found 349.0566.

(*E*)-1,3-Bis(phenylsulfonyl)-2-butene (11). Eluent: ethyl acetate−hexane (2:7), R_f = 0.07. Yield: 38% (in pure product after chromatography). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.85−7.41 (m, 10 H), 6.77 (tq, 1 H, J = 1.6 and 8.1 Hz), 3.94 (d, 2 H, J = 8.1 Hz) and 1.57 (bs, 3 H). MS: 337 (80, M^+ + 1).

Ethyl (*E*)-2-Acetyl-3-methyl-5-(phenylsulfonyl)-4-pentenoate (12a). Carbonate: **2a**. Nucleophile: ethyl acetoacetate. Solvent: THF at room temperature. Reaction time: 18 h. Eluent: ethyl acetate−hexane (1:15), R_f = 0.39 in ethyl acetate−hexane (1:3). Yield: 43%. Isomer ratio **12A**/**12B** = 55:45. Diastereoisomer **12A:** ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.85−7.82 (m, 2 H), 7.63−7.49 (m, 3 H), 6.89 (dd, 1 H, J = 8.1 and 15.1 Hz), 6.34 (dd, 1 H, J = 1.1 and 15.1 Hz), 4.01 (q, 2 H, J = 7.1 Hz), 3.43 (d, 1 H, J = 9.0 Hz), 3.20−3.13 (m, 1 H), 2.21 (s, 3 H), 1.15 (t, 3 H, J = 7.1 Hz), 1.09 (d, 3 H, J = 8.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 200.6, 167.6, 147.0, 140.3, 133.4, 131.2, 129.2, 127.6, 64.2, 63.7, 34.9, 29.8, 16.6, 13.9. Diastereoisomer **12B:** ^{1}H NMR (300 MHz, $CDCl_3$) (significant signals) δ: 6.88 (dd, 1 H, J = 8.0 and 15.1 Hz), 6.33 (dd, 1 H, J = 1.1 and 15.1 Hz), 4.13 (q, 2 H, J = 7.1 Hz), 3.46 (d, 1 H, J = 8.4 Hz), 2.14 (s, 3 H), 1.23 (t, 3 H, J = 7.1 Hz), 1.07 (d, 3 H, J = 8.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) (significant signals) δ: 200.8, 167.5, 147.4, 140.2, 61.8, 35.1, 29.9, 17.1, 14.0.

3-(Ethoxycarbonyl)-2,4-dimethyl-5-[(phenylsulfonyl)-methyl]-4,5-dihydrofuran (13). Carbonate: **2a**. Nucleophile: ethyl acetoacetate. Solvent: THF−toluene (1:1). Reaction time: 3.5 h. Eluent: ethyl acetate−hexane (1:15), R_f = 0.24 in ethyl acetate−hexane (1:3). Yield: 76%. Isomer ratio *trans*-**13**(4*R**,5*R**)/*cis*-**13**(4*R**,5*S**) = 78:22. Diastereoisomer *trans*-**13:** ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.98−7.91 (m, 2 H), 7.71−7.52 (m, 3 H), 4.61 (ddd, 1 H, J = 4.8, 4.8 and 8.6 Hz), 4.26−4.01 (m, 2 H), 3.47 (dd, 1 H, J = 8.1 and 14.5 Hz), 3.24 (dd, 1 H, J = 4.8 and 14.5 Hz), 3.02−2.89 (m, 1 H), 1.90 (bs, 3 H), 1.26 (t, 3 H, J = 7.0 Hz) and 1.20 (d, 3 H, J = 7.0 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 166.1, 165.4, 139.9, 133.9, 129.1, 128.2, 107.3, 82.4, 60.2, 59.5, 42.7, 19.5, 14.2 and 13.7. Diastereoisomer *cis*-**13:** ^{1}H NMR (200 MHz,$CDCl_3$) (significant signals) δ: 4.93 (ddd, 1 H, J = 4.8, 8.6 and 8.6 Hz), 4.26−4.01 (m, 2 H), 3.56 (dd, 1 H, J = 8.1 and 14.5 Hz), 3.43 (dd, 1 H, J = 4.3 and 15.1 Hz), 3.30−3.15 (m, 1 H), 2.01 (bs, 3 H), 1.25 (t, 3 H, J = 7.0 Hz) and 0.98 (d, 3 H, J = 7.0 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) (significant signals) δ: 166.9, 165.3, 139.4, 108.7, 78.7, 56.6, 39.4 and 13.8. MS: 325 (100, M^+ + 1), 279 (20, M^+ + 1 −EtOH). HRMS: exact mass calcd for $C_{16}H_{21}O_5S$ (M^+ + 1) 325.1109, found 325.1106.

3-(Ethoxycarbonyl)-4-methyl-2-phenyl-5-[(phenylsulfonyl)methyl]-4,5-dihydrofuran (14). Carbonate: **2a**. Nucleophile: ethyl benzoylacetate. Solvent: THF−toluene (1:1). Reaction time: 4 h. Eluent: ethyl acetate−hexane (1:15), R_f = 0.25 in ethyl acetate−hexane (1:5). Yield: 63%. Isomer ratio: *trans*-**14**(4*R**,5*R**)/*cis*-**14**(4*R**,5*S**) = 83:17. Diastereoisomer *trans*-**14:** ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.98−7.89 (m, 2H), 7.63−7.18 (m, 8H), 4.75 (ddd, 1H, J = 4.3, 4.3 and 8.0 Hz), 4.10 (q, 2 H, J = 7.0 Hz), 3.62 (dd, 1 H, J = 8.1 and 14.5 Hz), 3.31 (dd, 1 H, J = 4.3 and 14.5 Hz), 3.15 (dq, 1 H, J = 4.3 and 7.0 Hz), 1.32 (d, 3 H, J = 6.5 Hz), 1.17 (t, 3 H, J = 7.0 Hz).^{13}C NMR (75 MHz, $CDCl_3$) δ: 164.7, 163.2, 139.9, 133.8, 130.5, 129.4, 129.3, 129.1, 128.4, 128.3, 127.4, 107.5, 81.9, 60.5, 59.9, 44.5, 19.8, 14.1. Diastereoisomer *cis*-**14:** ^{1}H NMR (200 MHz, $CDCl_3$) (significant signals) δ: 5.10 (ddd, 1 H, J = 4.3, 8.0 and 8.0 Hz), 4.12 (q, 2 H, J = 7.0 Hz), 3.66 (dd, 1 H, J = 8.1 and 15.1 Hz), 3.51 (dd, 1 H, J = 4.3 and 15.1 Hz), 3.51−3.33 (m, 1 H), 1.19 (d, 3 H, J = 7.0 Hz), 1.14 (t, 3 H, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) (significant signals) δ: 163.7, 139.5, 130.6, 129.2, 128.2, 109, 78.6, 56.7, 41.3, 14.3. MS: 387 (55, M^+ + 1), 341 (92, $M^+ + 1 - EtOH$), 245 (19, $M^+ + 1 - PhSO_2H$). HRMS (*cis*-**14**+*trans*-**14**): exact mass calcd for $C_{21}H_{23}O_5S$ (M^+ + 1) 387.1266, found 387.1251.

3-Acetyl-2,4-dimethyl-5-[(phenylsulfonyl)methyl]-4,5-dihydrofuran (15). Carbonate: **2a**. Nucleophile: 2,4-pentanedione. Solvent: THF. Reaction time: 2.5 h. Eluent: ethyl acetate−hexane [1:5 (R_f = 0.05)]. Yield: 79%. Isomer ratio *trans*-**15**(4*R**,5*R**)/*cis*-**15**(4*R**,5*S**) = 75:25. Diastereoisomer

trans-**15:** ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.94−7.89 (m, 2 H), 7.70−7.51 (m, 3 H), 4.58 (ddd, 1 H, J = 3.6, 4.8 and 8.2 Hz), 3.42 (dd, 1 H, J = 7.9 and 14.5 Hz), 3.23 (dd, 1 H, J = 4.8 and 14.5 Hz), 3.04−2.97 (m, 1 H), 2.17 (s, 3H), 1.91 (s, 3 H), 1.18 (d, 3 H, J = 6.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 193.9, 165.6, 139.8, 133.8, 129.2, 128.1, 117.8, 82.5, 60.0, 43.1, 29.2, 20.0, 14.8. Diastereoismer *cis*-**15:** ^{1}H NMR (300 MHz, $CDCl_3$) (significant signals) δ: 4.88 (ddd, 1 H, J = 4.6, 8.2 and 8.2 Hz), 3.54 (dd, 1 H, J = 8.1 and 14.6 Hz), 3.43 (dd, 1 H, J = 4.6 and 14.5 Hz), 3.27−3.18 (m, 1 H), 2.20 (s, 3 H), 2.04 (s, 3 H) and 0.97 (d, 3 H, J = 6.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) (significant signals) δ: 193.6, 166.5, 139.4, 134.0, 128.2, 119.7, 78.8, 56.4, 39.9, 19.7 and 15.1. MS (*cis*-**15**+*trans*-**15**): 295 (100, $M^+ + 1$), 153 (18, $M^+ + 1 - PhSO_2H$). HRMS (*cis*-**15**+*trans*-**15**): exact mass calcd for $C_{15}H_{19}O_4S$ ($M^+ + 1$) 295.1004, found 295.0999.

4,5,6,7-Tetrahydro-3-methyl-2-[(phenylsulfonyl)methyl]-4(2*H*)-benzofuranone (16). Carbonate: **2a**. Nucleophile: 1,3-cyclohexanedione. Solvent: THF−toluene (1:1). Reaction time: 20 h. Eluent: ethyl acetate−hexane (1:9, 1:5, and 1:2), R_f = 0.4 in ethyl acetate−hexane (1.1). Yield: 89%. Isomer ratio *trans*-**16**(2*R**,3*R**)/*cis*-**16**(2*R**,3*S**) = 75:25. Diastereoisomer *trans*-**16:** ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.95−7.89 (m, 2 H), 7.68−7.51 (m, 3 H), 4.69 (ddd, 1 H, J = 4.7, 4.7 and 8.0 Hz), 3.47 (dd, 1 H, J = 8.0 and 14.6 Hz), 3.29 (dd, 1 H, J = 4.5 and 14.6 Hz), 3.01−2.93 (m, 1 H), 2.30−1.87 (m, 6 H), 1.19 (d, 3 H, J = 6.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 195.2, 175.4, 139.6, 133.9, 129.2, 128.0, 117.0, 85.2, 60.3, 40.3, 36.6, 23.5, 21.5, 18.7. Diastereoisomer *cis*-**16:** ^{1}H NMR (300 MHz, $CDCl_3$) (significant signals) δ: 5.08 (ddd, 1 H, J = 3.7, 9.0 and 9.0 Hz), 3.53 (dd, 1 H, J = 8.9 and 14.7 Hz), 3.41 (dd, 1 H, J = 3.7 and 14.8 Hz), 3.32−3.25 (m, 1 H), 0.99 (d, 3 H, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) (significant signals) δ: 195.0, 175.7, 139.4, 133.9, 128.1, 118.1, 81.0, 56.6, 36.7, 36.5, 21.4, 13.7. MS (*cis*-**16**+*trans*-**16**): 307 (100, $M^+ + 1$), 165 (29, $M^+ + 1 - PhSO_2H$). HRMS (*cis*-**16**+*trans*-**16**): exact mass calcd for $C_{16}H_{19}O_4S$ ($M^+ + 1$) 307.1004, found 307.1019.

2,4-Dimethyl-3-(phenylsulfonyl)-5-[(phenylsulfonyl)-methyl]-4,5-dihydrofuran (17). Carbonate: **2a**. Nucleophile: (phenylsulfonyl)acetone. Ligand: dppf (20 mol %). Solvent: THF−toluene (1:1). Reaction time: 6.5 h. Eluent: ethyl acetate−hexane (1:10, 1:8, and 1:5), R_f = 0.28 in ethyl acetate−hexane (1:1). Yield: 80%. Isomer ratio *trans*-**17**(4*R**, 5*R**)/*cis*-**17**(4*R**, 5*S**) = 75:25. Diastereoisomer *trans*-**17**: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.92−7.79 (m, 4 H), 7.70−7.49 (m, 6 H), 4.57 (ddd, 1 H, J = 4.9, 4.9 and 7.6 Hz), 3.34 (dd, 1 H, J = 7.6 and 14.5 Hz), 3.12 (dd, 1 H, J = 4.9 and 14.5 Hz), 2.95−2.90 (m, 1 H), 2.02 (d, 3 H, J = 1.4 Hz) and 1.14 (d, 3 H, J = 6.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 165.2, 142.7, 139.6, 133.0, 129.3, 129.2, 126.6, 114.2, 82.9, 59.8, 43.8, 19.3 and 13.4. Diastereoisomer *cis*-**17**: ^{1}H NMR (300 MHz, $CDCl_3$) (significant signals) δ: 4.91 (ddd, 1 H, J = 4.3, 8.5 and 8.5 Hz), 3.50 (dd, 1 H, J = 8.4 and 14.6 Hz), 3.35 (dd, 1 H, J = 4.5 and 14.5 Hz), 3.15−3.05 (m, 1 H), 2.09 (d, 3 H, J = 1.2 Hz), 1.06 (d, 3 H, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 165.7, 134.1, 134.0, 128.2, 128.1, 126.7, 115.6, 79.2, 56.2, 40.7, 14.4. MS (*cis*-**17**+*trans*-**17**): 393 (44, $M^+ + 1$), 251 (8, $M^+ + 1 - PhSO_2H$). HRMS (*cis*-**17**+*trans*-**17**): exact mass calcd for $C_{19}H_{21}O_5S_2$ ($M^+ + 1$) 393.0830, found 393.0836.

(4*R,5*R**)-3-(Ethoxycarbonyl)-4-*n*-hexyl-2-methyl-5-[(phenylsulfonyl)methyl]-4,5-dihydrofuran (*trans*-18).** Carbonate: **2b**. Nucleophile: ethyl acetoacetate. Solvent: THF−toluene (1:1). Reaction time: 4 h. Eluent: ethyl acetate−hexane [1:15 (R_f = 0.04)]. Yield: 79%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.94−7.90 (m, 2 H), 7.67−7.23 (m, 3 H), 4.75 (ddd, 1 H, J = 4.0, 4.0 and 8.9 Hz), 4.18−4.03 (m, 2 H), 3.46 (dd, 1 H, J = 8.9 and 14.5 Hz), 3.17 (dd, 1 H, J = 4.0 and 14.5 Hz), 2.85−2.82 (m, 1 H), 1.81 (bs, 3 H), 1.71−1.37 (m, 2 H), 1.36−1.16 (m, 8 H), 1.20 (t, 3 H, J = 6.9 Hz), 0.88−0.84 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.3, 165.5, 140.2, 133.7, 129.1, 128.2, 105.9, 80.4, 60.9, 59.6, 48.0, 33.0, 31.6, 29.2, 25.9, 22.6, 14.3, 14.1, 13.8. MS: 395 (24, $M^+ + 1$), 349 (100, $M^+ + 1 - EtOH$). HRMS: exact mass calcd for $C_{21}H_{31}O_5S$ ($M^+ + 1$) 395.1892, found 395.1891. [(4*R*,5*R*)-**18**, $[\alpha]^{25}_D$ = −56.5 (c = 1.49, $CHCl_3$) (prepared from (*S*)-**2b**[21])].

(4*R,5*R**)-3-(Ethoxycarbonyl)-4-*n*-hexyl-2-phenyl-5-[(phenylsulfonyl)methyl]-4,5-dihydrofuran (*trans*-19).** Carbonate: **2b**. Nucleophile: ethyl benzoylacetate. Solvent: THF−toluene (1:1). Reaction time: 5 h. Eluent: ethyl acetate−hexane (1:15), R_f = 0.28 in ethyl acetate−hexane (1:5). Yield: 57%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.98−7.90 (m, 2 H), 7.66−7.18 (m, 8 H), 4.91 (ddd, 1 H, J = 3.7, 3.7, 8.9 Hz), 4.16−4.05 (m, 2H), 3.64 (dd, 1 H, J = 8.9 and 14.9 Hz), 3.24 (dd, 1 H, J = 3.6 and 14.5 Hz), 3.08−3.03 (m, 1 H), 1.80−1.50 (m, 2 H), 1.40−1.10 (m, 8 H), 1.16 (t, 3 H, J = 6.9 Hz), 0.89−0.78 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 164.6, 163.3, 140.0, 133.7, 130.5, 129.4, 129.3, 128.5, 128.3, 127.3, 106.0, 79.8, 61.1, 59.8, 49.5, 33.4, 31.6, 29.2, 25.9, 22.6 and 14.0. MS: 457 (30, $M^+ + 1$), 411 (69, $M^+ + 1 - EtOH$). HRMS: exact mass calcd for $C_{26}H_{33}O_5S$ ($M^+ + 1$) 457.2049, found 457.2030.

(4*R,5*R**)-3-Acetyl-4-*n*-hexyl-2-methyl-5-[(phenylsulfonyl)methyl]-4,5-dihydrofuran (*trans*-20).** Carbonate: **2b**. Nucleophile: 2,4-pentanedione. Solvent: THF−toluene (1:1). Reaction time: 3 h. Eluent: ethyl acetate−hexane (1:15), R_f = 0.10 in ethyl acetate−hexane (1:10). Yield: 67%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.95−7.90 (m, 2 H), 7.70−7.51 (m, 3 H), 4.76 (ddd, 1 H, J = 3.9, 3.9 and 8.6 Hz), 3.45 (dd, 1 H, J = 8.6 and 14.9 Hz), 3.17 (dd, 1 H, J = 3.9 and 14.9 Hz), 2.94−2.89 (m, 1 H), 2.19 (s, 3 H), 1.91 (bs, 3 H), 1.69−1.40 (m, 1 H), 1.39−1.14 (m, 9 H), 0.95−0.83 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 193.8, 165.6, 140.0, 133.7, 129.1, 128.1, 116.4, 80.3, 60.6, 48.3, 33.2, 31.6, 29.2, 29.1, 25.9, 22.5, 14.8, 14.0. MS: 365 (100, $M^+ + 1$), 223 (29, $M^+ + 1 - PhSO_2H$). HRMS: exact mass calcd for $C_{20}H_{29}O_4S$ ($M^+ + 1$) 365.1786, found 365.1779.

(4*R,5*R**)-3-(Ethoxycarbonyl)-4-isopropyl-2-methyl-5-[(phenylsulfonyl)methyl]-4,5-dihydrofuran (*trans*-21).** Carbonate: **2c**. Nucleophile: ethyl acetoacetate. Solvent: THF−toluene (1:1). Reaction time: 6 h. Eluent: ethyl acetate−hexane (1:15), R_f = 0.35 in ethyl acetate−hexane (1:3). Yield: 38%. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.96−7.91 (m, 2 H), 7.70−7.51 (m, 3 H), 4.86 (ddd, 1 H, J = 3.2, 3.2, and 9.1 Hz), 4.24−4.01 (m, 2H), 3.49 (dd, 1 H, J = 9.1 and 15.0 Hz), 3.10 (dd, 1 H, J = 3.2 and 15.1 Hz), 2.83−2.80 (m, 1 H), 2.18−2.00 (m, 1 H), 1.84 (d, 3 H, J = 1.1 Hz), 1.24 (t, 3 H, J = 7.5 Hz), 0.88 (d, 3 H, J = 7.0 Hz), 0.74 (d, 3 H, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.6, 165.6, 140.2, 133.7, 129.3, 129.2, 128.2, 127.7, 127.6, 104.5, 76.7, 61.5, 59.6, 53.8, 32.2, 29.7, 28.9, 19.9, 16.3, 14.3, 13.7. MS: 307 (44, $M^+ + 1 - EtOH$). HRMS: exact mass calcd for $C_{18}H_{25}O_5S$ ($M^+ + 1$) 353.1423, found 353.1420.

(4*R,5*R**)-3-(Ethoxycarbonyl)-4-isopropyl-2-phenyl-5-[(phenylsulfonyl)methyl]-4,5-dihydrofuran (*trans*-22).** Carbonate: **2c**. Nucleophile: ethyl benzoylacetate. Solvent: THF−toluene (1:1). Reaction time: 6 h. Yield: 14%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.99−7.19 (m, 10H), 5.02 (ddd, 1H, J = 3.2, 3.2, and 9.1 Hz), 4.09 (q, 2H, J = 6.9 Hz), 3.68 (dd, 1H, J = 9.1 and 14.5 Hz), 3.16 (dd, 1H, J = 3.2 and 14.6 Hz), 3.03 (t, 1H, J = 3.2 Hz), 2.25−2.13 (m, 1H), 1.16 (t, 3H, J = 7.3 Hz), 0.98 (d, 3H, J = 6.9 Hz), 0.88 (d, 3H, J = 6.9 Hz).

(4*R,5*R**)-3-Acetyl-4-isopropyl-2-methyl-5-[(phenylsulfonyl)methyl]-4,5-dihydrofuran (*trans*-23).** Carbonate: **2c**. Nucleophile: 2,4-pentanedione. Solvent: THF−toluene (1:1). Reaction time: 7 h. Eluent: ethyl acetate−hexane (1:15), R_f = 0.10 in ethyl acetate−hexane (1:3). Yield: 14%. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.96−7.92 (m, 2 H), 7.67−7.53 (m, 3 H), 4.88 (ddd, 1 H, J = 3.8, 3.8 and 8.6 Hz), 3.46 (dd, 1 H, J = 9.1 and 15.0 Hz), 3.11 (dd, 1 H, J = 3.8 and 14.5 Hz), 2.95−2.90 (m, 1 H), 2.20 (s, 3 H), 2.11−2.02 (m, 1 H), 1.91 (d, 3 H, J = 1.0 Hz), 0.91 (d, 3 H, J = 7.0 Hz), 0.72 (d, 3 H, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 194.0, 165.9, 140.2, 133.8, 129.1, 128.2, 115.3, 76.4, 61.3, 54.3, 29.4, 28.8, 20.1, 16.0, 14.8. MS: 323 (74, $M^+ + 1$), 181 (16, $M^+ + 1 - PhSO_2H$). HRMS: exact mass calcd for $C_{17}H_{23}O_4S$ ($M^+ + 1$) 323.1317, found 323.1325.

3-(Ethoxycarbonyl)-2-methyl-5-[(*p*-tolylsulfonyl)methyl]-4,5-dihydrofuran (24). Carbonate: **2d**. Nucleophile: ethyl acetoacetate. Solvent: THF−toluene (1:1). Reaction time: 17.5 h. Eluent: ethyl acetate−hexane (1:7 and 1:3), R_f = 0.3 in ethyl acetate−hexane (1:1). Yield: 41%. mp: 89−93 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.80 (d, 2 H, J = 8.3 Hz), 7.35 (d, 2 H, J = 8.3 Hz), 5.00 (dddd, 1 H, J = 5.7, 6.9, 6.9 and 10.3 Hz), 4.13 (q, 2 H, J = 7.2 Hz), 3.52 (dd, 1 H, J = 6.9 and 14.3

Hz), 3.28 (dd, 1 H, J = 5.6 and 14.4 Hz), 3.09 (ddq, 1 H, J = 1.6, 10.3 and 15.1 Hz), 2.65 (ddq, 1 H, J = 1.6, 6.9, 15.0 Hz), 2.45 (s, 3 H), 1.98 (t, 3 H, J = 1.6 Hz) and 1.24 (t, 3 H, J = 7.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.6, 165.5, 145.0, 136.7, 129.8, 128.2, 101.8, 75.5, 61.1, 59.6, 35.4, 21.6, 14.3 and 13.6. MS: 325 (14, $M^+ + 1$), 279 (100, $M^+ + 1 -$ EtOH). HRMS: exact mass calcd for $C_{16}H_{21}O_5S$ ($M^+ + 1$) 325.1110, found 325.1096.

4,5,6,7-Tetrahydro-2-[(*p*-tolylsulfonyl)methyl]-4(2*H*)-benzofuranone (25). Carbonate: **2d**. Nucleophile: 1,3 cyclohexanedione. Solvent: THF−toluene (1:1). Reaction time: 18 h. Eluent: dichloromethane and dichloromethane−ethyl acetate (10:1 and 4:1). R_f = 0.23 in dichloromethane−ethyl acetate (2:1). Yield: 42%. mp: 168−170 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.79 (d, 2 H, J = 8.3 Hz), 7.36 (d, 2 H, J = 8.1 Hz), 5.96 (dddd, 1 H, J = 5.3, 7.2, 7.2 and 10.2 Hz), 3.55 (dd, 1 H, J = 7.2, 14.4 Hz), 3.33 (dd, 1 H, J = 5.3 and 14.5 Hz), 2.99 (ddt, 1 H, J = 1.8, 10.4 and 14.9 Hz), 2.51 (ddt, 1 H, J = 1.8, 7.2 and 14.9), 2.44 (s, 3 H), 2.41−2.16 (m, 4H), 2.02−1.89 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 195.1, 176.3, 145.2, 136.5, 129.9, 128.1, 112.5, 78.5, 61.2, 36.3, 31.8, 23.5, 21.6, 21.4. MS: 307 (85, $M^+ + 1$). HRMS exact mass calcd for $C_{16}H_{19}O_4S$ ($M^+ + 1$) 307.1004, found 307.1007.

(*R*)-Dimethyl 2-[(*E*)-1-Methyl-3-(phenylsulfonyl)-2-propen-1-yl]malonate [(*R*)-26]. $[\alpha]_D = -9.0$ (c = 1.03, $CHCl_3$); $[\alpha]_D$ lit.[23,5a] = −10.3 (c = 1.02, $CHCl_3$). ee >96% [determined by ^{1}H NMR with Pr(hfc)$_3$]. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.90−7−84 (m, 2H), 7.66−7.51 (m, 3H), 6.97 (dd, 1H, J = 8.1 and 15.2 Hz), 6.38 (dd, 1H, J = 0.7 and 15.2 Hz), 3.69 (s, 3H), 3.59 (s, 3H), 3.42 (d, 1H, J = 8.1 Hz), 3.20−3.07 (m, 1H), 1.17 (d, 3H, J = 6.8 Hz).

(2*S*,3*R*,4*R*,5*R*)-3-(Ethoxycarbonyl)-4-*n*-hexyl-2-methyl-5-[(phenylsulfonyl)methyl]tetrahydrofuran (27) and (2*R*,3*R*,4*R*,5*R*)-(28). To a stirred solution of **18** (71 mg, 0.18 mmol) in trifluoroacetic acid (3.44 mL) was added triethylsilane (10 equiv, 320 μL). The reaction mixture was heated at 60 °C for 19 h. After cooling at room temperature, the mixture was concentrated in vacuo and then azeotropic removal of residual trifluoroacetic acid with toluene. The residue was purified by flash chromatography (eluting with ethyl acetate−hexane 1:7. R_f = 0.37 in ethyl acetate−hexane 1:3) to give a mixture of **27** and **28**. Yield: 70%. Isomer ratio **27/28** = 86:14. $[\alpha]^{25}_D = -25.1$ (c = 0.97, $CHCl_3$). Isomer **27:** ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.95−7.90 (m, 2 H), 7.65−7.58 (m, 1 H), 7.55−7.48 (m, 2 H), 4.22 (ddd, 1 H, J = 3.2, 5.9 and 9.0 Hz), 4.11 (q, 2 H, J = 7.1 Hz), 3.85 (qd, 1 H, J = 6.0 and 8.1 Hz), 3.46 (dd, 1 H, J = 8.6 and 14.5 Hz), 3.27 (dd, 1 H, J = 3.3 and 14.5 Hz), 2.33−2.15 (m, 1 H), 2.23 (dd, 1 H, J = 8.1 and 8.3 Hz), 1.52−1.36 (m, 1 H), 1.29−1.16 (m, 9 H), 1.22 (t, 3 H, J = 7.1 Hz), 1.10 (d, 3 H, J = 6.1 Hz), 0.86 (t, 3 H, J = 6.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 172.7, 140.1, 133.5, 128.9, 128.2, 78.0, 77.7, 60.9, 60.5, 57.9, 50.0, 33.2, 31.5, 29.2, 27.4, 22.5, 19.8, 14.1 and 14.0. ^{1}H NMR (300 MHz, C_6D_6) δ: 7.98−7.91 (m, 2 H), 7.05−6.95 (m, 3 H), 4.40 (ddd, 1 H, J = 4.3, 6.4 and 8.0 Hz), 4.00−3.81 (m, 1 H), 3.93 (dq, 2 H, J = 1.1 and 7.0 Hz), 3.30 (dd, 1 H, J = 8.1 and 14.5 Hz), 3.15 (dd, 1H, J = 4.3 and 14.5 Hz), 2.48−2.36 (m, 1H), 2.21 (dd, 1 H, J = 8.1 and 8.6 Hz), 1.31−1.19 (m, 10 H), 1.09 (d, 3 H, J = 6.0 Hz), 0.95 (t, 3 H, J = 7.0 Hz), 0.93 (t, 3 H, J = 7.0 Hz). Isomer **28:** ^{1}H NMR (300 MHz, $CDCl_3$) (significant signals) δ: 4.16−4.09 (m, 1 H), 3.97 (ddd, 1 H J = 3.4, 7.8, and 7.8 Hz), 3.53 (dd, 1 H, J = 8.1 and 14.5 Hz), 3.40 (dd, 1 H, J = 3.4 and 14.5 Hz), 2.66 (dd, 1 H, J = 5.2 and 7.5 Hz) and 0.99 (d, 3 H, J = 6.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) (significant signals) δ: 128.8, 128.4, 128.2, 78.2, 76.0, 61.0, 60.6, 54.1, 48.2, 32.5, 27.6, 16.8, 14.2. Anal. Calcd for $C_{21}H_{32}O_5S$ (mixture **27**+**28**): C, 63.61; H, 8.13 and S, 8.08, found C, 64.14; H, 7.82 and S 8.09.

Acknowledgment. Financial support from DGICYT(Ministerio de Educación y Cultura, project PB96-0021) is gratefully acknowledged. The authors are also greatly indebted to Dr. Concepción Pedregal and Ms. Virginia Magro for some previous work in this field and to Prof. Dieter Enders for sending us the complete characterization data of compound (*R*)-**26**.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra for compounds **2a**−**d**, **4a**−**c**, **6**, **7**, **12a**, **13**−**21**, **24**, **25**, and **27**+**28**; ^{1}H NMR spectra of **9Z**, **11**, **23**, and **26**; HRMS spectra for **2b**, **4a**−**c**, **6**, **9Z**, **13**−**21**, and **23**−**25** (83 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.

JO981391R