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Carbolithiation of Cinnamyl Methyl Ethers and 2-Cinnamyl-2-methyl-1,3-dioxolane: High Diastereoselectivity after Electrophilic Substitution

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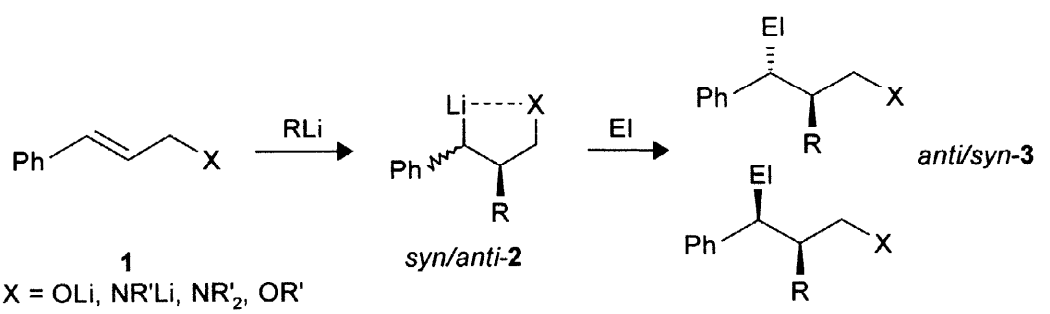
Abstract: The carbolithiation of cinnamyl methyl ether **4** with *tert*-butyllithium, benzyllithium, and allyllithium is achieved in good yields. Consecutive treatment with electrophiles yields in all three cases a good diastereoselectivity thus confirming earlier results obtained in the reaction of secondary and tertiary cinnamyl amines. The ethylene acetal of 4-phenyl-3-buten-2-one **20** can also be carbolithiated with *tert*-butyllithium and the products exhibit even higher diastereomeric excesses.

tert-Butyllithium has been added to α-methylcinnamyl methyl ether **17** showing complete diastereoselection in the nucleophilic addition step.

Cinnamyl alcohol[1] and both secondary[2] and tertiary[3] cinnamyl amines have been carbolithiated with success and treatment of the benzylic lithium compounds with electrophiles leads with high diastereoselectivity to the substituted products **3**. Amines give *anti* products while the alkoxide compounds have been shown to yield mainly the *syn* substituted diastereomers of **3**. This has been attributed to the oligomeric nature of the addition products of cinnamyl alcohol (**2**, X=OLi) under the reaction conditions.[2]



1
X = OLi, NR'Li, NR'_2, OR'

syn/anti-**2**

Scheme 1

In the group of O- and N-substituted cinnamyl compounds, only the ethers have not yet been explicitely investigated concerning their diastereoselectivity. Normant et al. have reported the

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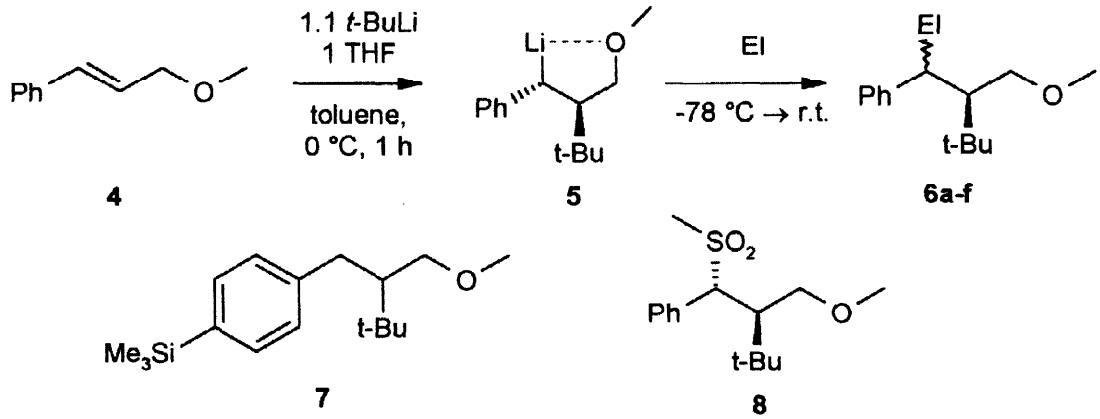
carbolithiation of *tert*-butyl cinnamyl ether in the presence of (-)-sparteine, but have not discussed the reaction with electrophiles other than proton. Cinnamyl ethers as well as tertiary cinnamyl amines can be deprotonated by the lithium alkyls to give 1-alkoxy or 1-dialkylamino allyllithium compounds. This side reaction may compete seriously with the desired nucleophilic addition reaction.

Carbolithiation of cinnamyl methyl ether 4

The addition reaction of lithium alkyls in neat THF or hydrocarbon solvents fails due to the side reaction already mentioned, yielding deprotonation products or mixtures. Fortunately, in the presence of only one equivalent of tetrahydrofuran (THF), *tert*-butyllithium adds smoothly to cinnamyl methyl ether **4** in toluene. The following treatment of the lithium compound **5** with electrophiles at -78 °C gives the products **6a-f** in moderate to good yields (Scheme 2, Table 1).[4]

The reaction conditions seem to promote the specific formation of a THF-solvated aggregate of *tert*-butyllithium that prefers addition over deprotonation. A tetrasolvated dimer of *tert*-butyllithium has been characterized by NMR spectroscopy as a stable but reactive species in the presence of two equivalents of diethyl ether in hydrocarbon solutions.[5]



Scheme 2

Table 1 Treatment of **5** with several electrophiles

Compound	El (reagent)	Yield (%)[a]	d.r (*anti*:*syn*)
6a	H (MeOH)	79	-
6b	D (MeOD)	73	90 : 10
6c	COOH (CO_2)	79	85 : 15
6d	SCH_3 (MeSSMe)	61	98 : 2[b]
6e	CH_3 (MeI)	60	13 : 87[c]
6f	n-C_4H_9 (n-BuI)	49	2 : 98[b][c]
7	Me_3Si (TMSCl)	58	-

[a] Yield of distilled products.
[b] Only one diastereomer appears in the ^1H NMR spectrum.
[c] Inversion of configuration is assumed.

In the case of deuteration, it is possible based on a low coupling constant ^3J between the benzylic proton and the proton at C_β to assign the *anti* configuration of **6b**. The reasoning is based on the assumed preferred conformation of the molecule in solution.[2] Since deuteration with methanol proceeds under retention of the configuration,[6,7] the *anti* configuration of the adduct **5** has been confirmed.

The methyl sulfide **6d** can be oxidized with sodium perborate to give the sulfone **8**. This compound gives crystals suitable for X-ray crystallographic analysis revealing the *anti* configuration. The molecular structure of the sulfone is shown in Fig. 1. The thiomethylation of this benzyllithium compound has therefore also taken place with retention of the configuration. We propose the same mechanism for the carboxylation due to the similar result with a structurally related cinnamyl acetal (see below). It must be mentioned, however, that some benzylic and dipole-stabilized lithium compounds have been reported to react with carbon dioxide in a metalloinverse fashion.[8,9]

Similarily, alkylation with alkyl halides has also been shown to occur under inversion at the nucleophilic centres.[6,7,9] We have not proven the relative configuration of the alkylation products **6e** and **6f** but assume the same stereospecifity in these cases. Accordingly, the two ethers are mainly formed as the *syn* diastereomers.

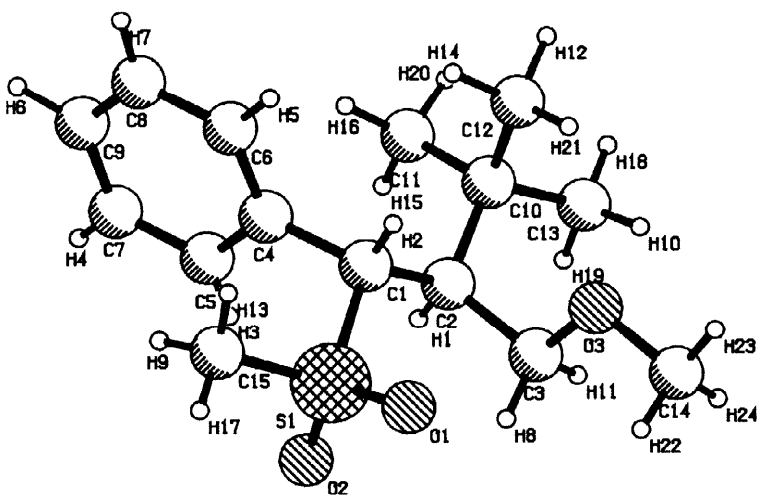


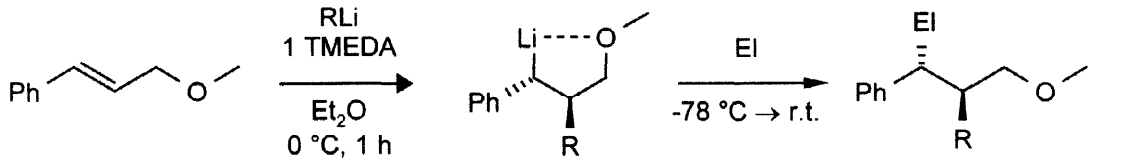
Fig. 1 Molecular structure of the sulfone **8** in the crystal, obtained upon oxidation of the *anti* methyl sulfide **6d**. Dihedral angles: C4-C1-C2-C10 63.5°, S1-C1-C2-C10 -173.8°, S1-C1-C2-C3 -43.8°, C4-C1-C2-C3 -166.5°.

The preparative value of the reaction is rather limited, as only a few electrophiles were successfully employed. The low reactivity of the benzyllithium compound is obviously caused by steric hindrance of the nucleophilic centre through the bulky *tert*-butyl group. In one case **5** reacts with pivalinic aldehyde, but the yield is lower and two diastereomers are formed in a 3 : 1 ratio due to the chiral centre of the newly generated secondary alcohol.

Surprisingly, the reaction of **5** with trimethylsilyl chloride (TMSCl) does not result in the formation of the expected trimethyl benzyl silane, but the para-silyl-substituted **7**. Such attack at the para-position of a benzyllithium compound has not yet been reported, although some benzylic Grignard reagents were found to yield similar products with Michael acceptors.[10,11] This unexpected behaviour again shows the low reactivity of the benzylic position.

9 **10**

Attempts to add *n*-butyllithium to **5** fail due to the deprotonation reaction mentioned above. Instead of using alkyllithium compounds we have turned to the delocalized and thereby „softer" allyllithium **9** and benzyllithium **10** which are expected to be more nucleophilic and less basic towards the substrate. Using diethyl ether (Et_2O) together with one equivalent of tetramethylethylenediamine (TMEDA) as solvent in the reaction of these organolithium compounds turns out to be superior to toluene/THF used with *tert*-butyllithium. Allyl- and benzyllithium are prepared in situ by transmetalation with methyllithium from the corresponding trimethyltin precursors.[12] After addition of the cinnamyl ether **4**, carbolithiation is complete after 1 h at 0 °C (Scheme 3). The electrophile is added at -78 °C and the products are obtained in reasonable yields after aqueous workup (Table 2).



4

11 (R = $-CH_2Ph$)
13 (R = $-CH_2CH{=}CH_2$)

12a-e (R = $-CH_2Ph$)
14a-e (R = $-CH_2CH{=}CH_2$)

Scheme 3

Table 2 Treatment of **11** and **13** with several electrophiles

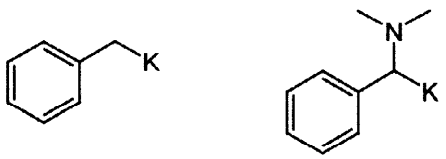
Compound	RLi	El (reagent)	Yield (%)[a]	d.r (*anti:syn*)
12a	$PhCH_2Li$	H (MeOH)	64	-
12b	$PhCH_2Li$	D (MeOD)	68	98 : 2[b]
12c	$PhCH_2Li$	COOH (CO_2)	66	98 : 2[b]
12d	$PhCH_2Li$	SCH_3 (MeSSMe)	61	95 : 5
12e	$PhCH_2Li$	CH_3 (MeI)	67	11 : 89[c]
14a	$H_2C{=}CH\text{-}CH_2Li$	H (MeOH)	65	-
14b	$H_2C{=}CH\text{-}CH_2Li$	D (MeOD)	63	80 : 20
14c	$H_2C{=}CH\text{-}CH_2Li$	COOH (CO_2)	68	87 : 13
14d	$H_2C{=}CH\text{-}CH_2Li$	SCH_3 (MeSSMe)	68	61 : 39
14e	$H_2C{=}CH\text{-}CH_2Li$	CH_3 (MeI)	59	16 : 84[c]

[a] Yield of distilled products.
[b] Only one diastereomer appears in the ^1H NMR spectrum.
[c] Inversion of configuration is assumed.

The observed selectivities of the benzyl substituted products **12b-e** are somewhat higher than for the *tert*-butyl substituted diastereomers **6b-e**, but lower for the allyl substituted **14b-e**. Steric demand of the benzyl vs. the *tert*-butyl group is clearly smaller so the higher selectivity seems to be influenced by

the change of the reaction conditions rather than by steric factors. The bidentate ligand TMEDA is most likely to coordinate the lithium cations in diethyl ether solutions, so the electrophile encounters a different environment of the benzylic nucleophile compared to the reaction in toluene/THF. Changes of the ion pair structure are also evident from the colours of the benzyllithium intermediates **5** (dark-orange) and **11**/**13**(yellow) in their respective solvent. This, however, does not explain the resulting stereoselectivity.

The addition of allyllithium **9** and benzyllithium **10** is one of the few examples of intermolecular carbolithiation with *functionalized* alkyllithium compounds. Further transformations, esp. of the terminal double bond, might extend the scope of this reaction, even if the diastereoselectivities in some cases are low.



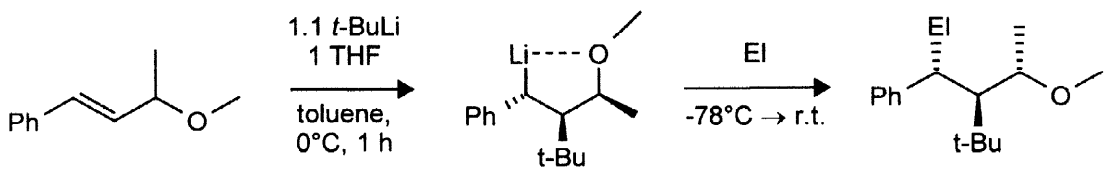
15 **16**

Addition of benzylpotassium **15** and the functionalized α-dimethylaminobenzylpotassium **16** (prepared by deprotonation of toluene and N,N-dimethylbenzylamine with *n*-butyllithium/*t*-BuOK) to cinnamyl methyl ether in THF give nearly the same yields as in the reaction of benzyllithium. However, as expected for organic compounds of the heavier alkali metals, the diastereoselectivites in the reactions of **15** and **16** with cinnamyl methyl ether **4** drop to very low ratios and the preparative value is therefore limited.[4]

Carbolithiation of α-methylcinnamyl methyl ether 17

The large excess of one diastereomer in the products **6**, **12** and **14** stimulates the idea of controlling the stereochemistry in the target molecule by employing a cinnamyl ether which already contains an asymmetric carbon atom. If the carbolithiation step was highly selective, it would allow the subsequent formation of the second and third stereogenic centre with high diastereomeric excess.

Felkin *et al.* have reported a high *anti* diastereoselectivity in the addition of *iso*-propyllithium to α-methylallyl alcohol.[13] α-Methylcinnamyl alcohol has also been carbolithiated with *n*-butyllithium with a selectivity of about 70 % *de*.[1] This encouraged us to explore the selectivity in the addition of *tert*-butyllithium to α-methylcinnamyl methyl ether **17**. Conditions used for carbolithiation and substitution were the same as with **5** (Scheme 4, Table 3).



17 **18** **19a-d**

Scheme 4

Indeed, after hydrolysis, only one single diastereomer of **19a** is found in the ^{1}H and ^{13}C NMR spectra. Deuteration, carboxylation and thiomethylation gave diastereomeric ratios similar to those observed in the reaction of cinnamyl methyl ether **4**. The new carbon-carbon bond is formed with high

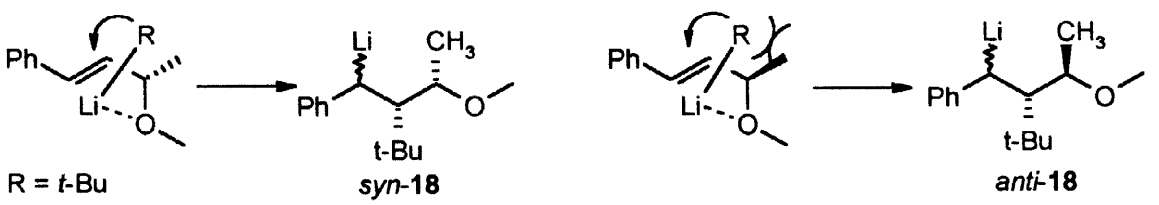
diastereoselectivity. The sulfone obtained after oxidation of **19d** does not crystallize well, therefore investigation by X-ray analysis is not possible. Nevertheless, the *anti* configuration between the *tert*-butyl and the methyl group can be proven by preparing **19b** in a different approach with known stereospecifity (see below).

Table 3 Results of the reaction of **17** with *tert*-butyllithium and electrophiles

Compound	El (reagent)	Yield (%) [a]	d.r (*anti*:*syn*)[b]
19a	H (MeOH)	84	-
19b	D (MeOD)	83	94 : 6
19c	COOH (CO_2)	75	73 : 27
19d	SCH_3 (MeSSMe)	64	98 : 2[c]

[a] Yield of distilled products.
[b] Relative configuration between *t*-Bu and El.
[c] Only one diastereomer can be seen in the ^{1}H NMR spectrum.

We obtained the *anti* diastereomer of **19a** in almost 100 % de. This parallels the earlier findings for the allyl and cinnamyl alcohols. A simple, tentative model (Scheme 5) for the transition structure based on the concept of heteroatom directed carbometalation contradicts the experimental results: The assumed chelation of the lithium cation with both the hetero atom (OLi or OCH_3) and the π-bond during the carbolithiation step would give rise to more steric repulsion between the attacking nucleophilic *tert*-butyl group and the methyl substituent in the *anti*-pathway. This assumption is supported by *ab initio* MO calculations.[14] To explain the high stereoselecitivity in both reactions, the transition structure for nucleophilic addition of alkyllithiums to lithiated α-methylallyl alcohol and α-methylcinnamyl ether might therefore lack a metal oxygen contact.



R = *t*-Bu *syn*-**18** *anti*-**18**

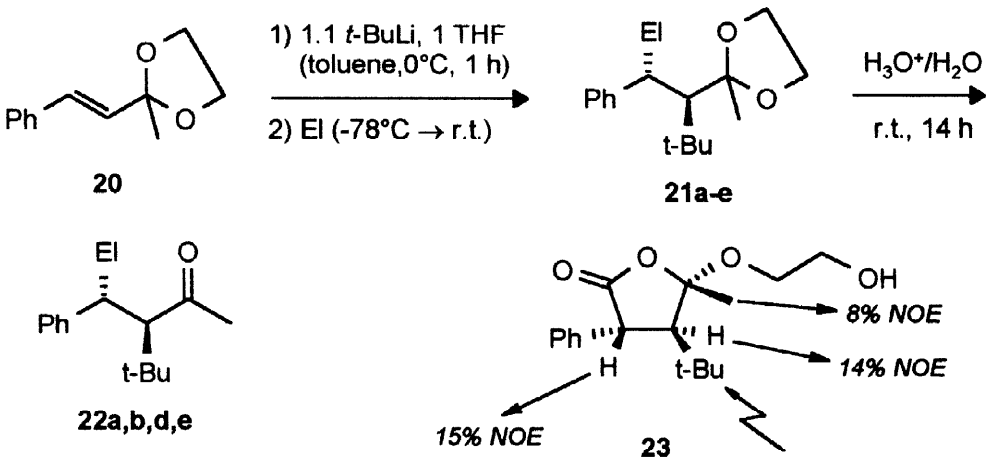
Scheme 5

Carbolithiation of 2-cinnamyl-2-methyl-1,3-dioxolane 20

Dioxolanes are widely used as protected carbonyl functionalities.[15] The cinnamyl acetal resembles the ether and similar reactivity towards nucleophilic alkyllithiums might be expected. The carbolithiation step represents a 3,4-addition of the organolithium compound to the Michael acceptor, a reaction that has earlier been reported for the corresponding diethyl acetal of 4-phenyl-3-buten-2-one but without electrophilic substitution.[16]

The electrophilic substitution of the carbolithiated acetal proceeds with a diastereoselectivity even better than the intermediates described above. Acid hydrolysis of the acetals **21** releases the ketones in acceptable yields (Scheme 6, Table 4). The carboxylic acid readily forms the lacton **23** with fixed conformation from the hemiacetal intermediate. Nuclear Overhauser effects of the benzylic proton and the methyl group attached to the acetal carbon with the *tert*-butyl group indicate the *trans* configuration of the phenyl group and the *cis* configuration of the methyl group with respect to the *tert*-butyl

substituent. Thereby, a *direct* proof of the configuration of **23** is possible.



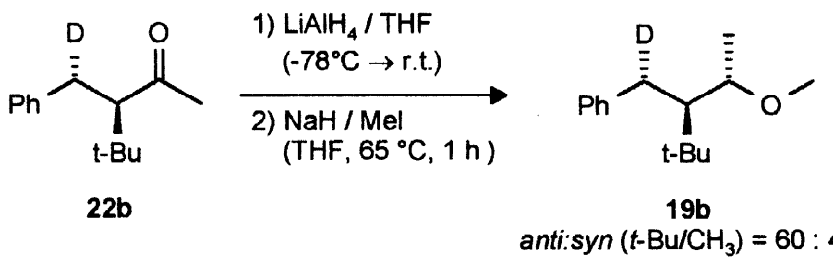
Scheme 6

The deuterated ketone **22b** is used to determine the configuration of the carbolithiation product **19b**, obtained from α-methyl cinnamyl methyl ether **17** (Scheme 7). According to Cram's rule for nucleophilic addition, reduction with a hydride donor would favour the *anti* diastereomer concerning the *tert*-butyl and the methyl group of the alcohol produced.

Table 4 Results of the carbolithiation of **20** on treatment with *tert*-butyllithium and electrophilic substitution

Compound	El (reagent)	Yield (%)[a]	d.r (*anti* : *syn*)
22a	H (MeOH)	77	-
22b	D (MeOD)	69	92 : 8
23	COOH (CO_2)	55[b]	98 : 2[c]
22d	SCH_3 (MeSSMe)	70	98 : 2[c]
22e	CH_3 (MeI)	47	2 : 98[c][d]

[a] Yield of distilled products.
[b] Lactone **23**. Yield after recrystallization from *c*-C_6H_{12}.
[c] Only one diastereomer can be seen in the ^1H NMR.
[d] Inversion of configuration is assumed.



Scheme 7

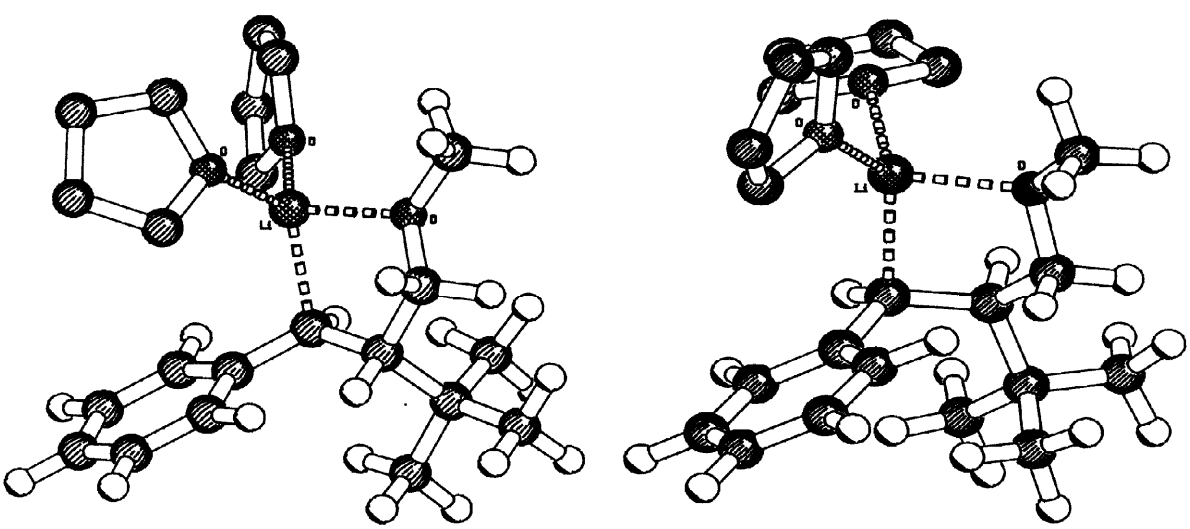
Indeed a 60 : 40 ratio of two ethers **19b** is found after methylating the reduction product, of which the *major* isomer is identical with the sole diastereomer that stems from the carbolithiation procedure with **17**. Therefore the *anti* configuration between the CH_3 and the *tert*-butyl group is obvious. Furthermore, both **22b** and **19b** have the same relative configuration of *tert*-butyl group and deuterium, which implies the predominating formation of the *anti* products in both electrophilic substitution reactions.

This makes it highly probable, that the carboxylation has also taken place under *retention* of the configuration of the benzylic position, as the *anti* configuration of **23** has been explicitely proven.

Discussion

To explain product configurations from the mechanism, one needs information about both the stereochemical nature of the intermediates and the mechanism of substitution. NMR spectroscopic data showed *anti-N*,3-dilithio-2-*tert*-butyl-3-phenylpropylamine (**2**, R = *t*-Bu, X = NLi(CH_3)) as the prevailing species in THF solution, which was supported by semiempirical calculations.[2] This underlines the idea of a strong thermodynamic preference of one diastereomer, which reacts stereospecifically with electrophiles. In the case of a non-ionic group X, the intramolecular interaction of the heteroatom with the benzylic lithium after carbolithiation is presumably weaker, as the solvation of the cation is less exothermic than an ionic interaction.

To evaluate the energy difference between the two epimers of **5** in solution, we have performed PM3[17] calculations as in the case of the lithiated secondary amines. We have assumed a monomeric benzyllithium species and modeled the solvation by two THF ligands at the lithium cation. The geometries of the two isomers are depicted in Fig. 2. *Anti*-**5** is the preferred isomer, although the stabilization against the *syn* diastereomer is only 0.7 kcal mol^{-1}. This value is well within the error margins of the PM3 method and cannot serve as evidence for a thermodynamic preference of one epimeric intermediate. For the lithiated secondary amine, the energy gap between the two diastereomers has been calculated to be much wider (4.7 kcal mol^{-1}). Here, the situation is more complex as *syn*- and *anti*-**5** are nearly isoenergetic.



a) *anti*-**5**·2THF, ΔH_f = -132.60 kcal mol^{-1} b) *syn*-**5**·2THF, ΔH_f = -131.90 kcal mol^{-1}

Fig. 2 PM3-optimized geometries of the diastereomers of **5**, solvated with two equivalents of THF, hydrogens at the solvent are omitted for clarity.

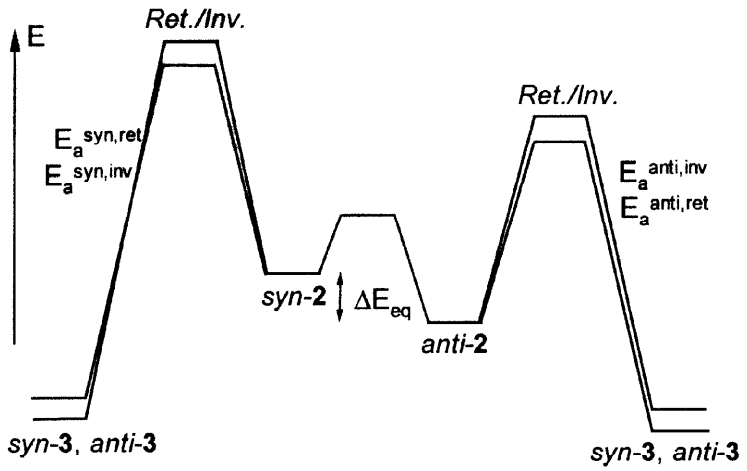


Fig. 3 Generalized energetic scheme of the electrophilic substitution of benzylic lithium species **2**.

If one draws a tentative energy diagram of the reaction, the barrier of epimerization of the both isoenergetic benzylic lithium intermediates **2** is presumably lower than the barrier of electrophilic substitution (Fig. 3). In such case, it is not possible to draw any conclucions on the configuration of the reacting intermediates from the product configuration. According to the Curtin-Hammett principle, all four barriers of electrophilic substitution must be compared and it cannot be concluded from the experiment which barrier is the lowest and which diastereomer is the more reactive species. High diastereoselectivity is even possible if both diastereomers supposed to exist in solution do indeed react but with opposite stereospecifity.

Our knowlegde at the moment is therefore too limited to propose a model to explain the origin of the high diastereoselectivity in the carbolithiation and electrophilic substitution of heterosubstituted cinnamyl compounds. However, based on the PM3-results, it is to be expected that the product distribution after electrophilic reaction is controlled by kinetic rather than by thermodynamic factors and the preference of one diastereomeric lithium intermediate is not responsible for the observed product ratios.

Conclusion

Cinnamyl methyl ether **4** and 2-cinnamyl-2-methyl-1,3-dioxolane **20** have been carbolithiated with several organolithium compounds and the resulting benzylic lithium compounds have been electrophilically substituted with good diastereoselectivities. Due to the poor nucleophilicity of the benzylic lithium intermediate, only a few electrophiles were reacted with success. The observed diastereomeric ratios are similar to the ones reported earlier for cinnamyl alcohols and amines. The dioxolanes can be hydrolysed to the α,β-disubstituted ketones **22** as almost pure diastereomers.

The highly diastereoselective carbolithiation with the sterically crowded *tert*-butyllithium can be performed on the chiral α-methylcinnamyl ether **15**. This allows in the case of **17d** the formation of three adjacent stereocentres in almost 100 % de.

Experimental Part

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AM-400 spectrometer. Chemical shifts are reported in ppm against tetramethylsilane as an internal standard and *J* values are given in Hz. Values in

brackets { } refer to the minor diastereomer (if present). Combustion analyses were carried out with a Carlo-Erba 1106 instrument. Mass spectra were taken on a Varian MAT 311 A using an ionization potential of 70 keV.

Cinnamyl methyl ether **4** was prepared by treatment of cinnamyl alcohol with sodium hydride and methyl iodide in THF. α-Methylcinnamyl methyl ether **17** was prepared by reduction of 3-phenyl-3-butene-2-one with $NaBH_4$ and *O*-methylation as described before. Trimethylbenzylstannane was prepared by deprotonation of toluene with *n*-butyllithium/KO*t*Bu in THF and reaction with trimethyl tin chloride. Trimethylallylstannane was prepared from trimethyl tin chloride and allyl magnesium bromide.[12] Condensation of 4-phenyl-prop-3-en-2-one with 1,2-ethanediol to give 2-cinnamyl-2-methyl-1,3-dioxolane **20** was achieved in refluxing benzene in the presence of catalytic amounts of p-toluene sulfonic acid under removal of water.

tert-Butyllithium was purchased from the Metallgesellschaft Frankfurt and its concentration was determined by titration of diphenylacetic acid[18] prior to use. All lithium compounds were handled under a protective argon atmosphere.

1-Lithio-3,3-dimethyl-2-methoxymethyl-1-phenylbutane (**5**): 445 mg (3 mmol) Cinnamyl methyl ether and 216 mg (3 mmol) THF in 2 ml toluene were added to a solution of 3.3 mmol *tert*-butyllithium/pentane in 8 ml toluene at -10..-5 °C. The solution was stirred for 1 h at that temperature, then it was cooled down to -75 °C and the electrophile added. For workup, the temperature was raised to room temperature, 20 ml aqueous NH_4Cl (10 %) were added, the phases separated and the aqueous phase extracted with 15 ml Et_2O three times. The combined organic phases were dried over $MgSO_4$, the solution was then filtrated and the solvent removed in vacuo.

3,3-Dimethyl-2-methoxymethyl-1-phenylbutane (**6a**): 500 µl CH_3OH were added as electrophile and the reaction mixture warmed to room temperature, then worked up. Distillation gave **6a** (655 mg, 79 % (scale of the experiment: 4 mmol)) as a colourless liquid, b.p. 60 °C/0.2 torr. (Found: C, 81.37; H, 11.38. Calc. for $C_{14}H_{22}O$: C, 81.50; H, 10.75 %); δ_H (400 MHz, $CDCl_3$) 1.0 (9 H, s, $C(CH_3)_3$), 1.51 (1 H, m_c, -CH(*t*-Bu)-), 2.53 (1 H, dd, *J* 13.5/10.6) and 2.78 (1 H, dd, *J* 13.5/3.4) ($PhCH_2$), 3.16 (3 H, s, OCH_3), 3.20 (1 H, dd, *J* 9.8/4.5) and 3.31 (1 H, dd, *J* 9.8/3.5) (OCH_2), 7.10-7.35 (5 H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 28.6 ($C(CH_3)_3$), 33.2 ($C(CH_3)_3$), 33.6 (Ph-CH_2), 50.9 (-CH(*t*-Bu)-), 58.4 (OCH_3), 71.9 (OCH_2), 125.5 (C_p), 128.1, 129.2 (C_o,C_m), 142.6 (C_i).

1-Deuterio-3,3-dimethyl-2-methoxymethyl-1-phenylbutane (**6b**): 500 µl CH_3OD were added and the reaction mixture warmed to room temperature, then worked up. Distillation gave **6b** (452 mg, 73 %) as a colourless liquid, b.p. 65 °C/0.4 torr. (Found: C, 81.25; H, 10.84. Calc. for $C_{14}H_{21}DO$: C, 81.10; H/D, 10.75 %); δ_H (400 MHz, $CDCl_3$) 1.0 (9 H, s, $C(CH_3)_3$), 1.49 (1 H, m_c(br), -CH(*t*-Bu)-), 2.75 {2.52} (1 H, s(br), Ph-CHD-), 3.15 (3 H, s, OCH_3), 3.19 (1.H, dd, *J* 9.8/4.5) and 3.30 (1 H, dd,*J* 9.8/3.5) (OCH_2), 7.10-7.40 (5 H, m, Ph); δ_C (100 MHz, $CDCl_3$) 28.6 ($C(CH_3)_3$), 33.16 ($C(CH_3)_3$), 33.24 (t, $^1J_{CD}$ 19.5, Ph-CHD-), 50.9 (-*C*H(*t*Bu)-), 58.4 (OCH_3), 71.9 (OCH_2), 125.5 (C_p), 128.1, 129.2 (C_o, C_m), 142.6 (C_i). d.r.=88:12 (integration of the PhC*H*D signal in the ^{1}H NMR spectrum).

4,4-Dimethyl-3-methoxymethyl-2-phenyl-pentanoic acid (**6c**): CO_2 was poured through the solution until the colour of the lithium intermediate had vanished. Then the solution was warmed to room temperature and worked up (2 n HCl was added instead of aqueous NH_4Cl). Distillation gave **6c** (594 mg, 79 %), b.p. 95 °C/0.005 torr. (Found: C, 72.00; H, 8.67. Calc. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86 %); δ_H (400 MHz, $CDCl_3$) 0.90 {0.98} (9 H, s, $C(CH_3)_3$), 2.03 {2.33} (1 H, m_c, -CH(*t*Bu)-), 3.13 {2.82} (3 H, s, OCH_3), 3.59 (1 H, dd, *J* 10.1 / 5.0) and 3.65 (1 H, dd, *J* 10.0 / 4.7) (OCH_2), 3.90 {3.80} (1 H, d, *J* 6.0 {8.8}, PhCH), 7.15-7.40 (5 H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 29.0 {28.8} ($C(CH_3)_3$), 34.1 {33.8} ($C(CH_3)_3$), 51.3 {51.5}, 53.1 {49.8} and 58.1 {58.0} (Ph-*C*H(COOH), -*C*H(*t*Bu)-, OCH_3), 71.1 {70.9} (OCH_2), 127.1 (C_p), 128.4, 128.9 (C_o, C_m), 139.9 {137.4} (C_i), 178.9 {181.3} (COOH). d.r.=85:15 (integration of the PhCH signal in the ^{1}H NMR spectrum).

3,3-Dimethyl-2-methoxymethyl-1-methylsulfanyl-1-phenylbutane (**6d**): 377 mg (4 mmol) CH_3SSCH_3 were added in 1 ml toluene. Distillation gave **6d** (464 mg, 61 %), b.p. 75 °C/0.005 torr. (Found: C, 71.51 %; H, 9.88 %. Calc. for $C_{15}H_{24}OS$: C, 71.38 %; H, 9.58 %); δ_H (400 MHz, $CDCl_3$) 1.02 (9 H, s, $C(CH_3)_3$), 1.82 (3 H, s, SCH_3), 1.91 (1 H, m, -CH(*t*-Bu)-), 3.25 (3 H, s, OCH_3), 3.59 (1 H, dd, *J* 10.0/5.0) and 3.69 (1 H, dd, *J* 10.0/5.0) (OCH_2), 3.93 (1 H, d, *J* 3.5, PhCH), 7.10-7.35 (5 H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 15.5

(SCH_3), 29.0 ($C(CH_3)_3$), 34.2 ($C(CH_3)_3$), 53.0, 54.6, 58.1 (PhCH, -CH(*t*-Bu)-, OCH_3), 71.2 (OCH_2), 126.4 (C_p), 128.2, 128.5 (C_o, C_m), 144.5 (C_i).

3,3-Dimethyl-2-methoxymethyl-1-sulfomethyl-1-phenylbutane (**8**): 0.13 mmol (34 mg) of **6d** were oxidized by stirring with 0.5 mmol (77 mg) $NaBO_3 \cdot 4H_2O$ in 4 ml acetic acid (99%) at 50 °C for 18 h.[19] After addition of 5 ml H_2O and threefold extraction with 5 ml CH_2Cl_2, the organic phase was dried over $MgSO_4$. The major part of the solvent was removed in vacuo, the rest at the air to give quantitative yield (0.13 mmol, 37 mg) of the sulfone **8**, obtained as white crystals suitable for X-ray analysis.

δ_H (400 MHz, $CDCl_3$) 0.90 (9 H, s, $C(CH_3)_3$), 2.44 (1 H, m_c, -CH(*t*-Bu)-), 2.57 (3 H, s, SO_2CH_3), 3.39 (3 H, s, OCH_3), 3.84 (1 H, dd, *J* 10.0/3.9) and 4.12 (1 H, dd, *J* 9.9/7.2) (OCH_2), 4.39 (1 H, d, *J* 5.5, PhCH), 7.30-7.40 (3 H, m) and 7.51-7.61 (2 H, m) (Ar-H); δ_C (100 MHz, $CDCl_3$) 28.9 ($C(CH_3)_3$), 34.6 ($C(CH_3)_3$), 40.8 (SO_2CH_3), 52.6 (-CH(*t*-Bu)-), 58.1 (OCH_3), 70.2, 72.1 (OCH_2, PhCH), 128.6 (C_p), 128.9, 130.8 (C_o, C_m), 137.4 (C_i).

Single crystal structure analysis of **8**:[20] λ = 0.71073 Å, T = 293 K, monoclinic cell, $P2_1/n$, a = 9.139 Å, b = 10.500 Å, c = 16.540 Å, β = 91.569°, Z = 4, $-11 \le h \le 12$, $-12 \le k \le 12$, $-21 \le l \le 21$, $2\theta_{max}$ = 55.87°, R_1 = 0.0416 for 2183 $F_o > 4\sigma(F_o)$ and 0.0789 for all 3600 data. ωR_2 = 0.1153, GOF = 0.941.

2,2-Dimethyl-3-methoxymethyl-4-phenylpentane (**6e**): 710 mg (5 mmol) CH_3I were added in 1 ml toluene. Distillation gave **6e** (532 mg, 60 %), b.p. 65 °C/0.02 torr. (Found M^+, 220.1824. Calc. for $C_{15}H_{24}O$: M, 220.1827); δ_H (400 MHz, $CDCl_3$) 0.98 (9 H, s, $C(CH_3)_3$), 1.28 {1.40} (3 H, d, *J* 7.1 {7.3}, CH_3), 1.70 {1.59} (1 H, m_c, -CH(*t*-Bu)-), 3.09 (1 H, dq, *J* 3.2/7.2, PhCH) 3.18 {3.11} (3 H, s, OCH_3), 3.49 (2 H, m, OCH_2), 7.08-7.35 (5 H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 17.5 (CH_3) 29.5 ($C(CH_3)_3$), 34.1 ($C(CH_3)_3$), 38.3 (PhCH), 53.2 (-CH(*t*-Bu)-), 58.1 (OCH_3), 71.4 (OCH_2), 125.3 (C_p), 127.6, 128.1 (C_o, C_m), 149.9 (C_i). d.r.=87:13 (integration of the -CH(*t*-Bu)-signal in the ^1H NMR spectrum)

2,2-Dimethyl-3-methoxymethyl-4-phenyloctane (**6f**): 736 mg (4 mmol) *n*-C_4H_9I were added in 2 ml toluene. Distillation gave **6f** as a single diastereomer, b.p. 70 °C/0.005 torr. (Found M^+, 262.2302. Calc. for $C_{18}H_{30}O$: M, 252.2297); δ_H (400 MHz, $CDCl_3$) 0.81 (3 H, t, *J* 7.3, CH_2CH_3), 0.9-1.4 (4 H, m, CH_2CH_2), 0.97 (9 H, s, $C(CH_3)_3$), 1.63 (1 H, m_c, -CH(*t*-Bu)-), 1.65-1.85 (2 H, m, $-CH_2-$), 2.84 (1 H, dt, *J* 11.5/2.9, PhCH), 3.24 (3 H, s, OCH_3), 3.52 (1 H, dd, *J* 10.0/4.8) and 3.59 (1 H, dd, *J* 10.0/6.4) (OCH_2), 7.05-7.38 (5 H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 14.1 (CH_3), 22.9 (CH_2), 29.0 ($C(CH_3)_3$), 30.5, 30.8 (CH_2), 34.3 ($C(CH_3)_3$), 44.9, 54.0 (PhCH, -CH(*t*-Bu)-), 58.1 (OCH_3), 71.4 (OCH_2), 125.3 (C_p), 128.1, 128.3 (C_o, C_m), 148.1 (C_i).

3,3-Dimethyl-2-methoxymethyl-1-(4-trimethylsilyl)phenylbutane (**7**): 400 mg $(CH_3)_3SiCl$ were added to the solution of **5** through a syringe and the reaction mixture worked up as described above. Distillation gave **7** (345 mg, 58 %), b.p. 65 °C/0.005 torr. (Found: C, 73.51; H, 11.22. Calc. for $C_{17}H_{30}SiO$: C, 73.31; H, 10.86 %). δ_H(400 MHz, $CDCl_3$) 0.25 (9 H, s, $Si(CH_3)_3$), 1.01 (9 H, s, $C(CH_3)_3$), 1.50 (1 H, m_c, like dq, -CH(*t*-Bu)-), 2.53 (1 H, dd, *J* 13.5/10.6) and 2.76 (1 H, dd, *J* 13.5/3.3) (Ph-CH_2), 3.18 (3 H, s, OCH_3), 3.22 (dd, *J* 9.8/3.5) and 3.32 (dd, *J* 9.9/4.4) (OCH_2), 7.18 (2 H, d, *J* 7.7, H-C_m), 7.42 (2 H, d, *J* 7.7, H-C_o); δ_C(100 MHz, $CDCl_3$) -1.0 ($Si(CH_3)_3$), 28.6 ($C(CH_3)_3$), 33.2 ($C(CH_3)_3$), 33.5 ($PhCH_2$), 50.9 (-CH(*t*-Bu)-), 58.4 (OCH_3), 72.0 (OCH_2), 128.6, 133.2 (C_o, C_m), 136.9 (C_p), 143.3 (C_i).

1,4-Diphenyl-1-lithio-2-methoxymethylbutane (**11**): To a solution of 637 mg (2.5 mmol) benzyltrimethylstannane and 291 mg (2.5 mmol) TMEDA in 10 ml Et_2O 2.5 mmol MeLi/Et_2O were added dropwise at -5 °C. The solution was stirred for 1 h, then 372 mg (2.5 mmol) cinnamyl methyl ether **4** were added. After stirring at -5 °C for another hour, the solution was cooled to -75 °C and then treated with the electrophile to give the products **12a-e**. All products were worked up by warming to room temperature and addition of 20 ml NH_4Cl (10% solution). The phases were separated, the aqueous phase extracted with Et_2O and the combined organic extracts dried over $MgSO_4$. After filtration, the solvent was removed in vacuo and the remaining crude products were distilled.

2-Methoxymethyl-1,3-diphenylpropane (=(2,2-Dibenzyl)ethyl methyl ether) (**12a**): To the solution of lithium compound **11** were added 500 µl of CH_3OH. After workup, distillation gave **12a** (385 mg, 64 %) as a colourless liquid, b.p. 75 °C/0.005 torr. (Found: C, 85.00; H, 8.47. Calc. for $C_{17}H_{20}O$: C, 84.96; H, 8.39 %); δ_H(400 MHz, $CDCl_3$) 2.14 (1 H, m_c, Bz_2CH-), 2.62 (2 H, dd, *J* 13.6/6.5) and 2.69 (2 H, dd, *J* 13.6/7.9) ($PhCH_2$), 3.13 (2 H, d, *J* 4.9, OCH_2), 3.27 (3 H, s, OCH_3), 7.10-7.35 (5 H, m, Ar-H); δ_C(100 MHz, $CDCl_3$) 37.5 ($PhCH_2$), 42.6 (Bz_2CH-), 58.7 (OCH_3), 73.4 (OCH_2), 125.8, 128.2, 129.2, 140.7 (Ph).

1-Deuterio-2-methoxymethyl-1,3-diphenylpropane (**12b**): To the solution of lithium compound **11** were added 500 µl CH_3OD. After workup and distillation **12b** (413 mg, 68 %) was obtained as a colourless liquid, b.p. 75 °C/0.005 torr. (Found: C, 84.25; H/D, 8.41. Calc. for $C_{17}H_{19}OD$: C, 84.60; H/D, 8.40 %). δ_H(400 MHz, $CDCl_3$) 2.13 (1 H, m_c, Bz_2CH-), 2.62 (2 H, dd, *J* 13.1/6.5, 1 $PhCH_2$ and PhCHD), 2.68 (1 H, dd, *J* 13.6/7.9, 1 $PhCH_2$), 3.12 (2 H, d, *J* 4.8, OCH_2), 3.25 (3 H, s, OCH_3), 7.10-7.35 (5 H, m, Ar-H); δ_C(100 MHz, $CDCl_3$) 37.1 (t, J_{CD} 19.3, Ph*C*HD), 37.5 (PhCH_2), 42.5 (Bz_2CH-), 58.6 (OCH_2), 73.3 (OCH_3), 125.8, 128.2, 129.2, 140.6 (Ph).

3-Methoxymethyl-2,4-diphenylbutanoic acid (**12c**): CO_2 was poured through the solution of **11** until the dark red colour had vanished. Then the solution was warmed to room temperature and worked up (2 n HCl was added instead of aqueous NH_4Cl). Distillation (b.p. 140 °C/0.2 torr) gave **12c** (466 mg, 66 %) as a white solid, m.p. 106-107 °C. (Found: C, 75.97; H, 7.58. Calc. for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09 %). δ_H(400 MHz, $CDCl_3$) 2.44-2.54 (1 H, m_c, -CH(Bz)-), 2.69 (1 H, dd, *J* 9.4/3.6) and 2.97 (1 H, dd, *J* 9.4/3.0) (OCH_2), 2.77-2.83 (2 H, m, $PhCH_2$), 3.07 (3 H, s, OCH_3), 3.77 (1 H, d, *J* 10.7, PhCH), 7.0-7.45 (10 H, m, Ar-H), 11.5 (1 H, s(br), COOH); δ_C(100 MHz, $CDCl_3$) 35.7 ($PhCH_2$), 44.1 (PhCH(COOH)), 53.6 (-CH(Bz)-), 58.5 (OCH_3), 69.2 (OCH_2), 126.1, 127.6 (2 C_p), 128.2, 128.6, 128.7, 129.4 (2 C_o, 2 C_m), 136.9, 140.0 (2 C_i).

2-Methoxymethyl-1-methylsulfanyl-1,3-diphenylpropane (**12d**): To the solution of lithium compound **11** 283 mg (3 mmol) CH_3SSCH_3 in 2 ml Et_2O were added. After workup distillation yielded **12d** (437 mg, 61 %) as a colourless liquid, b.p. 110 °C/0.005 torr. (Found: C, 76.18; H, 7.48. Calc. for $C_{18}H_{22}OS$: C, 75.48; H, 7.74 %). (Found: M^+, 286.139. Calc for $C_{18}H_{22}OS$: M, 286.1391). δ_H(400 MHz, $CDCl_3$) 1.84 {1.83} (3 H, s, SCH_3), 2.24-2.35 {2.16-2.26} (1 H, m_c, -CH(Bz)-), 2.42 (1 H, dd, *J* 13.3/10.2) and 2.72 (1 H, dd, *J* 13.3/4.3) ($PhCH_2$), 3.12 (1 H, dd, *J* 9.5/5.1) and 3.49 (1 H, dd, *J* 9.5/4.1) (OCH_2), 3.28 (3 H, s, OCH_3), 3.96 {3.87} (1 H, d, *J* 7.7 {8.7}, PhCH(SMe)-), 7.05-7.40 (5 H, m, Ar-H); δ_C(100 MHz, $CDCl_3$) 14.8 (SCH_3), 34.8 (PhCH_2), 46.4 (-*C*H(Bz)-), 52.7 (Ph*C*H(SMe)), 58.6 (OCH_3), 70.7 (OCH_2), 126.0, 127.0, 128.1, 128.3, 129.1, 130.1, 140.4, 140.8 (Ph). d.r.=95:5 (integration of the PhCH(SMe) signal in the ^1H NMR spectrum)

2-Methoxymethyl-1,3-diphenylbutane (**12e**): To the solution of lithium compound **11** were added 426 mg (3 mmol) CH_3I in 2 ml Et_2O. After workup distillation yielded **12e** (427 mg, 67 %) as a colourless liquid, b.p. 80 °C/0.005 torr. (Found: C, 84.97; H, 8.75. Calc. for $C_{18}H_{22}O$: C, 84.99; H, 8.72 %). δ_H(400 MHz, $CDCl_3$) 1.34 {1.31} (3 H, d, *J* 7.0 {7.2}, CH_3), 2.00 (1 H, m_c, -CH(Bz)-), 2.57 {2.41} (1 H, dd, *J* 13.5/9.6 {13.5/10.0}) and 2.78 (1 H, dd, *J* 13.5/4.7) ($PhCH_2$), 2.88 (1 H, dd, *J* 9.4/4.6) and 3.04 {3.33} (1 H, dd, *J* 9.4/5.3 {9.3/4.1}) (OCH_2), 2.98 (1 H, quintett, *J* 7.2, PhCH(CH_3)), 3.14 (3 H, s, OCH_3), 7.05-7.35 (5 H, m, Ar-H); δ_C(100 MHz, $CDCl_3$) 18.1 {18.9} (CH_3), 34.2 {35.3} ($PhCH_2$), 39.9 {40.3} (-*C*H(Bz)-), 47.3 {47.2} (Ph*C*H(CH_3)-), 58.5 {58.7} (OCH_3), 71.9 {71.2} (OCH_2), 125.7, 126.0, 127.7, 128.2, 128.3, 129.2, 141.1, 146.1 (Ph). d.r.=89:11 (integration of the OCH_3 signal in the ^1H NMR spectrum).

1-Lithio-2-methoxymethyl-1-phenylpent-4-ene (**13**): This lithio compound was prepared in an analogous way as **11**, starting from allyltrimethylstannane.

2-Methoxymethyl-1-phenylpent-4-ene (**14a**): To the solution of lithium compound **13** in Et_2O were added 500 µl of methanol. After workup, distillation gave **14a** (305 mg, 65 %) as a colourless liquid, b.p. 80 °C/0.9 torr. (Found: C, 82.66; H, 10.09. Calc. for $C_{18}H_{18}O$: C, 82.06; H, 9.53 %. Found M^+-CH_3OH 158.1098, Calc. for $C_{18}H_{18}O$: M-(CH_3OH) 158.1096). δ_H(400 MHz, $CDCl_3$) 1.96 (1 H, m_c) 2.10 (2 H, m_c) (C*HCH*$_2$CH=CH_2), 2.60 (dd, *J* 13.6/6.8) and 2.66 (dd, *J* 13.5/7.3) (2 H, $PhCH_2$), 3.22 (2 H, d, *J* 5.5, OCH_2), 3.30 (3 H, s, OCH_3), 4.95-5.10 (2 H, m, =CH_2), 5.79 (1 H, m_c, -CH=), 7.10-7.35 (5 H, m, Ar-H); δ_C(100 MHz, $CDCl_3$) 35.4 (CH_2), 37.2 ($PhCH_2$), 40.3 (-CH(Allyl)-), 58.7 (OCH_3), 74.3 (OCH_3), 116.4 (=CH_2), 125.8 (C_p), 128.2, 129.3 (C_o, C_m), 136.8 (-CH=), 140.6 (C_i).

1-Deuterio-2-methoxymethyl-1-phenylpent-4-ene (**14b**): To the solution of lithium compound **13** (2 mmol) were added 500 µl CH_3OD. After workup and distillation **14b** (241 mg, 63 %) was obtained as a colourless liquid, b.p. 80 °C/0.9 torr. (Found: C, 81.83; H/D, 9.71. Calc. for $C_{13}H_{17}OD$: C, 81.63; H/D, 9.54 %). δ_H(400 MHz, $CDCl_3$) 1.96 (1 H, m_c) 2.10 (2 H, m_c) (C*HCH*$_2$CH=CH_2), 2.58 {2.64} (2 H, d, *J* 6.7 {7.1}, PhCHD), 3.22 (2 H, d, *J* 5.5, OCH_2), 3.30 (3 H, s, OCH_3), 4.95-5.10 (2 H, m, =CH_2), 5.79 (1 H, m_c, -CH=), 7.10-7.35 (5 H, m, Ar-H); δ_C(100 MHz, $CDCl_3$) 35.4 (CH_2), 36.9 (t, $^1J_{CD}$ 19.4 , PhCHD), 40.2 (-CH(Allyl)-), 58.7 (OCH_3), 74.3 (OCH_3), 116.4 (=CH_2), 125.8 (C_p), 128.2, 129.3 (C_o, C_m), 136.8 (-CH=), 140.6 (C_i). d.r.=80:20 (integration of the PhCHD signal in the ^1H NMR spectrum).

3-Methoxymethyl-2-phenylhex-5-enoic acid (**14c**): CO_2 was poured through the solution of **13** until the dark red colour had vanished. Then the solution was warmed to room temperature and worked up (2 n HCl was added instead of aqueous NH_4Cl). Distillation (b.p. 95 °C/0.005 torr) gave **14c** (357 mg, 68 %) as a white solid, m.p. 93 °C. (Found: C, 71.92; H, 7.88. Calc. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74 %). δ_H(400 MHz, $CDCl_3$) 2.20-2.40 (3 H, m, C*H*C*H*$_2$-CH=CH_2), 2.86 (1 H, dd, *J* 9.5/4.4) and 3.18 (1 H, dd, *J* 9.4/3.2) (OCH_2), 3.11 (3 H, s, OCH_3), 3.66 {3.61} (1 H, d, *J* 9.9 {10.3}, PhC*H*(COOH)), 4.98-5.13 (2 H, m, =CH_2), 5.73-5.88 (1 H, m, -C*H*=CH_2), 7.10-7.38 (5 H, m, Ar-H), 11.6 (s(br), COOH), δ_C(100 MHz, $CDCl_3$) 34.1 (-CH_2CH=CH_2), 41.5 (-*C*H(Allyl)-), 53.1 (PhCH(COOH)), 58.6 (OCH_3), 70.5 (OCH_2), 117.1 (=CH_2), 127.5 (C_p), 128.4, 128.8 (C_o, C_m), 135.9 (-CH=CH_2), 136.8 (C_i), 179.5 (COOH). d.r.=87:13 (integration of the PhC*H*(COOH) signal in the ^{1}H NMR spectrum).

2-Methoxymethyl-1-methylsulfanyl-1-phenylpent-4-ene (**14d**): To the solution of lithium compound **13** were added 283 mg (3 mmol) CH_3SSCH_3 in 2 ml Et_2O. After workup distillation yielded **14d** (370 mg, 68 %) as a colourless liquid, b.p. 65 °C/0.005 torr. (Found: C, 71.14; H, 8.78. Calc. for $C_{14}H_{20}OS$: C, 71.14; H, 8.53 %). δ_H(400 MHz, $CDCl_3$) 1.83 {1.82} (3 H, s, SCH_3), 1.85-2.55 (3 H, m, -C*H*C*H*$_2$CH=CH_2) 2.99 (dd, *J* 9.3/5.5, OCH_2), 3.34 {3.18} (s, OCH_3), 3.33 (dd, *J* 9.4/5.3, OCH_2), 3.53 (dd, *J* 9.4/4.9) (together 5 H), 3.91 {3.83} (1 H, d, *J* 7.8 {8.2}, PhCH(SMe)), 4.88-5.12 (2 H, m, =CH_2), 5.63-5.88 (1 H, m, -CH=), 7.15-7.40 (5 H, m, Ar-H); δ_C(100 MHz, $CDCl_3$) 14.8 (SCH_3), 33.1 (-CH_2CH=CH_2), 43.7 {44.3} (-CH(Allyl)-), 52.7 {53.4} (PhCH(SMe)), 58.8 {58.6} (OCH_3), 71.8 {71.9} (OCH_2), 116.6 {116.8} (=CH_2), 126.9 (C_p), 128.2, 128.8 (C_o, C_m), 136.5 {136.5} (C_i), 140.6 {141.2} (-CH=CH_2). d.r.=61:39 (integration of the PhCH(SMe) signal in the ^{1}H NMR spectrum).

3-Methoxymethyl-2-phenyl-hex-5-ene (**14e**): To the solution of lithium compound **13** were added 436 mg (3 mmol) CH_3I in 2 ml Et_2O. After workup distillation yielded **14e** (254 mg, 59 %) as a colourless liquid, b.p. 70 °C/0.15 torr. (Found: C, 82.69; H, 10.28. Calc. for $C_{14}H_{20}O$: C, 82.30; H, 9.87 %). δ_H(400 MHz, $CDCl_3$) 1.27 (3 H, d, *J* 7.2, CH_3), 1.84 (1 H, m_c), 2.00-2.20 and 2.20-2.32 (2 H, m) (-C*H*C*H*$_2$-CH=), 2.86 (1 H, m_c, like dq, *J* 7/7, PhCH), 3.02 {3.28} (1 H, dd, *J* 9.4/6.0 {9.0/4.4}) and 3.17 {3.39} (1 H, dd, *J* 9.4/5.2 {9.4/4.8}) (OCH_2), 3.20 {3.31} (3 H, s, OCH_3), 4.85-5.10 (2 H, m, =CH_2), 5.60-5.90 (1 H, m, -CH=), 7.10-7.35 (5 H, Ar-H); δ_C(100 MHz, $CDCl_3$) 18.2 {18.8} (CH_3), 32.5 {33.5}, (CH_2-CH=), 39.6 {40.0} (-CH(Allyl)-), 44.6 {44.5} (PhCH), 58.6 {58.7} (OCH_3), 72.9 {72.4} (OCH_2), 116.2 (=CH_2), 125.9 (C_p), 127.7, 128.2 (C_o, C_m), 137.0 {137.3} (-CH=), 146.1 (C_i). d.r.=84:16 (Averaged intensities of five signals in the ^{13}C NMR spectrum: $CHCH_2CH=CH_2$, OCH_2 and OCH_3).

2,2-Dimethyl-3-(phenyllithio)methyl-4-methoxypentane (**18**): To a solution of 3.3 mmol *t*-BuLi/pentane in 9 ml toluene, 487 mg (3 mmol) α-methylcinnamyl methyl ether **17** and 216 mg (3 mmol) THF in 1 ml toluene were added dropwise at -5 °C. The solution was stirred for 1 hour, then cooled to -75 °C and treated with the electrophile to give the products **19a-d**. All products were worked up by warming up to room temperature and hydrolysis (20 ml NH_4Cl (10%), 20 ml HCl (2n) in case of the carboxylic acids). The phases were separated, the aqueous phase extracted with Et_2O and the combined organic extracts dried over $MgSO_4$. After filtration, the solvent was removed in vacuo and the remaining crude products were distilled.

3-Benzyl-4-methoxy-2,2-dimethylpentane (**19a**): The solution of **18** was treated with 500 µl CH_3OH. After workup, distillation yielded **19a** (553 mg, 84 %) as a colourless liquid, b.p. 50 °C/0.005 torr. (Found: C, 81.43; H, 11.24. Calc. for $C_{15}H_{24}O$: C, 81.76; H, 10.98 %). δ_H(400 MHz, $CDCl_3$) 0.96 (s, $C(CH_3)_3$) and 0.97 ((d, partly hidden), CH_3) (12 H), 1.54 (1 H, m_c, -CH(*t*-Bu)-), 2.68 {2.61} (1 H, dd, *J* 15.0/4.6 {14.6/5.9}) and 2.86 {2.76} (1 H, dd, *J* 15.0/6.8 {14.7/6.0}) ($PhCH_2$), 3.24 (3 H, s, OCH_3), 3.60 (1 H, qd, *J* 6.4/1.1, OCH), 7.05-7.35 (5 H, m, Ar-H); δ_C(100 MHz, $CDCl_3$) 18.7 (CH_3), 28.9 ($C(CH_3)_3$), 31.1 ($PhCH_2$), 34.4 (*C*$(CH_3)_3$), 55.5, 55.7 (OCH_3, -*C*H(*t*-Bu)-), 76.8 (OCH), 125.2, 128.1, 128.9, 144.6 (Ph).

4-Methoxy-2,2-dimethyl-3-(phenyldeuterio)methylpentane (**19b**): The solution of **18** was treated with 500 µl CH_3OD. After workup, distillation yielded **19b** (551 mg, 83 %) as a colourless liquid, b.p. 50 °C/ 0.005 torr. (Found M^+, 221.1891. Calc. for $C_{15}H_{23}OD$: M, 221.1890). δ_H(400 MHz, $CDCl_3$) 0.96 (s, $C(CH_3)_3$) and 0.97 ((d, partly hidden, *J* -, CH_3) (12 H), 1.54 (1 H, d, *J* 4.5, -CH(*t*-Bu)-), 2.66 (1 H, m_c, PhCHD), 3.24 (3 H, s, OCH_3), 3.60 (1 H, qd, *J* 6.4/1.0, OCH), 7.05-7.30 (5 H, m, Ar-H); δ_C(100 MHz, $CDCl_3$) 18.7 (CH_3), 28.9 ($C(CH_3)_3$), 30.75 (t, J_{CD} 19.3, PhCHD), 34.3 ($C(CH_3)_3$), 55.3, 55.7 (OCH_3, -CH(*t*-Bu)-), 76.7 (OCH), 125.1, 128.0, 128.9, 144.6 (Ph). d.r.=94:6 (integration of the PhCHD signal in the ^{1}H NMR spectrum).

4,4-Dimethyl-3-(1-methoxy)ethyl-2-phenylpentanoic acid (**19c**): CO_2 was poured through the solution of **18** until the colour had vanished. After workup, distillation (b.p. 110 °C/0.005 torr) yielded **19c** (591 mg, 75 %) as a white solid, m.p. 100-101 °C. (Found: C, 72.62; H, 9.15. Calc. for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15 %). δ_H(400 MHz, $CDCl_3$) 0.81 {1.01} (9 H, s, $C(CH_3)_3$), 1.16 {1.30} (3 H, d, *J* 6.3 {6.6}, CH_3), 2.14 {2.32} (1 H, dd, *J* 8.8/3.5 {9.1/1.8}, -CH(*t*-Bu)-), 3.22 {3.10} (3 H, s, OCH_3), 3.55 {3.45} (1 H, m_c, OCH), 3.84 {3.90} (1 H, d, 8.8 {9.1}, PhCH), 7.15-7.50 (5 H, m, Ar-H); δ_C(100 MHz, $CDCl_3$) 21.1 (CH_3), 29.0 ($C(CH_3)_3$), 29.3 (PhCH(COOH)-), 34.5 ($C(CH_3)_3$), 56.1, 58.4 (OCH_3, -CH(*t*-Bu)-), 76.9 (OCH), 126.9, 128.3, 129.2, 140.1 (Ph), 178.8 (COOH). d.r.=73:27 (integration of the -C*H*(*t*-Bu)- signal in the ^{1}H NMR spectrum).

2,2-Dimethyl-4-methoxy-3-(phenyl-methylsulfanyl)methylpentane (**19d**): 337 mg (4 mmol) CH_3SSCH_3 were added in 1 ml toluene. After workup, distillation gave **19d** (511 mg, 64 %) as a colourless liquid, b.p. 75 °C/0.005 torr. (Found: C, 72.44; H, 10.22. Calc. for $C_{16}H_{26}OS$: C, 72.13; H, 9.84 %). δ_H(400 MHz, $CDCl_3$) 1.05 (3 H, d, *J* 6.6, CH_3), 1.14 (9 H, s, $C(CH_3)_3$), 1.82 (3 H, s, SCH_3), 1.87 (1 H, dd like t, *J* 2.3, -CH(*t*-Bu)-), 3.13 (3 H, s, OCH_3), 3.62 (1 H, qd, *J* 6.6/2.2, OCH), 3.98 (1 H, d, *J* 2.7, PhCH), 7.17 (1 H, t, *J* 7.2, C_p), 7.29 (2 H, t, *J* 7.8, C_m), 7.55 (2 H, d, *J* 7.2, C_o); δ_C(100 MHz, $CDCl_3$) 15.6, 19.6 (CH_3, SCH_3), 29.8 ($C(CH_3)_3$), 35.1 ($C(CH_3)_3$), 53.4, 55.7, 59.8 (PhCH(SCH_3), OCH_3, -CH(*t*-Bu)-), 77.4 (OCH), 126.2, 128.0, 129.0, 144.1 (Ph).

Carbolithiation of 2-cinnamyl-2-methyl-1,3-dioxolane **20**: To a solution of 3.3 mmol *t*-BuLi/pentane in 9 ml toluene, 571 mg (3 mmol) **20** and 216 mg (3 mmol) THF in 2 ml toluene were added dropwise at -5 °C. The solution was stirred for 1 hour, then cooled to -75 °C and treated with the electrophile. After warming up to room temperature, the solution was treated with 20 ml NH_4Cl (10%) and extracted with three portions of diethyl ether. The solvent of the organic phase was removed in vacuo, the remaining acetal stirred overnight with 20 ml dilute HCl (2 n). After extraction with Et_2O, the organic phase was dried over $MgSO_4$, the solvent removed in vacuo and the remaining crude product distilled.

3-Benzyl-4,4-dimethylpentan-2-one (**22a**): 500 µl CH_3OH were added as electrophile. Distillation gave **22a** (470 mg, 77 %) as a colourless liquid, b.p. 60 °C/0.02 torr. (Found: C, 82.02; H, 10.59. Calc. for $C_{14}H_{20}O$: C, 82.30; H, 9.87 %). δ_H (400 MHz, $CDCl_3$) 1.04 (9 H, s, *t*-Bu), 1.78 (3 H, s, CH_3), 2.68-2.91 (3 H, m, $PhCH_2$ and -CH(*t*-Bu)-), 7.05-7.30 (5 H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 28.0 ($C(CH_3)_3$), 33.7 ($C(CH_3)_3$) 34.7 ($PhCH_2$), 35.1 (-CH(*t*-Bu)-), 64.3 ($COCH_3$), 126.1 (C_p), 128.5, 128.8 (C_o, C_m), 140.6 (C_i), 213.3 (C=O).

3-(Phenyldeuterio)methyl-4,4-dimethylpentan-2-one (**22b**): 500 µl CH_3OD were added as electrophile. Distillation gave **22b** (425 mg, 69 %) as a colourless liquid, b.p. 70 °C/0.09 torr. (Found: C, 82.00; H, 10.46. Calc. for $C_{14}H_{19}OD$: C, 81.90; H/D, 9.87 %). δ_H (400 MHz, $CDCl_3$) 1.04 (9 H, s, *t*-Bu), 1.77 (3 H, s, CH_3), 2.73 {2.84} (2 H, 2 m, PhCHD and -CH(*t*-Bu)-), 7.05-7.30 (5 H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 27.9 ($C(CH_3)_3$), 33.7 ($C(CH_3)_3$), 34.4 (t, $^1J_{CD}$ 20, PhCHD), 35.1 (-CH(*t*-Bu)-), 64.1 ($COCH_3$), 126.0 (C_p), 128.4, 128.7 (C_o, C_m), 140.5 (C_i), 213.3 (C=O). d.r.=92:8 (integration of the multipletts at 2.73 and 2.84 ppm in the ^{1}H NMR spectrum)

3-(Phenyl-methylsulfanyl)methyl-4,4-dimethylpentan-2-one (**22d**): 377 mg (4 mmol) CH_3SSCH_3 were added in 2 ml toluene as electrophile. Distillation gave **22d** (521 mg, 70 %) as a colourless liquid, b.p. 80 °C/0.005 torr. (Found: C, 72.15; H, 9.06. Calc. for $C_{15}H_{22}SO$: C, 71.95; H, 8.86 %). δ_H (400 MHz, $CDCl_3$) 0.75 (9 H, s, *t*-Bu), 1.73 (3 H, s, CH_3), 2.35 (3 H, s, SCH_3), 3.05 (1 H, d, *J* 11.4, -CH(*t*-Bu)-), 3.89 (1 H, d, *J* 11.5, PhCH), 7.18-7.40 (5 H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 15.1 (SCH_3), 28.9 ($C(CH_3)_3$), 34.8 ($C(CH_3)_3$), 35.1 (-CH(*t*-Bu)-), 51.1 (PhCH), 65.0 ($COCH_3$), 127.3 (C_p), 128.4, 128.8 (C_o, C_m), 141.6 (C_i), 210.8 (C=O).

3-(1-Phenyl)ethyl-4,4-dimethyl-pentan-2-one (**22e**): 568 mg (4 mmol) CH_3I were added in 2 ml toluene as electrophile. Distillation gave **22e** (295 mg, 47 %) as a colourless liquid, b.p. 65 °C/0.04 torr. (Found: M^+, 218.1677. Calc. for $C_{15}H_{22}O$: M, 218.1671). δ_H (400 MHz, $CDCl_3$) 0.80 (9 H, s, *t*-Bu), 1.18 (3 H, d, *J* 6.9, CH_3), 2.15 (3 H, s, $COCH_3$), 2.82 (1 H, d, *J* 9.1, -CH(*t*-Bu)-), 3.15 (1 H, dq, *J* 9.0/6.9, PhCH), 7.10-7.30 (5 H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 21.7 (CH_3), 29.1 ($C(CH_3)_3$), 34.0 ($C(CH_3)_3$), 35.5 (-CH(*t*-Bu)-), 39.5 (PhCH), 66.8 ($COCH_3$), 126.3 (C_p), 127.7, 128.4 (C_o, C_m), 146.8 (C_i), 213.2 (C=O).

2-Phenyl-3-(1,1-dimethyl)ethyl-4-(2-hydroxy)ethoxy-pentanolactone (**23**). CO_2 was poured through the solution as electrophile. After the usual workup, a white solid remained that was recyrstallized from

cyclohexane to give **23** (**484 mg, 55 %**), m.p. **109 °C**. (Found: C, 69.58; H, 8.28. Calc. for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27 %). δ_H (400 MHz, $CDCl_3$) 0.93 (9 H, s, *t*-Bu), 1.81 (3 H, s, CH_3), 2.47 (1 H, d, *J* 12.0, -CH(*t*-Bu)-), 3.60-3.88 (4 H, m, OCH_2CH_2O), 4.06 (1 H, d, *J* 11.9, PhCH-), 7.10-7.45 (5 H, m, Ar-H). δ_C (100 MHz, $CDCl_3$) 24.0 (CH_3), 29.6 ($C(CH_3)_3$), 32.7 ($C(CH_3)_3$), 50.0 (-CH(*t*Bu)-), 62.0, 64.3 (OCH_2CH_2O), 62.8 (PhCH), 109.7 (-C(O)(O)-), 127.7 (C_p), 128.6, 129.0 (C_o, C_m), 138.3 (C_i), 174.8 (C=O).

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[20] Crystallographic data (excluding structure factors) for the structure reported in this paper (**8**) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: int. code +44(1223)336-033, e-mail: deposit@ccdc.cam.ac.uk].