Regioselective S_N2 Opening of Vinylic Epoxides with Trialkylzincates and Trialkylaluminates

Olivier Equey,[a] Emmanuel Vrancken,[b] and Alexandre Alexakis*[a]

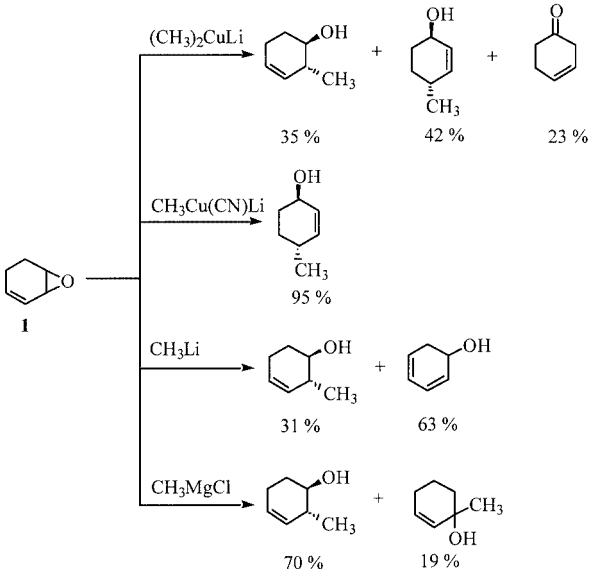
Keywords: Aluminum / Nucleophilic substitution / Regioselectivity / Vinylic epoxides / Zinc

The use of trialkylorganozincates and tetraalkylaluminates allows regioselective S_N2 nucleophilic opening of vinylic epoxides. The reaction occurs with an *anti*-substitution pattern and can be applied to a wide range of substrates. We also show that the solvent and the structure of the epoxide have an influence on the substitution products' ratio.

Introduction

Vinylic epoxides are interesting starting materials that are commonly used in organic synthesis.[1] The nucleophilic addition of organometallic reagents to vinylic epoxides provides 1,2- and 1,4-addition products,[2] with 1,4-addition predominating with organocopper reagents[3] and copper-catalysed reactions of organomagnesium[4,5] and organozinc compounds.[6−8] Marino et al.[9,10] have shown that the use of cyanocopper derivatives RCuCNLi affords exclusively the S_N2' products. On the other hand, Grignard reagents,[11−14] alkyllithium,[15−18] organoaluminum[19,20] and organozinc[21] species favor the 1,2-addition products, although a mixture of regioisomers is generally obtained (Scheme 1). Some exceptions exist. For example, Maruyama et al.[22] found that allylstannane exclusively gives the 1,2-adduct in the presence of $BF_3{\cdot}OEt_2$ with various vinylic epoxides. Recently, Zaidlewicz et al.[23] reported that allylboration of 3,4-epoxycycloalkenes of six- to eight-membered rings with allyldiethylborane and (2-cyclohexenyl)dicyclohexylborane favors the *cis*-1,2-addition. Xue et al.[24] reported that the use of diethylzinc in the presence of CF_3COOH gives the *cis*-1,2-addition product.

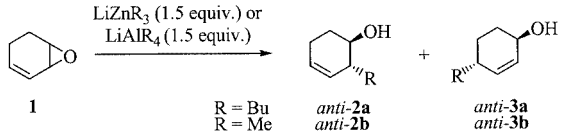
It might be predicted that a hard nucleophile should have a preference for the S_N2 process, whereas a soft nucleophile (such as a copper reagent) would prefer a softer center, and therefore an S_N2' process. Indeed, our group has reported that an RLi/BF_3 combination allows the regioselective S_N2 nucleophilic cleavage of a variety of cyclic as well as acyclic vinylic epoxides.[25,26] A clean *anti* process is involved and the reaction works well with a variety of RLi reagents (R = Me, *n*Bu, Ph, hexynyl, benzyl). However, the reaction must be performed at low temperatures (−75 to −116 °C) and with cyclopentadiene oxide a mixture of unidentified products was observed. This epoxide seems to be too sensitive to strongly basic or Lewis acidic conditions. That is the reason why we turned our attention to slightly less basic reagents such as zincates and aluminates. Here we want to report the regioselective S_N2 *anti* addition of trialkylzincates and tetraalkylaluminates to various vinylic epoxides at room temperature.



Scheme 1. Nucleophilic addition of various organometallic reagents to 1,3-cyclohexadiene monoepoxide **1**

[a] Département de Chimie Organique, Université de Genève, Sciences II,
30 quai Ernest-Ansermet, 1211 Genève 4, Switzerland
Fax: (internat.) + 41-22-379-3215
E-mail: alexandre.alexakis@chiorg.unige.ch
[b] Laboratoire de Chimie des Organoéléments, UMR 7611, Université Pierre et Marie Curie,
4 place Jussieu, 75252 Paris Cedex 05, France

Table 1. Regioselective opening of 1,3-cyclohexadiene monoepoxide (**1**)



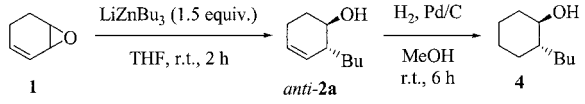
Entry	Reagent	Additive	Solvent	Temp.	Time	Yield (%)[a]	S_N2/S_N2'[b]
1	$LiZnBu_3$	$BF_3{\cdot}OEt_2$	Et_2O	−90 °C	10 min	74	95:5
2	$LiZnMe_3$	$BF_3{\cdot}OEt_2$	Et_2O	−90 °C	10 min	68	96:4
3	**$LiZnBu_3$**	−	**THF**	**room temp.**	**2 h**	**86**	**100:0**
4	$LiZnBu_3$	−	Et_2O	room temp.	2 h	85	100:0
5	$LiZnBu_3$	−	hexane	room temp.	2 h	89	97:3
6	$LiZnMe_3$	−	THF	room temp.	22 h	0	−
7	**$LiZnMe_3$**	−	**THF**	**reflux**	**15 h**	**61**	**100:0**
8	$LiZnMe_3$	−	Et_2O	room temp.	18 h	16	65:35
9	$LiZnMe_3$	−	hexane	room temp.	17 h	52	94:6
10	$LiAlBu_4$	−	Et_2O	room temp.	2 h	83	98:2
11	$LiAlBu_4$	−	hexane	room temp.	2 h	89	97:3
12	$AlBu_3$	−	Et_2O	room temp.	20 h	0	−
13	$LiAlMe_4$	−	THF	reflux	15 h	39	100:0
14	$LiAlMe_4$	−	hexane	room temp.	17 h	60	96:4

[a] Isolated yield after flash chromatography (FC). [b] Determined by ^1H NMR spectroscopy from the crude product.

Results and Discussion

Cyclic Vinylic Epoxides

We began our investigation with 1,3-cyclohexadiene monoepoxide (**1**) as a substrate (Table 1). The organozincate species can be generated by reaction of an equimolar amount of dialkylzinc and alkyllithium. When cyclohexadiene monoepoxide (**1**) was treated with 1.5 equiv. of tributyl- or trimethylzincate and 1.5 equiv. of $BF_3{\cdot}OEt_2$ at −90 °C, after 10 min we obtained a 95:5 mixture of the S_N2 and S_N2' products *anti*-**2a** and *anti*-**3a**, respectively, in 74% overall yield, for tributlyzincate and a 96:4 mixture of S_N2 and S_N2' products *anti*-**2b** and *anti*-**3b**, respectively, in 68% overall yield, for trimethylzincate (Entries 1 and 2). Hydrogenation of the double bond and comparison with the reported ^1H NMR spectrum of *trans*-2-butylcyclohexanol (**4**) allowed us to confirm that the addition product arises from a clean *anti* process (Scheme 2).



Scheme 2. Hydrogenation of the double bond of **2a**

Interestingly, the reaction could be performed at room temperature without the need for a Lewis acid. After 2 h at room temperature in THF, we obtained 86% of the pure S_N2 product *anti*-**2a** (Entry 3). The reaction could also be carried out in Et_2O; we obtained 85% of pure S_N2 product *anti*-**2a** (Entry 4). The use of a nonpolar solvent such as hexane gave a 97:3 mixture of S_N2 and S_N2' products *anti*-**2a** and *anti*-**3a** with 89% overall yield (Entry 5). In THF, with the less reactive trimethylzincate species, it was necessary to heat the solution overnight, because coordination of the zincate species by the solvent attenuated its reactivity. Indeed, we simply recovered the starting material when the reaction was performed at room temp. (Entry 6). After 15 h at reflux, we obtained 61% of the S_N2 product *anti*-**2b** only (Entry 7). On the other hand, in Et_2O the reaction could be done at room temp. Surprisingly, we obtained only 16% of a 65:35 mixture of substitution products *anti*-**2b** and *anti*-**3b** (Entry 8). In view of this bad result, we decided to avoid the use of Et_2O with trialkylzincates for the rest of our study. In hexane, we obtained a 94:6 mixture of S_N2 and S_N2' products *anti*-**2b** and *anti*-**3b**, respectively, in 52% overall yield (Entry 9). These results were quite surprising because organozincates are known to undergo a 1,4-conjugated addition reaction with α,β-unsaturated carbonyl compounds.[27−31]

We thought that it should be possible to use tetraalkylaluminate to open vinylic epoxides regioselectively. Indeed, we observed the same tendency as with triorganozincates. The reaction of tetrabutylaluminate with **1** afforded, after 2 h at room temp., a 98:2 mixture of *anti*-**2b** and *anti*-**3b** with 83% yield in Et_2O and a 97:3 mixture of *anti*-**2b** and *anti*-**3b** with 89% yield in hexane (Entries 10 and 11). When **1** was treated with 1.5 equiv. of $AlBu_3$ in Et_2O at room temp., only degradation products were observed (Entry 12). Tetrabutylaluminate can be readily obtained by treating *n*-butyllithium with aluminum chloride in a 4:1 ratio in Et_2O or in a hydrocarbon solvent. To avoid the tedious removal of the solvent, we decided to choose Et_2O as polar solvent with tetrabutylaluminate for our study instead of THF. The reaction carried out with tetramethylaluminate gave similar

results. In THF, after 15 h at reflux, we obtained 39% of *anti*-**2b** only and in hexane, after 17 h at room temp., a 96:4 mixture of *anti*-**2b** and *anti*-**3b** in 60% overall yield (Entries 13 and 14). The tetramethylaluminate species can be prepared by mixing 1 equiv. of trimethylaluminum with 1 equiv. of methyllithium [Scheme 3, Equation (1)]. Alternatively, the reaction can be performed with the tetramethylaluminate species prepared by adding 4 equiv. of methyllithium to aluminum chloride [Scheme 3, Equation (2)]. In both cases, we observed exactly the same regioselectivities.

$$AlMe_3 + MeLi \longrightarrow LiAlMe_4 \quad (1)$$

$$AlCl_3 + 4\ MeLi \longrightarrow LiAlMe_4 + 3\ LiCl \quad (2)$$

Scheme 3. Preparation of the tetraaluminate species

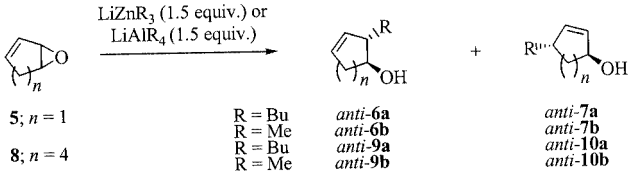
Encouraged by these initial results, we decided to expand the scope of the method and the reaction conditions were examined with various simple vinylic epoxides. We started with cyclopentadiene monoepoxide (**5**) (Table 2). The reaction of **5** with 1.5 equiv. of $LiZnBu_3$ in THF afforded, after 3 h at room temperature, 75% of the S_N2 product *anti*-**6a** (Entry 1). In hexane, we observed the formation of more S_N2' product *anti*-**7a** than with cyclohexadiene monoepoxide (**1**). We obtained an 84:16 mixture of *anti*-**6a** and *anti*-**7a** with 66% overall yield (Entry 2). With $LiAlBu_4$, the reaction gave a mixture of *anti*-**6a** and *anti*-**7a**, either in Et_2O or in hexane, but largely in favor of the product arising from the S_N2 substitution (Entries 3 and 4). The yields obtained for the transfer of a methyl group in the C-2 position of monoepoxide **5** were moderate. With $LiZnMe_3$, the reaction afforded, after 14 h at reflux in THF, only the S_N2 product *anti*-**6b** in 33% yield (Entry 5). In hexane, we obtained an 83:17 mixture of *anti*-**6b** and *anti*-**7b** with 34% overall yield after 15 h at room temp. (Entry 6). With $LiAlMe_4$, the yields were still lower. In THF, we did not isolate any product after flash chromatography (Entry 7), and in hexane we obtained a 95:5 mixture of *anti*-**6b** and *anti*-**7b** with only 18% overall yield (Entry 8).

Compared to monoepoxides **1** and **5**, 1,3-cyclooctadiene monoepoxide (**8**) is much less reactive, so that even with $LiZnBu_3$ and $LiAlBu_4$ the reaction required prolonged heating to go to completion. Moreover, we observed a great discrepancy between $LiZnBu_3$ and $LiZnMe_3$. When the reaction was carried out in THF, with $LiZnBu_3$, we obtained 54% of a 97:3 mixture of ring-opening products in favor of the S_N2 product *anti*-**9a**, while with $LiZnMe_3$ we obtained 72% of a 1:1 mixture of *anti*-**9b** and *anti*-**10b** (Entry 9 vs. Entry 12). This result was quite surprising since we normally obtained mainly the product of S_N2 substitution in polar solvent. The use of hexane, with $LiZnBu_3$ and $LiAlBu_4$, gave 85:15 and a 70:30 mixtures of *anti*-**9a** and *anti*-**10a** in favor of the S_N2 product, with 46% and 58% overall yield respectively (Entries 10 and 11).

Acyclic Vinylic Epoxides

We extended our study to acyclic vinylic epoxides. First, the reaction was examined with very simple substrates such as the monoepoxides **11** and **12** of 1,3-butadiene and isoprene, respectively (Table 3). In every case we observed the formation of almost all the regio- and stereoisomers possible, the ratio of these isomers depending strongly on the solvent used. When a solution of $LiZnBu_3$ and **11** in THF was stirred at room temperature for 4 h, we observed the formation of a 92:8 mixture of S_N2 and S_N2' products (En-

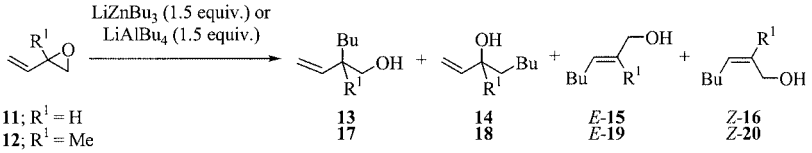
Table 2. Regioselective opening of cyclopentadiene monoepoxide (**5**) and 1,3-cyclooctadiene monoepoxide (**8**)



Entry	Substrate	Reagent	Solvent	Temp.	Time	Yield (%)[a]	S_N2/S_N2'[b]
1	**5**	$LiZnBu_3$	**THF**	**room temp.**	**3 h**	**75**	**100:0**
2	**5**	$LiZnBu_3$	hexane	room temp.	3 h	68	84:16
3	**5**	$LiAlBu_4$	Et_2O	room temp.	3 h	86	96:4
4	**5**	$LiAlBu_4$	hexane	room temp.	3 h	89	92:8
5	**5**	**$LiZnMe_3$**	**THF**	**reflux**	**14 h**	**33**	**100:0**
6	**5**	$LiZnMe_3$	hexane	room temp.	15 h	34	83:17
7	**5**	$LiAlMe_4$	THF	reflux	14 h	0	–
8	**5**	$LiAlMe_4$	hexane	room temp.	15 h	18	95:5
9	**8**	**$LiZnBu_3$**	**THF**	**reflux**	**16 h**	**54**	**97:3**
10	**8**	$LiZnBu_3$	hexane	reflux	19 h	46	85:15
11	**8**	$LiAlBu_4$	hexane	reflux	22 h	58	70:30
12	**8**	$LiZnMe_3$	THF	reflux	36 h	72	49:51

[a] Isolated yield after FC. [b] Determined by ^1H NMR spectroscopy from the crude product.

Table 3. Regioselective opening of 1,3-butadiene monoepoxide (**11**) and isoprene monoepoxide (**12**)



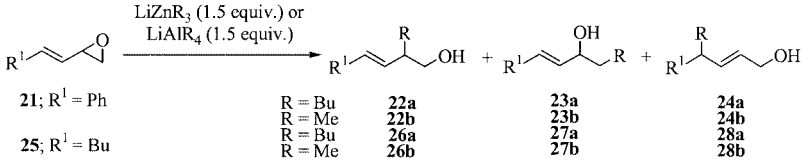
Entry	Substrate	Reagent	Solvent	Temp.	Time	Yield (%)[b]	**13**:**14**/**15**:**16** or **17**:**18**/**19**:**20**[a]	S_N2/S_N2'[a]
1	**11**	$LiZnBu_3$	THF	room temp.	4 h	55	63:29/6:2	92:8
2	**11**	$LiZnBu_3$	hexane	room temp.	3 h	80	83:0/16:1	83:17
3	**11**	$LiAlBu_4$	Et_2O	room temp.	3 h	56	12:1/42:45	13:87
4	**11**	$LiAlBu_4$	hexane	room temp.	4 h	70	55:1/39:5	56:44
5	**12**	$LiZnBu_3$	THF	room temp.	17 h	70	35:50/10:5	85:15
6	**12**	$LiZnBu_3$	hexane	room temp.	5 h	89	33:0/55:12	33:77
7	**12**	$LiAlBu_4$	Et_2O	room temp.	5 h	85	17:0/14:69	17:83
8	**12**	$LiAlBu_4$	hexane	room temp.	4 h	79	43:0/36:21	43:57

[a] Determined by ^1H NMR spectroscopy from the crude product. [b] Isolated yield after FC.

try 1). S_N2 substitution was favored, but we isolated a mixture of products of addition to both carbon atoms bearing the epoxide (**13** and **14**). In hexane, the reaction gave an 83:17 mixture of S_N2 and S_N2' products. In this case, we observed only the S_N2 substitution product **13** arising from a nucleophilic attack at the carbon atom of the epoxide next to the double bond (Entry 2). The product **14** was not formed. With $LiAlBu_4$ in Et_2O, the reaction afforded mainly both S_N2' products **15** and **16**, in a 1:1 ratio between (*E*) and (*Z*) isomers, while in hexane the reaction provided a 56:44 mixture of S_N2 and S_N2' products (Entries 3 and 4).

We thought that the presence of the methyl group would favor attack at the terminal position of the monoepoxide **12**, whereas in fact the reaction was shown to favor S_N2'

Table 4. Regioselective opening of (2*E*)-2-styryloxirane (**21**) and (*E*)-2-(hex-1-enyl)oxirane (**25**)



Entry	Substrate	Reagent	Solvent	Temp.	Time	Yield (%)[b]	**22**:**23**:**24** or **26**:**27**:**28**[a]	S_N2/S_N2'[a]
1	**21**	**$LiZnBu_3$**	**THF**	**room temp.**	**2 h**	**84**	**91:3:6**	**94:6**
2	**21**	$LiZnBu_3$	hexane	room temp.	2 h	83	81:0:19	81:19
3	**21**	$LiAlBu_4$	Et_2O	room temp.	2 h	65	82:0:18	82:18
4	**21**	$LiAlBu_4$	hexane	room temp.	2 h	81	81:0:19	81:19
5	**21**	**$LiZnMe_3$**	**THF**	**reflux**	**22 h**	**77**	**94:5:1**	**99:1**
6	**21**	$LiZnMe_3$	hexane	room temp.	22 h	94	91:0:9	91:9
7	**21**	$LiAlMe_4$	THF	reflux	5 d	0	–	–
8	**21**	$LiAlMe_4$	Et_2O	room temp.	16 h	74	92:0:8	92:8
9	**21**	$LiAlMe_4$	hexane	room temp.	21 h	65	76:0:24	76:24
10	**25**	$LiZnBu_3$	THF	room temp.	4 h	65	90:8:2	98:2
11	**25**	**$LiZnBu_3$**	**hexane**	**room temp.**	**2 h**	**69**	**99:0:1**	**99:1**
12	**25**	$LiAlBu_4$	Et_2O	room temp.	2 h	63	92:4:4	96:4
13	**25**	$LiAlBu_4$	hexane	room temp.	2 h	66	97:0:3	97:3
14	**25**	$LiZnMe_3$	THF	room temp.	23 h	53	96:1:3	97:3
15	**25**	$LiZnMe_3$	hexane	room temp.	20 h	66	95:0:5	95:5
16	**25**	$LiAlMe_4$	THF	room temp.	5 d	0	–	–
17	**25**	**$LiAlMe_4$**	**Et_2O**	**room temp.**	**41 h**	**48**[c]	**99:0:1**	**99:1**
18	**25**	$LiAlMe_4$	hexane	room temp.	20 h	62	98:0:2	98:2

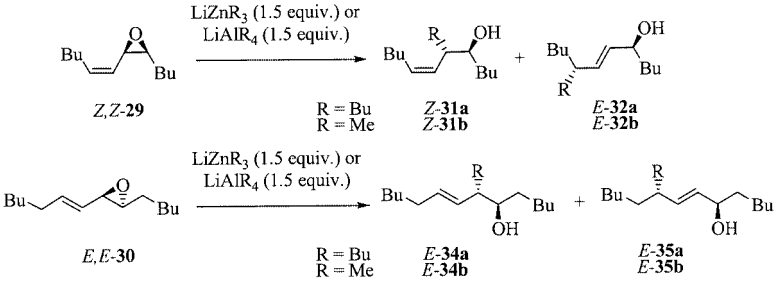
[a] Determined by ^1H NMR spectroscopy from the crude product. [b] Isolated yield after FC. [c] Conversion: 75%.

substitution. When the reaction was carried out with $LiZnBu_3$ in THF, we obtained an 85:15 mixture of S_N2 and S_N2' products with 70% overall yield; the product **18** arising from an S_N2 substitution at the terminal carbon atom of the epoxide was obtained to a much greater extent than with monoepoxide **11** (Entry 5 vs. Entry 1). In hexane, the reaction afforded a 33:77 mixture favoring the (*E*)-S_N2' product **19**, with 89% overall yield (Entry 6). Again, in Et_2O $LiAlBu_4$ favored formation of the S_N2' products, but with a preference for the (*Z*) isomer **20** (Entry 7). In hexane, we obtained a 43:57 mixture of S_N2 and S_N2' products with 79% overall yield (Entry 8).

At this stage, we thought that the absence of any substituent at the terminal olefinic carbon atom could be responsible for the bad regioselectvities observed with monoepoxides **11** and **12**. In order to check this assumption, we prepared two vinylic epoxides through the two-step sequence described by Matteson et al.[32] Monoepoxide **21** was synthesized starting from cinnamaldehyde. $LiZnBu_3$ was used first. In THF, after 2 h at room temperature, the reaction afforded mainly the S_N2 substitution products **22a**, with a good overall yield (84%) (Table 4, Entry 1). In hexane, the reaction gave a greater amount of S_N2' product **24a**, but the product **23a** arising from an S_N2 substitution on the terminal carbon atom of the epoxide was not formed (Entry 2). With $LiAlBu_4$, we observed no difference of regioselectivity between polar and apolar solvents (Entries 3 and 4). The results obtained with $LiZnMe_3$ and $LiAlMe_4$ were quite similar to those obtained for the transfer of a butyl group. The best regioselectivity was obtained in THF with $LiZnMe_3$ (Entry 5). After 22 h at room temperature, we obtained a 99:1 mixture of S_N2 and S_N2' products with 77% overall yield. In hexane, the ratio between S_N2 and S_N2' products dropped to 91:9 (Entry 6). With $LiAlMe_4$, in Et_2O, we isolated a 92:8 mixture of S_N2 and S_N2' products with 74% overall yield (Entry 8). In hexane, this ratio dropped to 76:24 (Entry 9). In THF, after 5 d at room temperature, we only recovered the starting material (Entry 7).

The vinylic epoxide **25** possesses an alkyl group instead of a phenyl group at the terminal olefinic carbon atom. The regioselectivities observed in apolar solvents were better with epoxide **25** than with epoxide **21**. With $LiZnBu_3$, in THF, we obtained a 98:2 mixture of S_N2 and S_N2' products (Entry 10). However, both S_N2 substitution products **26a** and **27a** were formed. In hexane, the ratio was 99:1 in favor of the S_N2 substitution product **26a** (Entry 11). Interestingly, we observed only one product arising from an S_N2 substitution. With $LiAlBu_4$ in Et_2O, we obtained a 96:4 mixture of S_N2 and S_N2' products and we observed both S_N2 substitution products **26a** and **27a** (Entry 12). In hexane, the ratio was 97:3 in favor of the S_N2 substitution product **26a** (Entry 13). The reaction was performed with $LiZnMe_3$ and $LiAlMe_4$. With $LiZnMe_3$, after 23 h at room temperature in THF, we obtained a 97:3 mixture of S_N2

Table 5. Regioselective opening of (5*Z*,7*Z*)-5,7-dodecadiene monoepoxide (**29**) and (6*E*,8*E*)-6,8-tetradecadiene monoepoxide (**30**)

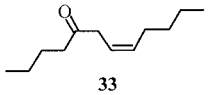


Entry	Substrate	Reagent	Solvent	Temp.	Time	Yield (%)[a]	S_N2/S_N2'[b]
1	**29**	$LiZnBu_3$	THF	room temp.	6 d	54[c]	95:5
2	**29**	**$LiZnBu_3$**	**THF**	**reflux**	**16 h**	**96**	**95:5**
3	**29**	$LiZnBu_3$	hexane	room temp.	2 h	94	76:24
4	**29**	$LiAlBu_4$	Et_2O	room temp.	16 h	8	88:12
5	**29**	$LiAlBu_4$	hexane	room temp.	2 h	89	71:29
6	**29**	$LiZnMe_3$	THF	room temp.	7 d	26[d]	99:1
7	**29**	**$LiZnMe_3$**	**THF**	**reflux**	**18 h**	**77**	**99:1**
8	**29**	$LiZnMe_3$	hexane	room temp.	64 h	75	65:35
9	**30**	$LiZnBu_3$	THF	room temp.	5 d	43[e]	87:13
10	**30**	$LiZnBu_3$	hexane	room temp.	3 h	77	73:27
11	**30**	**$LiAlBu_4$**	**Et_2O**	**room temp.**	**24 h**	**75**	**91:9**
12	**30**	$LiAlBu_4$	hexane	room temp.	4 h	83	41:59
13	**30**	$LiZnMe_3$	THF	room temp.	6 d	0	–
14	**30**	**$LiZnMe_3$** [f]	**THF**	**room temp.**	**12 d**	**84**	**79:21**
15	**30**	$LiZnMe_3$	hexane	room temp.	6 d	88	39:61

[a] Isolated yield after FC. [b] Determined by ^1H NMR spectroscopy from the crude product. [c] Conversion: 70%. [d] Conversion: 45%. [e] Conversion: 62%. [f] The reaction was carried out with 5 equiv. of $LiZnMe_3$.

and S_N2' products with 53% overall yield, while in hexane we obtained a 95:5 mixture of S_N2 and S_N2' products with 66% overall yield (Entries 14 and 15). With $LiAlMe_4$, after 5 d in THF, we simply recovered the starting material (Entry 16). In Et_2O, after 41 h at room temperature, the conversion was not complete, but we obtained 48% of a 99:1 mixture of S_N2 and S_N2' products (Entry 17). In hexane, after 20 h at room temperature, the reaction gave a 98:2 mixture of S_N2 and S_N2' products with 62% overall yield (Entry 18).

Finally, the reaction was extended to acyclic vinylic epoxides having the same substitution pattern at C-1 and C-4 (Table 5). We thought that with an unbiased system we would no longer observe products arising from an S_N2 substitution at the terminal carbon atom of the epoxide. (5*Z*,7*Z*)-5,7-Dodecadiene monoepoxide (**29**) and (6*E*,8*E*)-6,8-tetradecadiene monoepoxide (**30**) were selected as representative substrates. We observed a slight difference of reactivity between both substrates. The monoepoxide **29** reacted faster than the monoepoxide **30**. This difference should arise from the fact that both substituents on the epoxide **29** are on the same side, so that the carbon atom of the epoxide next to the double bond is sterically less hindered.[3,26] Moreover, the regioselectivities observed with monoepoxide **29** were slightly better. When the reaction was carried out with $LiZnBu_3$ in THF, after 6 d at room temperature we isolated 54% of a 95:5 mixture of S_N2 and S_N2' products in favor of *anti*-**31a** (Entry 1). It is noteworthy that the (*Z*) double bond retained its configuration and that no *cis*-1,2-addition products were formed. The conversion was not complete (70%), but when the solution was heated at reflux, after 16 h the reaction was complete. We isolated 96% of products of substitution with exactly the same ratio in favor of the S_N2 substitution product **31a** (Entry 2). In hexane, the reaction was much faster, as after 2 h at room temperature we obtained 94% of ring-opening products (Entry 3). However, more S_N2' product was formed (76:24 in favor of *anti*-**31a**). The reaction has also been run with $LiAlBu_4$. In Et_2O, only 8% of an 88:12 mixture of addition products was formed (Entry 4). We isolated mainly the homoallyl ketone **33** in 75% yield (Scheme 4). In hexane, as with the reaction with $LiZnBu_3$, we obtained a 71:29 mixture of S_N2 and S_N2' products in favor of *anti*-**31a** (Entry 5).



33

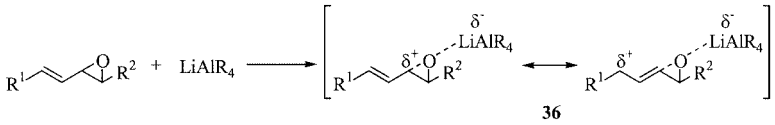
Scheme 4. Homoallyl ketone **33**

The reaction was also studied with $LiZnMe_3$. In THF, after 7 d at room temperature, the ratio was excellent (99:1 in favor of *anti*-**31b**) but the conversion was not complete (45%) (Entry 6). Again, when the reaction mixture was heated to reflux, after 18 h we obtained a better yield (77%) and the same regioselectivity (Entry 7). In hexane, after 64 h at room temperature, we obtained a 65:35 mixture of S_N2 and S_N2' products with 75% overall yield (Entry 8). These results confirmed that S_N2 substitution is preferred in polar solvents such as THF.

The reaction was then carried out with monoepoxide **30**. This epoxide possesses a *trans* configuration. In THF with $LiZnBu_3$, we obtained an 87:13 mixture of S_N2 and S_N2' products **34a** and **35a**, respectively, with 43% overall yield (conv. 62%; Entry 9). Here also, the double bond retained its configuration and only *anti*-S_N2 substitution products were detected. In hexane, after 3 h at room temperature, we obtained a 73:27 mixture of substitution products in favor of *anti*-**34a** (Entry 10). With $LiAlBu_4$ in Et_2O, we obtained 75% of a 91:9 mixture of substitution products in favor of *anti*-**34a** (Entry 11). In hexane, after 4 h at room temperature, more S_N2' substitution products were formed (41:59) but the overall yield was better (83%; Entry 12). The reaction was then performed with $LiZnMe_3$. It was very slow. After 6 d at room temperature we just recovered the starting material (Entry 13). With 5 equiv. of $LiZnMe_3$, after 12 d at room temperature we obtained a 79:21 mixture of S_N2 and S_N2' products in favor of *anti*-**34b** with an overall yield of 84% (Entry 14). In hexane, after 6 d at room temperature, we obtained a 39:61 mixture of ring-opening products in favor of the S_N2' substitution product *anti*-**35b** with a good overall yield (88%; Entry 15).

Influence of the Solvent

The influence of the solvent on the substitution products ratio can be explained with the following model (Scheme 5).[33] In a non-coordinating solvent, the lithium salts of the "ate" complexes must exist essentially in the form of contact ion pairs. One can then imagine the formation of complex **36** between the organometallic species and the vinylic epoxide. Such a complex activates not only the carbon atom of the epoxide next to the double bond but also the terminal carbon atom of the double bond, because the positive charge can be stabilized by the mesomeric effect.[22] In polar solvents such as THF, the "ate" complexes exist in the form of ion pairs separated by solvents. Therefore a complex between the oxygen atom of the epoxide bridge and the organometallic species cannot be formed. Such complex formation explains also the difference in reactivity observed in THF and in hexane.



36

Scheme 5. Model for the influence of the solvent on regioselectivity

The nature of the organometallic species also plays a role as "ate" complexes are not as hard as an alkyllithium species, for example, but are harder than an organocopper species. This intermediate softness can also explain why we observe more S_N2' substitution in non-polar solvents.

Conclusion

We have demonstrated with several examples that trialkylorganozincates and tetraalkylaluminates provide a convenient way to introduce alkyl substituents at the allylic position of 1,3-diene monoepoxides regio- and diastereoselectively. We have also shown that the solvent has an influence on the substitution products' ratio. A polar solvent such as THF favors addition at the allylic position. We observed more S_N2' substitution with non-coordinating solvents such as hydrocarbons. We have also observed that polar solvents slow down the reaction rate and that organoaluminates are more sensitive than organozincates to this effect. Moreover, the presence of a substituent at the double bond is essential, otherwise we observe formation of a large amount of S_N2' substitution product. The presence of a Lewis acid is not necessary with our method and the reaction can be carried out at room temperature. Heating of the solution in some cases shortens the reaction time, but without having any influence on the substitution products ratio. For these reasons, our method is a good alternative to the already existing methods.

Experimental Section

General Remarks: THF and Et_2O were freshly distilled from sodium/benzophenone. Other solvents were obtained from commercial sources and used as received. Flash column chromatography was carried out on Baker silica gel (0.03−0.06 mm). TLC was carried out on Macherey−Nagel plastic sheets of silica gel 60 F_{254}. A solution of 25 g of phosphomolybdic acid, 10 g of $Ce(SO_4)_2{\cdot}4H_2O$, 60 mL of concd. H_2SO_4 and 940 mL of H_2O was used to reveal the TLC spots. ^1H and ^{13}C NMR spectra were recorded either with a Varian Gemini 200 or with a Bruker AC-400 spectrometer. Chemical shifts are expressed in ppm relative to tetramethylsilane (δ = 0 ppm) and coupling constants are reported in Hz. Deuterated chloroform was used as solvent. Spin multiplicities are described with the following symbols: s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet), br. (broad). Mass spectra were obtained with a Finnigan 4023 instrument and IR spectra were recorded with a Perkin−Elmer 1420 spectrometer.

Preparation of the Epoxides: All the epoxides have already been described. They were prepared according to the procedure of Crandall et al.,[34] except for the oxiranes **21** and **25**, which were prepared according to the two-step procedure described by Matteson et al.[32] and Lautens et al.[35]

General Procedure for the Nucleophilic Opening of Epoxides with Lithium Tributylzincate: In a 25-mL, two-necked flask equipped with a thermometer was placed 3 mL (3 mmol) of a 1 M solution of $ZnBu_2$ in hexane in the required solvent (7 mL) under nitrogen. The solution was cooled to −20 °C and 1.6 mL (3 mmol) of a 1.9 M solution of *n*BuLi in hexane was added dropwise. The solution was stirred for 30 min at room temp. It was then cooled to −10 °C before addition of a solution of epoxide (2 mmol) in the required solvent (3 mL). The solution was then stirred at room temp. until all the starting material had been consumed (the reaction was monitored by TLC). The reaction mixture was cooled to 0 °C, quenched with a 3:1 solution of NH_4Cl/NH_4OH (5 mL) and stirred for 30 min at room temp. before being transferred into a separating funnel. The aqueous phase was extracted three times with Et_2O. The combined organic phases were washed once with brine, dried with $MgSO_4$, filtered and the solvents were removed under reduced pressure. The crude product was then subjected to FC on SiO_2.

General Procedure for the Nucleophilic Opening of Epoxides with Lithium Trimethylzincate: In a 25-mL, two-necked flask equipped with a thermometer was placed 1.5 mL (3 mmol) of a 2 M solution of $ZnMe_2$ in toluene in the required solvent (6 mL) under nitrogen. The solution was cooled to −20 °C and 1.9 mL (3 mmol) of a 1.6 M solution of MeLi in Et_2O was added dropwise. The solution was stirred for 30 min at room temp. It was then cooled to −10 °C before addition of a solution of the epoxide (2 mmol) in the required solvent (3 mL). The solution was then stirred at room temp. until all the starting material had been consumed (the reaction was monitored by TLC). The reaction mixture was cooled to 0 °C, quenched with a 3:1 solution of NH_4Cl/NH_4OH (5 mL) and stirred for 30 min at room temp. before being transferred into a separating funnel. The aqueous phase was extracted three times with Et_2O. The combined organic phases were washed once with brine, dried with $MgSO_4$, filtered and the solvents were removed under reduced pressure. The crude product was then subjected to FC on SiO_2.

General Procedure for the Nucleophilic Opening of Epoxides with Lithium Tetrabutylaluminate: In a 25-mL, two-necked flask equipped with a thermometer was placed 406 mg (3 mmol) of $AlCl_3$ in the required solvent (9 mL) under nitrogen. The solution was cooled to −20 °C and 6.3 mL (12 mmol) of a 1.9 M solution of *n*BuLi in hexane was added dropwise. The solution was stirred for 1 h at room temp. and the formation of a white suspension was observed. The suspension was then cooled to −10 °C before addition of a solution of the epoxide (2 mmol) in the required solvent (3 mL). The solution was then stirred at room temp. until all the starting material had been consumed (the reaction was monitored by TLC). The reaction mixture was cooled to 0 °C, quenched with a 1 M solution of HCl (5 mL) and stirred for 30 min at room temp. before being transferred into a separating funnel. The aqueous phase was extracted three times with Et_2O. The combined organic phases were washed once with brine, dried with $MgSO_4$, filtered and the solvents were removed under reduced pressure. The crude product was then subjected to FC on SiO_2.

General Procedure for the Nucleophilic Opening of Epoxides with Lithium Tetramethylaluminate: In a 25-mL, two-necked flask equipped with a thermometer was placed 1.5 mL (3 mmol) of a 2 M solution of $AlMe_3$ in heptane in the required solvent (6 mL) under nitrogen. The solution was cooled to −20 °C and 1.9 mL (3 mmol) of a 1.6 M solution of MeLi in Et_2O was added dropwise. The solution was stirred for 30 min at room temp. until it became cloudy. It was then cooled to −10 °C before addition of a solution of the epoxide (2 mmol) in the required solvent (3 mL). The solution was then stirred at room temp. until all the starting material had been consumed (the reaction was monitored by TLC). The reaction mixture was cooled to 0 °C, quenched with a 1 M solution of HCl (5 mL) and stirred for 30 min at room temp. before being transferred into a separating funnel. The aqueous phase was extracted three times with Et_2O. The combined organic phases were

washed once with brine, dried with $MgSO_4$, filtered and the solvents were removed under reduced pressure. The crude product was then subjected to FC on SiO_2.

***trans*-2-Butyl-3-cyclohexen-1-ol (2a):** The product was isolated by FC (cyclohexane/EtOAc, 9:1) as a colorless oil. The NMR spectra of **2a** are identical to those reported previously.[26]

***trans*-2-Methyl-3-cyclohexen-1-ol (2b):** The product was isolated by FC (cyclohexane/EtOAc, 9:1) as a colorless oil. The NMR spectra of **2b** are identical to those reported previously.[36]

***trans*-2-Butyl-3-cyclopenten-1-ol (6a):** The product was isolated by FC (cyclohexane/EtOAc, 9:1) as a pale yellow oil. The NMR spectra of **6a** are identical to those reported previously.[37]

***trans*-2-Methyl-3-cyclopenten-1-ol (6b):**The product was isolated by FC (pentane/Et_2O, 3:1) as a slightly yellow oil. The NMR spectra of **6b** are identical to those reported previously.[38]

***trans*-2-Butyl-3-cycloocten-1-ol (9a):** The product was isolated by FC (cyclohexane/EtOAc, 19:1) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.71 (q, *J* = 8.1 Hz, 1 H), 5.23 (t, *J* = 9.8 Hz, 1 H), 3.50 (dt, *J* = 10.1, 3.6 Hz, 1 H), 2.45−2.40 (m, 1 H), 2.25−2.18 (m, 1 H), 2.11−2.08 (m, 1 H), 1.82−1.60 (m, 6 H), 1.47 (br. s, 1 H), 1.34−1.19 (m, 6 H), 0.89 (t, *J* = 7 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.9 (d), 131.4 (d), 75.9 (d), 42.5 (d), 34.8 (t), 32.1 (t), 30.0 (t), 29.2 (t), 27.6 (t), 22.9 (t), 22.0 (t), 14.2 (q) ppm. IR: ṽ = 3400, 2980, 1050, 730 cm^{-1}. $C_{12}H_{22}O$ (182.30): calcd. C 79.06, H 12.16; found C 79.04, H 12.12.

2-Butyl-4-phenyl-3-buten-1-ol (22a): The product was isolated by FC (cyclohexane/EtOAc, 9:1) as a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41−7.21 (m, 5 H), 6.51 (d, *J* = 15.9 Hz, 1 H), 6.01 (dd, *J* = 15.9, 9.0 Hz, 1 H), 3.65 (dd, *J* = 10.6, 5.2 Hz, 1 H), 3.52 (dd, *J* = 10.6, 8.1 Hz, 1 H), 2.42−2.37 (m, 1 H), 1.74−1.69 (m, 1 H), 1.53−1.50 (m, 1 H), 1.40−1.31 (m, 5 H), 0.92 (t, *J* = 6.0 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.2 (s), 132.4 (d), 131.7 (d), 128.6 (d), 127.3 (d), 126.2 (d), 66.1 (t), 46.4 (d), 30.9 (t), 29.4 (t), 22.8 (t), 14.1 (q) ppm. IR: ṽ = 3420, 3025, 2960, 1640, 1330, 1070, 970, 690 cm^{-1}. $C_{14}H_{20}O$ (204.31): calcd. C 82.30, H 9.87; found C 82.25, H 9.91.

2-Methyl-4-phenyl-3-buten-1-ol (22b):[39] The product was isolated by FC (cyclohexane/EtOAc, 9:1) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40−7.22 (m, 5 H), 6.50 (d, *J* = 16 Hz, 1 H); 6.01 (dd, *J* = 15.9, 7.9 Hz, 1 H), 3.61 (dd, *J* = 10.5, 5.7 Hz, 1 H), 3.53 (dd, *J* = 10.5, 7.5 Hz, 1 H), 2.58−2.53 (m, 1 H), 1.66 (br. s, 1 H), 1.13 (d, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.3 (s), 132.6 (d), 130.9 (d), 128.6 (d), 127.2 (d), 126.2 (d), 67.4 (t), 40.2 (d), 16.5 (q) ppm.

2-Butyl-3-octen-1-ol (26a): The product was isolated by FC (cyclohexane/EtOAc, 19:1) as a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.52 (dt, *J* = 15.3, 6.8 Hz, 1 H), 5.12 (ddt, *J* = 15.3, 8.9, 1.3 Hz, 1 H), 3.50 (dd, *J* = 10.4, 5.1 Hz, 1 H), 3.31 (dd, *J* = 10.4, 8.5 Hz, 1 H), 2.16−2.10 (m, 1 H), 2.03−1.99 (m, 2 H), 1.64 (br. s, 1 H), 1.35−1.19 (m, 10 H), 0.90−0.85 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.9 (d), 131.3 (d), 66.0 (t), 45.9 (d), 32.4 (t), 31.7 (t), 30.8 (t), 29.3 (t), 22.7 (t), 22.2 (t), 14.0 (q), 13.9 (q) ppm. IR: ṽ = 3370, 3080, 2960, 1640, 1435, 1050, 990, 910 cm^{-1}. $C_{12}H_{24}O$ (184.32) calcd. C 78.20, H 13.12; found C 78.11, H 13.18.

2-Methyl-3-octen-1-ol (26b): The product was isolated by FC (cyclohexane/EtOAc, 9:1) as a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.55−5.47 (m, 1 H), 5.27−5.20 (m, 1 H), 3.44−3.42 (m, 1 H), 3.36−3.31 (m, 1 H), 2.31−2.24 (m, 1 H), 2.01−1.98 (m, 2 H), 1.83 (br. s, 1 H), 1.34−1.20 (m, 5 H), 0.96 (d, *J* = 6.8 Hz, 3 H), 0.89−0.86 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 132.2 (d), 132.2 (d), 67.3 (t), 39.7 (d), 32.3 (t), 31.7 (t), 22.2 (t), 22.2 (t), 16.6 (q), 13.9 (q) ppm. The IR spectrum[40] and the elemental analysis[41] have already been reported.

***trans*-(7*Z*)-6-Butyl-7-dodecen-5-ol (31a):** The product was isolated by FC (cyclohexane/EtOAc, 29:1) as a colorless oil. The NMR spectra of **31a** are identical with those reported.[26]

***trans*-(7*Z*)-6-Methyl-7-dodecen-5-ol (31b):** The product was isolated by FC (cyclohexane/EtOAc, 29:1) as a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.40 (dt, *J* = 11.1, 7.8 Hz, 1 H), 5.20 (t, *J* = 9.9 Hz, 1 H), 3.39−3.32 (m, 1 H), 2.57−2.48 (m, 1 H), 2.10−1.99 (m, 2 H), 1.57−1.42 (m, 3 H), 1.38−1.26 (m, 8 H), 0.98 (d, *J* = 6.8 Hz, 3 H), 0.91−0.88 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 132.1 (d), 130.6 (d), 75.9 (d), 38.0 (d), 34.1 (t), 32.0 (t), 28.3 (t), 27.4 (t), 22.8 (t), 22.4 (t), 16.6 (q), 14.1 (q), 14.0 (q) ppm. IR: ṽ = 3410, 3015, 2910, 1020, 740 cm^{-1}. $C_{13}H_{26}O$ (198.34): calcd. C 78.72, H 13.21; found C 78.65, H 13.26.

***trans*-(8*E*)-7-Butyl-8-tetradecen-6-ol (34a):** The product was isolated by FC (cyclohexane/EtOAc, 9:1) as a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.48 (dt, *J* = 15.3, 6.8 Hz, 1 H), 5.18 (dd, *J* = 15.3, 9.3 Hz, 1 H), 3.37 (br. s, 1 H), 2.06−2.00 (m, 2 H), 1.94−1.88 (m, 1 H), 1.57−1.23 (m, 21 H), 0.90−0.86 (m, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.5 (d), 130.3 (d), 73.8 (d), 49.2 (d), 34.6 (t), 32.7 (t), 32.0 (t), 31.3 (t), 30.8 (t), 29.7 (t), 29.2 (t), 25.4 (t), 22.7 (t), 22.7 (t), 22.5 (t), 14.1 (q), 14.1 (q) ppm. IR: ṽ = 3320, 2910, 1430, 1030, 960 cm^{-1}. $C_{20}H_{40}O$ (296.53): calcd. C 81.01, H 13.60; found C 81.92, H 13.54.

***trans*-(8*E*)-7-Methyl-8-tetradecen-6-ol (34b):** The product was isolated by FC (cyclohexane/EtOAc, 9:1) as a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.51 (dt, *J* = 15.3, 6.7 Hz, 1 H), 5.30 (dd, *J* = 15.4, 8.5 Hz, 1 H), 3.31 (br. s, 1 H), 2.15−2.07 (m, 1 H), 2.05−1.99 (m, 2 H), 1.52−1.26 (m, 15 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 0.91−0.87 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.0 (d), 131.7 (d), 74.8 (d), 43.2 (d), 34.3 (t), 32.3 (t), 32.0 (t), 31.3 (t), 28.6 (t), 25.6 (t), 22.6 (t), 22.5 (t), 16.9 (q), 14.1 (q), 14.1 (q) ppm. IR: ṽ = 3390, 2970, 1470, 1060, 780 cm^{-1}. $C_{17}H_{34}O$ (254.45): calcd. C 80.24, H 13.47; found C 80.17, H 13.51.

Acknowledgments

We thank the Swiss National Science Foundation (No. 20-068095.02) for financial support.

[1] *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), Pergamon Press, New York, **1991**, vol. 6.
[2] J. G. Smith, *Synthesis* **1984**, 629−656.
[3] J. A. Marshall, *Chem. Rev.* **1989**, *89*, 1503−1511.
[4] E. R. Lee, I. Lacomy, P. Bigler, R. Scheffold, *Helv. Chim. Acta* **1991**, *74*, 146.
[5] M. E. Jung, D. C. D'Amico, *J. Am. Chem. Soc.* **1995**, *117*, 7379.
[6] B. H. Lipshutz, K. Woo, T. Gross, D. J. Buzard, R. Tirado, *Synlett* **1997**, 477−478.
[7] F. Badalassi, P. Crotti, F. Macchia, M. Pineschi, A. Arnold, B. L. Feringa, *Tetrahedron Lett.* **1998**, *39*, 7795−7798.
[8] F. Bertozzi, P. Crotti, F. Macchia, M. Pineschi, B. L. Feringa, *Angew. Chem. Int. Ed.* **2001**, *40*, 930−932.
[9] J. P. Marino, D. P. Floyd, *Tetrahedron Lett.* **1979**, *20*, 675−678.
[10] J. P. Marino, R. Fernandez de la Pradilla, E. Laborde, *J. Org. Chem.* **1987**, *52*, 4898−4913.
[11] R. J. Anderson, *J. Am. Chem. Soc.* **1970**, *92*, 4978−4979.

[12] C. B. Rose, S. K. Taylor, *J. Org. Chem.* **1974**, *39*, 578.
[13] A. J. Bloodworth, R. J. Curtis, M. D. T. Spencer, N. A. Tallant, *Tetrahedron* **1993**, *49*, 2729.
[14] B. C. Söderberg, L. R. Austin, C. A. Davis, J. E. Nyström, J. O. Vagborg, *Tetrahedron* **1994**, *50*, 61.
[15] R. W. Herr, C. R. Johnson, *J. Am. Chem. Soc.* **1970**, *92*, 4979−4981.
[16] J. Staroscik, B. Rickborn, *J. Am. Chem. Soc.* **1971**, *93*, 3046−3047.
[17] D. M. Wieland, C. R. Johnson, *J. Am. Chem. Soc.* **1971**, *93*, 3047−3049.
[18] G. Stork, C. Kowalski, G. Garcia, *J. Am. Chem. Soc.* **1975**, *97*, 3258−3260.
[19] G. A. Crosby, R. A. Stephenson, *J. Chem. Soc., Chem. Commun.* **1975**, 287−288.
[20] A. J. Briggs, K. A. M. Walker, *J. Org. Chem.* **1990**, *55*, 2962−2964.
[21] J. J. Eshelby, P. J. Parsons, P. J. Crowley, *J. Chem. Soc., Perkin Trans. 1* **1996**, 191.
[22] Y. Naruta, K. Maruyama, *Chem. Lett.* **1987**, 963−966.
[23] M. Zaidlewicz, M. P. Krzeminski, *Org. Lett.* **2000**, *2*, 3897−3899.
[24] S. Xue, Y. Li, K. Han, W. Yin, M. Wang, Q. Guo, *Org. Lett.* **2002**, *4*, 905−907.
[25] N. Bernard, F. Chemla, J. F. Normant, *Tetrahedron Lett.* **1998**, *39*, 6715.
[26] A. Alexakis, E. Vrancken, P. Mangeney, F. Chemla, *J. Chem. Soc., Perkin Trans. 1* **2000**, 3352−3353.
[27] M. Isobe, S. Kondo, N. Nagasawa, T. Goto, *Chem. Lett.* **1977**, 679−682.
[28] W. Tückmantel, K. Oshima, H. Nozaki, *Chem. Ber.* **1986**, *119*, 1581−1593.
[29] C. A. Musser, H. G. Richey Jr., *J. Org. Chem.* **2000**, *65*, 7750−7756.
[30] D. Seebach, H.-O. Kalinowski, W. Langer, C. Gerhard, E.-M. Wilka, *Org. Synth.* **1983**, *61*, 24−34.
[31] B. L. Feringa, A. H. M. de Vries, *Adv. Catal. Processes* **1995**, *1*, 151−192.
[32] K. M. Sadhu, D. S. Matteson, *Tetrahedron Lett.* **1986**, *27*, 795.
[33] G. Boireau, D. Abenhaim, E. Henry-Basch, *Tetrahedron* **1980**, *36*, 3061−3070.
[34] J. K. Crandall, D. B. Banks, R. A. Colyer, R. J. Watkins, J. P. Arrington, *J. Org. Chem.* **1968**, *33*, 423−425.
[35] M. Lautens, M. L. Maddess, E. L. O. Sauer, S. G. Ouellet, *Org. Lett.* **2002**, *4*, 83−86.
[36] R. L. Danheiser, C. Martinez-Davila, H. Sard, *Tetrahedron* **1981**, *37*, 3943−3950.
[37] M. Ito, M. Matsuumi, M. G. Murugesh, Y. Kobayashi, *J. Org. Chem.* **2001**, *66*, 5881−5889.
[38] J. J. Partridge, N. K. Chadha, M. R. Uskovic, *J. Am. Chem. Soc.* **1973**, *95*, 532−540.
[39] Y. Ohfune, M. Tomita, *J. Am. Chem. Soc.* **1982**, *104*, 3511−3513.
[40] C. Hirai, Y. Sakai, T. Matsumoto, *Yakagatu* **1966**, *15*, 306−310.
[41] W. E. Parham, H. E. Holmquist, *J. Am. Chem. Soc.* **1954**, *76*, 1173−1175.

Received December 3, 2003

