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Addition of 2-(Chloromagnesiomethyl)-2-alkenyl Ethers to Epoxides followed by Pd(0)-Catalyzed Cyclization: A One-pot Synthesis of 3-Methylenetetrahydropyrans

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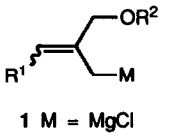
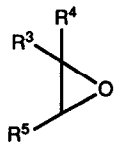
Abstract: *Addition of 2-(chloromagnesiomethyl)-2-propenyl ethers* ***1a*** *and* ***1b*** *to epoxides* ***3*** *affords ring opening products* ***6*** *or* ***7*** *which are converted by Pd(0) to 3-methylenetetrahydropyrans* ***9****. Cyclization of the addition products is best effected by a catalyst system generated in situ from* $Pd(OAc)_2$ *and* $(i\text{-}PrO)_3P$.

The tetrahydropyran system is a structural feature characteristic of many naturally occurring substances. Together with the tetrahydrofurans and spiroketal systems, tetrahydropyrans appear frequently in polyether antibiotics (ionophores[1]) and are important structural units in several marine natural products.[2] Consequently, there is much interest in developing efficient methods for the preparation of these six-membered oxacycles.[3] Besides S_N2 displacement[4] and intramolecular ketalization,[5] ring expansion of tetrahydrofurans,[6] iodocyclization,[7] hydroxyepoxide isomerization,[8] [4+2] cycloaddition,[9] carbenium ion-olefin cyclization,[10] palladium-promoted reactions[11] and condensation reactions of 1,3-bifunctional reagents[12] have been employed.

Recently, we demonstrated that the trimethylenemethane moiety of the bifunctional conjunctive reagents **1** or **2** can be added to alkenes,[13] 1-(trimethylsilyl)-1-alkynes,[14] and aldehydes, ketones and imines.[15] Among trimethylenemethane equivalents,[16] 2-(metallomethyl)-2-alkenyl ethers **1** and **2** stand out by their ability to sustain a carbon-metal center of relatively high nucleophilicity.This suggested that in particular Grignard reagents **1** might be used as nucleophiles towards epoxides **3**,[17] whereafter our usual protocol, *i.e.* adding a catalytic amount of Pd(0) to the reaction mixture and heating for several hours, might cause the addition products **4** to cyclize, forming 3-methylenetetrahydropyrans **5**. Epoxide ring opening might also be accomplished under conditions of Cu(I)-catalysis.[18] In this paper we describe the results of our investigation.[19]



1 M = MgCl
2 M = ZnBr



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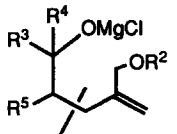

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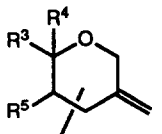

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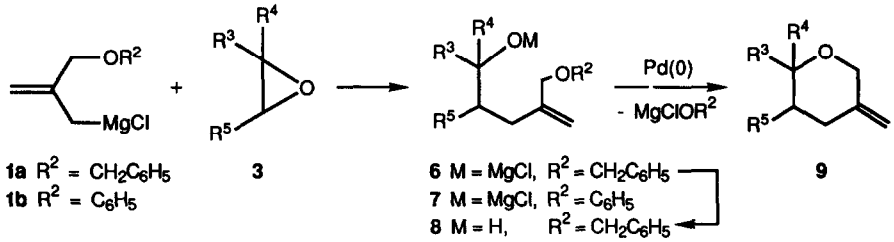
RESULTS AND DISCUSSION

3-Methylenetetrahydropyrans from epoxides 3 and 2-(chloromagnesiomethyl)-2-propenyl ethers 1a,b.

The synthesis of 5,6-substituted 3-methylenetetrahydropyrans by use of the simple 2-propenylmagnesium derivatives **1a** and **1b** was studied first (Scheme 1). The preparation of the latter has been described elsewhere.[14b] Since it is reported that Cu(I)-catalyzed ring opening of epoxides by Grignard reagents is unafflicted by premature isomerization to carbonyl compounds (a well-known complication accompanying the use of unmodified Grignard reagents[20-22]) this method seemed most promising. Six epoxides were subjected to the reaction, using **1a** (0.25 M, THF, 1.2 equiv.; 10 mol% CuI, -30 °C, 4 h, Table 1). A small portion of each reaction mixture was hydrolyzed and analyzed by GCMS/NMR. It turned out that Cu(I)-promoted ring opening was successful only in the case of propylene oxide (**3a**), cyclopentene oxide (**3d**) and cyclohexene oxide (**3e**). With methylenecyclohexane oxide **3b** and styrene oxide (**3c**) addition products were produced in moderate or low yields, respectively, together with several unidentified by-products. Cycloheptene oxide (**3f**) remained unchanged. Attack of **3a**, **3b** and **3c** by **1a** took place regiospecifically (> 97 %, NMR) at the unhindered position. The strong preference for β-attack of **3c** is opposite to that reported for the Cu(I)-catalyzed reaction of this epoxide with other Grignard reagents.[23] Addition to **3d** and **3e** gave exclusively products of *trans* ring opening (see below).



Scheme 1

In order to effect cyclization of the addition products (*i.e.* **6a,b,d,e**), the reaction mixtures were treated with 5 mol% [$Pd(PPh_3)_4$] and heated for 24 h at 65 °C. It was found that smooth conversion of **6** to **9** could only be accomplished for alkoxides derived from cyclopentene oxide and cyclohexene oxide (**3d,e**). Cyclization of **6a,b** required severe reaction conditions (100 °C, 70 h). Use of other solvents (25 % DMF/THF, 25 % HMPA/THF, DMF, HMPA) did not result in faster reaction. The greater ease of ring closure of **6d,e** may be related to the fact that the -OMgCl and 2-(benzyloxymethyl)-2-propenyl groups are held in each others vicinity in these systems while greater loss of rotational freedom is incurred on establishing the transition states of cyclization of **6a** and **6b**. Also, **6a** and **6b**, being less hindered, may be more aggregated and/or solvated (and thereby more stabilized) than cyclic **6d** and **6e**.

In view of the difficulties encountered it was decided to abandon the use of Cu(I) and to perform the addition reaction in the conventional way, using **1b** (1.3-1.6 M, THF, 1.2 equiv.; 0 °C, 0.5 h; room temperature, 4 h), while as catalyst for ring closure the more reactive system $Pd(OAc)_2/(i\text{-}PrO)_3P$[24] was chosen (5 mol% $Pd(OAc)_2$ and 30 mol% $(i\text{-}PrO)_3P$; 70-80 °C, 24-48 h). Results are given in Table 2. In almost all cases tested, addition was a smooth reaction again yielding only products of *trans* ring opening. The latter conclusion is based on the structures of the cyclization products **9** (see below). Since ring opening of epoxides by Grignard reagents is irreversible this reasoning is justified. Premature isomerization of epoxides was not observed. Again, **3a** and **3b** were attacked regiospecifically at the unhindered position, as were epoxides **3h** and **3i**. Reaction of **1b** with styrene oxide (**3c**), however, now took place predominantly at the α-position. As indicated by the structure of cyclization product **9j** (Table 2), the epoxide ring of **3j** was opened at

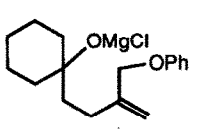
Table 1. 3-Methylenetetrahydropyrans **9** by Cu(I)-promoted Reaction of **1a** with Epoxides **3** followed by [$Pd(PPh_3)_4$]-catalyzed Cyclization.

Epoxide	R^4	R^3	R^5	Yield of **8** (%)[a,b]	Yield of **9** (%)[b]
3a	H	CH_3	H	87	61[c]
3b	-$(CH_2)_5$-		H	49	28[c]
3c	H	C_6H_5	H	14	
3d	H	-$(CH_2)_3$-		80	79
3e	H	-$(CH_2)_4$-		93	85
3f	H	-$(CH_2)_5$-		-[d]	

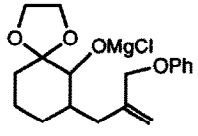
[a] After hydrolysis of **6**. [b] GLC yields, based on epoxide **3**. [c] Conditions of ring closure: 100°C, 70 h. [d] No ring opening.

the carbon atom nearest to the dioxolane ring. Precoordination between the magnesium atom of the organometallic reagent and the oxygen atoms of the dioxolane ring of **3j** may be the reason for this. Even after heating for 48 h at 80 °C, cyclooctene oxide (**3g**) and *exo*-norbornene oxide (**3k**) did not react.

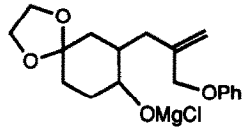
With the catalyst system generated *in situ* from $Pd(OAc)_2$ and $(i\text{-PrO})_3P$, most addition products could be cyclized smoothly. The finding that **7b** could not be converted to **9b** by using [$Pd(PPh_3)_4$] as a catalyst at 80 °C for 24 h while cyclization was easily effected by the $Pd(OAc)_2/(i\text{-PrO})_3P$ system, proves that the greater ease of the experiments contained in Table 2, as compared to those of Table 1, is not due to the replacement of $C_6H_5CH_2O^-$ as the leaving group by phenoxide but is a genuine effect of the use of $Pd(OAc)_2/(i\text{-PrO})_3P$. Even with the more active catalyst, ring closure of **7i** and **7j** was found to be incomplete after 48 hours, while partial decomposition had occurred. The slowness of ring closure of these compounds may be due to steric hindrance encountered during formation and/or conversion of the π-allyl palladium complex leading to **9** and, particularly in case of **7i**, to stabilization of this magnesium alkoxide by intramolecular coordination of the dioxolane oxygens. **9c''** Is probably formed from **9c'** (Table 2).



7b



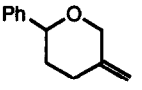
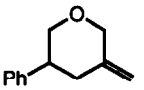
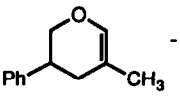
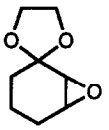
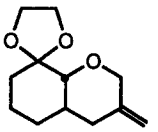
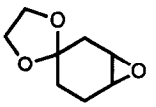
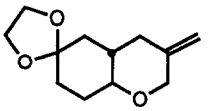
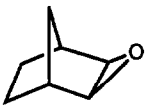
7i



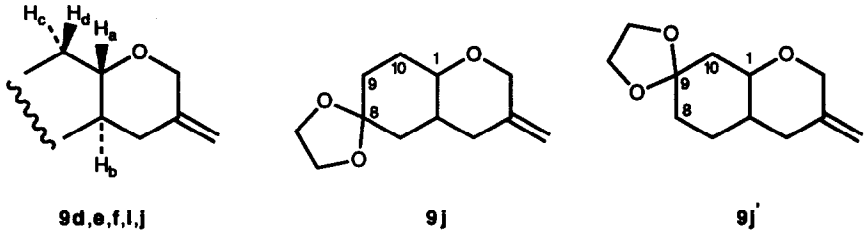
7j

The structure of the 3-methylenetetrahydropyrans **9** was assigned by ^1H NMR; characteristic are resonances for the trimethylenemethane moiety in **9** and those for the non-allylic ether proton(s) [typically **9a**: δ 4.78 (m, 2H, =CH_2), 4.08 (AB system, δ(A) = 4.17, dd, J(AB) = 12.3 Hz, ^4J = 1.8 Hz, 1H, =CCH_2O, δ(B) = 3.98, 1H, =CCH_2O), 3.62-3.47 (m, 1H, OC*H*), 2.33-2.18 (m, 2H, =CCH_2CH$_2$), 1.76 (dquintet, ^2J = 13.1 Hz, J = 2.5 Hz, 1H, =CCH$_2$CH_2), 1.48-1.31 (m, 1H, =CCH$_2$CH_2), 1.20 (d, ^3J = 6.2 Hz, 3H, CH_3)]. Assignment of the *trans*-relation of H_a and H_b of the tetrahydropyrans **9d,e,f,i,j** was based on the fact that the observed coupling constants $^3J_{ab}$, $^3J_{ac}$ and $^3J_{ad}$ of protons H_a, H_b, H_c and H_d (Figure 1) were closer to those calculated for the *trans*-fused ring systems than to those of the *cis*-fused systems (Table 3).

Table 2. 3-Methylenetetrahydropyrans **9** by Reaction of **1b** with Epoxides **3** followed by $Pd(OAc)_2/(i\text{-}PrO)_3P$-catalyzed Cyclization.

System	R^4	R^3	R^5	Product(s)	Yields[a] of **9** [b/c] (%)
a	H	CH_3	H	**9a**	83/-
b	-	$(CH_2)_5$ -	H	**9b**	- /94
c	H	C_6H_5	H	 **9c**  **9c'**  **9c''** 15 : 71 : 14	- /70
d	H	- $(CH_2)_3$ -		**9d**	- /85
e	H	- $(CH_2)_4$ -		**9e**	- /69
f	H	- $(CH_2)_5$-		**9f**	- /76
g	H	- $(CH_2)_6$ -		- [d]	
h	H	$CH(OC_2H_5)_2$	H	**9h**	68/-[e]
i				 **9i**	23/-
j				 **9j**	53/-[f]
k				- [d]	

[a] Yields are based on epoxide **3**. [b] GLC yields. [c] Isolated yields. [d] No ring opening.
[e] 60 mol% $(i\text{-}PrO)_3P$ + 10 mol% $Pd(OAc)_2$. [f] 138 mol% $(i\text{-}PrO)_3P$ + 23 mol% $Pd(OAc)_2$.



9d,e,f,i,j **9j** **9j'**

Fig. 1

Table 3. Observed and Calculated Values [Hz] of Coupling Constants of H_a, H_b, H_c and H_d in Tetrahydropyrans **9d,e,f,i,j**.

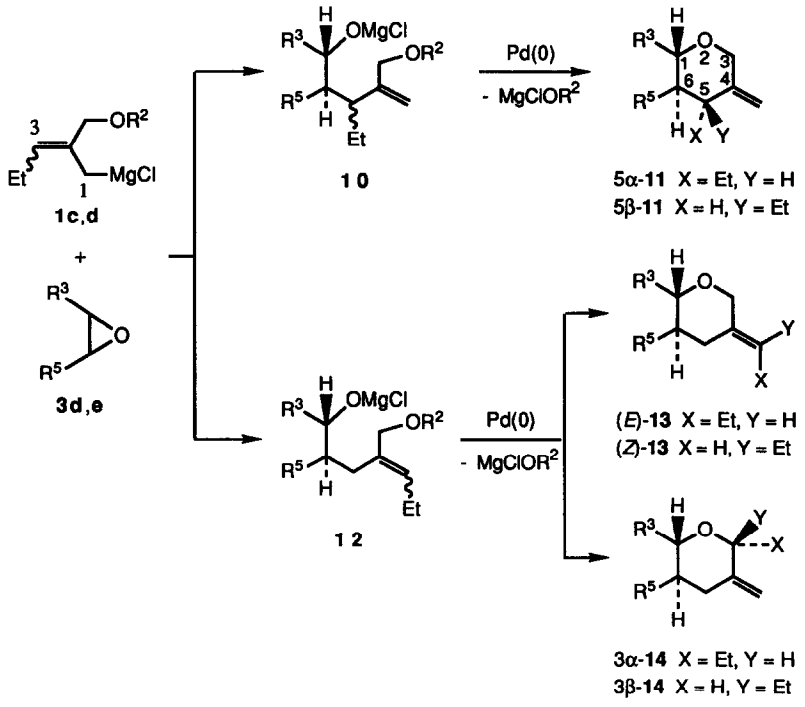
9	Observed[a]			Calculated *cis*-9			Calculated *trans*-9		
	$^3J_{ab}$	$^3J_{ac}$	$^3J_{ad}$	$^3J_{ab}$	$^3J_{ac}$	$^3J_{ad}$	$^3J_{ab}$	$^3J_{ac}$	$^3J_{ad}$
d	10.3	7.1	7.1	2.5	4.9	0.8	10.2	10.1	6.8
e	9.8	4.2	4.2	1.6	2.6	1.5	10.9	11.6	2.1
f	8.9	3.8	3.8	0.0	3.6	1.1	9.6	10.6	1.0
i	10.1	-	-	0.6	-	-	11.1	-	-
j	9.4	11.8	4.4	0.7	2.6	1.5	10.4	11.3	4.3

[a] The signal for H_a in the ^1H NMR spectra of **9d,e,f** consists of a pseudotriplet of doublets. It arises from two relatively large coupling constants ($^3J_{ab}$, and $^3J_{ac}$ *or* $^3J_{ad}$) which are approximately equal, and one relatively small coupling constant ($^3J_{ac}$ *or* $^3J_{ad}$).

The calculated values were obtained by first calculating lowest energy conformations of **9d,e,f,i,j** by molecular mechanics (MM2) which were then used for calculation of the coupling constants by the method of Haasnoot, De Leeuw and Altona.[25] The *trans* geometry of the ring systems **9d,e,f,i,j** confirms the *trans* stereoselectivity of the epoxide ring opening for both the Cu-catalyzed (**3d,e**) and the uncatalyzed reaction (**3d,e,f,i,j**), which is in agreement with other findings.[18,26] The position of the dioxolane ring in **9j** and, by consequence, the site of addition of **1b** to epoxide **3j**, was assigned by 2D COSY NMR, which established the subunit –C(8)-C(9)-C(10)-C(1)-O– contained in **9j**, thereby disproving the alternative structure **9j'** which would contain the sububunit –C(9)-C(10)-C(1)-O– (Figure 1).

Reactions of epoxides 3 with 2-(chloromagnesiomethyl)-2-pentenyl ethers 1c,d.

Reaction of epoxides with 3-alkyl-2-alkenylmagnesium compounds of type **1c,d** is reported to take place almost exclusively at the 3-position of the latter.[17] Accordingly, the addition of **1c,d** to **3** would lead to the "branched" addition products **10**, which upon Pd(0)-catalyzed cyclization would give more highly substituted tetrahydropyrans **11** (Scheme 2). On the other hand, Cu(I)-promoted ring opening of epoxides takes place almost exclusively by attack of C-1 of the allylic reagents.[18] Notwithstanding its limited applicability in the case of **1a**, it therefore seemed interesting to test the Cu(I)-catalyzed reaction as a route to linear addition products **12**, which on Pd(0)-catalyzed cyclization would give the tetrahydropyrans **13** and/or **14**.



1	R^2	3	R^3,R^5	11,13,14	R^3,R^5	10,12	R^2	R^3,R^5
c	$CH_2C_6H_5$	d	$-(CH_2)_3-$	a	$-(CH_2)_3-$	a	$CH_2C_6H_5$	$-(CH_2)_3-$
d	CH_3	e	$-(CH_2)_4-$	b	$-(CH_2)_4-$	b	$CH_2C_6H_5$	$-(CH_2)_4-$
						c	CH_3	$-(CH_2)_3-$
						d	CH_3	$-(CH_2)_4-$

Scheme 2

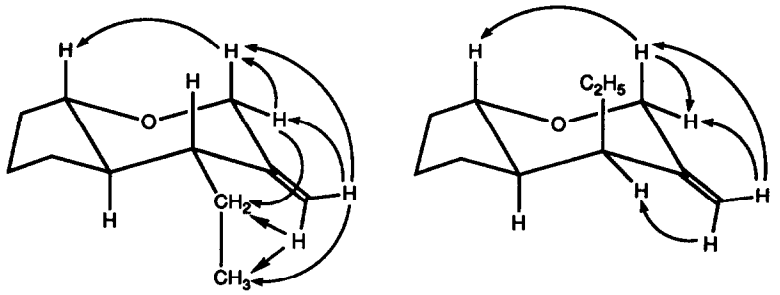
The preparation of the organometallics **1c** and **1d** has been described.[14b] The scope and limitations of the two reaction modes outlined above were investigated for two epoxides: cyclopentene oxide (**3d**) and cyclohexene oxide (**3e**). To effect cyclization, both $Pd(OAc)_2/(i\text{-}PrO)_3P$ and $[Pd(PPh_3)_4]$ were applied. Results are given in Table 4. The structure of the tetrahydropyrans **11**, **13** and **14** was assigned by ^1H NMR. The resonances for the ethyltrimethylenemethane moiety in these compounds readily confirmed the position of the ethyl group as depicted (Scheme 2). The stereochemistry of **11a**, **11b** and **14b** was determined by 2D NOESY NMR. Some selected results for **11a** and **11b** are shown in Figures 2 and 3. The NOESY spectrum of 3α-**14b** displays a large NOE between H(1) and H(3) which is absent in the NOESY spectrum of its epimer 3β-**14b**. The stereochemistry of **14a** was assigned by comparison of its ^1H NMR spectrum with that of **14b**. The position of the ethyl group in **13a** was assigned by NOE difference spectroscopy. One of the two protons H(3) of (*Z*)-**13a** displays a NOE with the CH_2 group of the ethyl substituent; such an effect is absent in the case of (*E*)-**13a**. The stereochemistry of **13b** was assigned by comparison of its ^1H NMR spectrum with that of **13a**.

Table 4. 3-Methylenetetrahydropyrans **11**, **13** and **14** from epoxides **3d**,**e** and 2-(chloromagnesiomethyl)-2-pentenyl ethers **1c**,**d** ($R^1 = C_2H_5$).

Entry	RM	Epoxide	Addition[a]	Cyclization[b] Catalyst	Products **11** %[c] (5α:5β)	**13** %[c] (*E*:*Z*)	**14** %[c] (3α:3β)
1	**1c**	**3d**	uncatalyzed	$Pd(OAc)_2/(i\text{-}PrO)_3P$	52 (54 : 46)	9 (50 : 50)	2 (85 : 15)
2	**1d**	**3d**	uncatalyzed	$Pd(OAc)_2/(i\text{-}PrO)_3P$	61 (53 : 47)	4 - [d]	3 - [d]
3	**1c**	**3d**	Cu-catalyzed	$Pd(OAc)_2/(i\text{-}PrO)_3P$		42 (50 : 50)	17 (85 : 15)
4	**1c**	**3d**	Cu-catalyzed	$[Pd(PPh_3)_4]$		45[e] (68 : 32)	7[e] (71 : 29)
5	**1c**	**3e**	uncatalyzed	$Pd(OAc)_2/(i\text{-}PrO)_3P$	31 (45 : 55)	10 (60 : 40)	2 (64 : 36)
6	**1d**	**3e**	uncatalyzed	$Pd(OAc)_2/(i\text{-}PrO)_3P$	33 (50 : 50)	4 - [d]	0 - [d]
7	**1c**	**3e**	Cu-catalyzed	$Pd(OAc)_2/(i\text{-}PrO)_3P$		45 (60 : 40)	13 (59 : 41)
8	**1c**	**3e**	Cu-catalyzed	$[Pd(PPh_3)_4]$		62[e] (91 : 9)	3[e] (22 : 78)

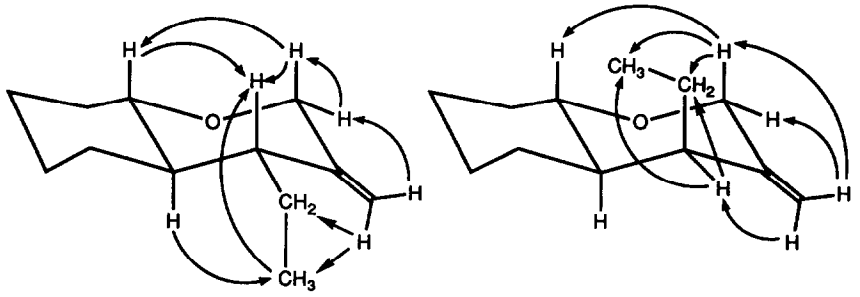
[a] Uncatalyzed ring opening: **1c**,**d** (0.80 M solution in THF, 1.2 equiv.), 0 °C, 1 h; room temperature, 23 h. Cu-catalyzed ring opening: **1c** (0.60 M solution in THF, 1.2 equiv.), 10 mol% CuI, -30 °C, 4 h. [b] 5- 10 mol% catalyst, 65 °C, 40 h. [c] GLC yields, based on epoxide **3**. [d] Ratio of diastereomers could not be determined. [e] Isolated yields.

Results obtained after Pd(0)-catalyzed cyclization (Table 4, entries 1,2 and 5,6) indicated that the uncatalyzed ring opening of **3d** and **3e** by the organometallics **1c** and **1d** was less regioselective than similar reactions involving other 2-alkenylmagnesium compounds which normally react for more than 97 % at their 3-position.[26] As indicated by the tetrahydropyrans **13** and **14**, accompanying **11**, the branched addition products **10** were produced together with the linear addition products **12**. Formation of **10** took place almost non-stereoselectively with respect to the ethyl group. This contrasts with the fair stereoselectivity observed in theaddition of **1c** to aldehydes, ketones and imines.[15b] The difference may be caused by the fact that a highly ordered chairlike transition state operates in additions to carbonyl compounds and imines,[27] whereas attack on epoxides probably involves an acyclic S_N2 mechanism[26] in which the two possible orientations of the ethyl group are of similar steric energy. The copper promoted reaction (Table 4, entries 3,4 and 7,8) gave regiospecifically and in good yields (GLC) the linear addition products **12** resulting from reaction at C-1 of the 2-alkenylmetal species. Pd(0)-catalyzed cyclization of **12** was more difficult than that of the branched addition products **10**. Even with $Pd(OAc)_2/(i\text{-}PrO)_3P$ it was impossible to conduct the ring closure reaction of **12a-d** to completion. Raising the temperature, extending the reaction time, concentrating the reaction mixture or increasing the amount of catalyst were of no avail. Apart from being cyclized, **12a-d** slowly decomposed when $Pd(OAc)_2/(i\text{-}PrO)_3P$ was used as catalyst. No decomposition was observed when $[Pd(PPh_3)_4]$ was used. The results suggest establishment of an equilibrium mixture between **12** on one hand, and **13** or **14** and benzyloxymagnesiumchloride or methoxymagnesium chloride on the other. In this case, the amount of **12** actually formed during the uncatalyzed ring opening of **3d**,**e** would be higher than indicated by the amounts of **13** and **14** (Table 4, entries 1,2 and 5,6).



5α-**11a** 5β-**11a**

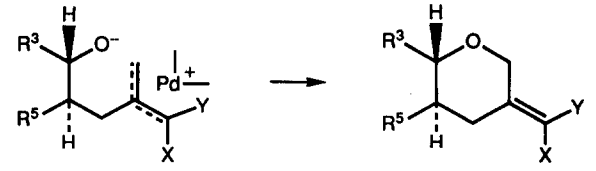
Fig. 2. NOESY data for **11a**.



5α-**11b** 5β-**11b**

Fig. 3. NOESY data for **11b**.

Predominance of cyclization through attack of -OMgCl at the unsubstituted CH_2 group of the allyl ether moiety of **12a-d** (preferential formation of **13**) is in agreement with the regioselectivity reported for Pd(0)-catalyzed allylations of the oxygen nucleophiles AcO^- and $C_6H_5OSn(C_4H_9)_3$.[28] With $[Pd(PPh_3)_4]$, regioselectivity was better than with $Pd(OAc)_2$/ $(i\text{-}PrO)_3P$. The stereoselectivity of formation of cyclization products **13a** and **13b** was much lower (50-91 % *E*) than usually observed in Pd(0)-catalyzed allylations which give more than 95 % of the *E*-isomer. π-Allyl palladium complexes, which most probably are intermediates, prefer the *syn*-configuration[29] leading to the *E*-allylation products.[30] Due to substitution at the central carbon atom of the allyl system this preference may be lost in the π-allyl palladium complexes **15a-d** (Scheme 3) which are formed from **12a-d**. The mixture of *syn*- and *anti*-**15a-d** then would yield a mixture of (*E*)- and (*Z*)-**13a,b**.[31]



syn-**15a-d** X = Et, Y = H (*E*)-**13a,b** X = Et, Y = H

anti-**15a-d** X = H, Y = Et (*Z*)-**13a,b** X = H, Y = Et

Scheme 3

CONCLUSION

Reaction of 2-(chloromagnesiomethyl)-2-alkenyl ethers with epoxides (uncatalyzed or Cu(I)-catalyzed), followed by Pd(0)-catalyzed cyclization, provides a new route to 3-methylenetetrahydropyrans, with substituents on several positions.

Acknowledgment.
We wish to thank Mr R.F. Schmitz for measuring the HRMS spectra.

EXPERIMENTAL SECTION

For general information, see preceding paper.

6,7-Epoxy-1,4-dioxaspiro[4.5]decane 3i.

To a magnetically stirred solution of 1,4-dioxaspiro[4.5]dec-6-ene (3.37 g, 24.1 mmol) in CH_2Cl_2 (5 ml), cooled at 0 °C, was added a solution of *m*-chloroperbenzoic acid (4.37 g, 25.3 mmol) in CH_2Cl_2 (40 ml) in 10 minutes. Stirring was continued for 1 h at 0 °C and, subsequently, for another 2 h at room temperature. The mixture was filtered and the filtrate was washed with 0.1 M $Na_2S_2O_5$ (1x), 0.5 M NaOH (3x) and water (1x), dried (Na_2SO_4) and concentrated *in vacuo*. Molecular distillation (100 °C, 16 Torr) gave 3i (1.88 g, 50 %). ^{1}H NMR (90 MHz): 4.27-3.90 (m, 4H, H(2,3)), 3.42-3.28 (m, 1H, H(7)), 3.03 (d, $^3J(6,7)$ = 4.0 Hz, 1H, H(6)), 2.30-1.30 (m, 6H, H(8,9,10)). MS: 156 (0.4, $M^{+\cdot}$), 127 (2), 99 (100), 86 (3), 68 (4), 55 (47).

7,8-Epoxy-1,4-dioxaspiro[4.5]decane 3j.

Prepared according to the same procedure as described for the synthesis of 3i. Molecular distillation (100 °C, 16 Torr) gave 3j in 66 % yield. ^{1}H NMR (90 MHz): 3.95 (m, 4H, H(2,3)), 3.21 (m, 2H, H(7,8)), 2.29-2.03 (m, 4H, H(6,9)), 2.03-1.30 (m, 2H, H(10)). MS: 129 (1), 127 (12), 100 (100), 99 (78), 98 (42), 86 (62), 55 (11), 53 (36). HRMS ($C_6H_7O_3$ [M-C_2H_5]$^+$): calc. 127.0395, found 127.0399.

General procedure for the preparation of 3-methylenetetrahydropyrans 9 by Cu(I)-promoted reaction of 1a with epoxides 3 followed by [$Pd(PPh_3)_4$]-catalyzed cyclization (Table 1).

To a magnetically stirred solution of **1a** in THF (0.25 M, 2.4 mmol), cooled at -30 °C, was added CuI (38 mg, 0.20 mmol). After stirring for 10 minutes, the epoxide (2.0 mmol) was added dropwise. *c*-Octane (1 mmol) was added as internal standard. Stirring was continued while the reaction mixture was kept at -30 °C for 4 h and then allowed to warm-up to room temperature overnight. The reaction mixture was analyzed by quenching a small portion with aqueous NH_4Cl. To the remainder of the mixture was added [$Pd(PPh_3)_4$] (0.116 g, 0.10 mmol) whereafter it was heated in standard glass equipment or, alternatively, in the Carius tube mentioned above at 65-100 °C for 24-70 h. After cooling, the mixture was poured onto saturated NH_4Cl solution and the aqueous phase was extracted three times with diethyl ether. The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated at reduced pressure. The crude reaction product was analyzed by GLC, GCMS and NMR. Yields are based on epoxide 3.

5-(Benzyloxymethyl)-5-hexen-2-ol 8a.

Prepared by reaction of **1a** with **3a** followed by hydrolysis (yield: 87 % [GLC]). ^{1}H NMR (90 MHz): 7.36 (s, 5H, C_6H_5), 5.07 (m, 1H, H(6)), 4.97 (bs, 1H, H(6)), 4.51 (s, 2H, O$CH_2C_6H_5$), 3.98 (s, 2H, C(5)CH_2O), 3.83 (sextet, $^3J(2,1) = {}^3J(2,3)$ = 6.2 Hz, 1H, H(2)), 2.35-2.05 (m, 2H, H(4)), 1.78-1.45 (m, 3H, H(3), OH), 1.21 (d, $^3J(1,2)$ = 6.2 Hz, 3H, H(1)). MS: 143 (1), 129 (4), 112 (9), 107 (14), 96 (5), 91 (100), 85 (4), 81 (11), 65 (9), 55 (9). HRMS ($C_7H_{13}O_2$ [M-$CH_2C_6H_5$]$^+$): calc. 129.0915, found 129.0899.

2-Methyl-5-methyleneoxane 9a.

Prepared by reaction of **1a** with **3a** followed by Pd(0)-catalyzed cyclization (yield: 61 % [GLC]). Conditions of ring closure: 100 ^{o}C, 70 h. Use of other solvents (25 % DMF/THF, 25 % HMPA/THF, DMF, HMPA) did not result in faster reaction. ^{1}H NMR (250 MHz): 4.78 (m, 2H, $=CH_2$), 4.08 (AB system, δ(A) = 4.17, dd, J(AB) = 12.3 Hz, ^{4}J = 1.8 Hz, 1H, H(6), δ(B) = 3.98, J(BA) = 12.3 Hz, 1H, H(6)), 3.62-3.47 (m, 1H, H(2)), 2.33-2.18 (m, 2H, H(4)), 1.76 (dquintet, ^{2}J = 13.1 Hz, J = 2.5 Hz, 1H, H(3)), 1.48-1.31 (m, 1H, H(3)), 1.20 (d, $^{3}J(CH_3,2)$ = 6.2 Hz, 3H, CH_3). MS: 112 (77, $M^{+\cdot}$), 97 (25), 83 (17), 79 (7), 71 (56), 67 (100), 55 (48), 53 (45). HRMS ($C_7H_{12}O$): calc. 112.0888, found 112.0893.

1-(3-(Benzyloxymethyl)-3-butenyl)cyclohexanol 8b.

Prepared by reaction of **1a** with **3b** followed by hydrolysis (yield: 49 % [GLC]). ^{1}H NMR (90 MHz): 7.36 (d, 5H, C_6H_5), 5.06 (bs, 1H, H(4')), 4.98 (bs, 1H, H(4')), 4.52 (s, 2H, $OCH_2C_6H_5$), 4.01 (bs, 2H, C(3')CH_2O), 2.35-2.05 (m, 2H, H(2')), 1.80-1.05 (m, 13H, H(2,3,4,5,6,1'), OH). MS: 256 (1, $M^{+\cdot}$), 165 (7), 148 (20), 135 (10), 119 (5), 105 (17), 99 (6), 95 (11), 91 (100), 79 (16), 67 (16), 55 (14). HRMS ($C_{18}H_{24}O$ $[M-H_2O]^{+}$): calc. 256.1827, found 256.1820.

3-Methylene-1-oxaspiro[5.5]undecane 9b.

Prepared by reaction of **1a** with **3b** followed by Pd(0)-catalyzed cyclization (yield: 28 % [GLC]). Conditions of ring closure: 100 ^{o}C, 70 h. ^{1}H NMR (250 MHz): 4.77 (m, 1H, $=CH_2$), 4.74 (m, 1H, $=CH_2$), 4.06 (s, 2H, H(2)), 2.32 (tt, ^{3}J = 6.5 Hz, J = 1.2 Hz, 1H, H(4)), 1.90-1.75 (m, 1H, H(4)), 1.70-1.21 (m, 12H, H(5,7,8,9,10,11)). MS: 166 (22, $M^{+\cdot}$), 148 (22), 137 (5), 123 (100), 110 (67), 99 (16), 96 (17), 91 (4), 81 (31), 67 (32), 55
(33). HRMS ($C_{11}H_{18}O$): calc. 166.1358, found 166.1359.

4-(Benzyloxymethyl)-1-phenyl-4-pentenol 8c.

Prepared by reaction of **1a** with **3c** followed by hydrolysis (yield: 14 % [GLC]). ^{1}H NMR (90 MHz): 7.33 (bs, 10H, C_6H_5), 5.16-4.94 (m, 2H, H(5)), 4.84-4.60 (m, 1H, H(1)), 4.50 (s, 2H, $OCH_2C_6H_5$), 3.98 (bs, 2H, C(4)CH_2O), 2.38-1.78 (m, 5H, H(2,3), OH).

2-(2-(Benzyloxymethyl)-2-propenyl)cyclopentanol 8d.

Prepared by reaction of **1a** with **3d** followed by hydrolysis (yield: 80 % [GLC]). ^{1}H NMR (250 MHz): 7.38-7.27 (m, 5H, C_6H_5), 5.12 (m, 1H, $=CH_2$), 5.01 (m, 1H, $=CH_2$), 4.52 (s, 2H, $OCH_2C_6H_5$), 4.00 (s, 2H, C(2')CH_2O), 3.86 (q, ^{3}J = 6.4 Hz, 1H, H(1)), 2.27- 1.84 (m, 5H), 1.81-1.49 (m, 4H), 1.31-1.12 (m, 1H). MS: 155 (2), 138 (12), 122 (6), 107 (16), 91 (100), 84 (19), 79 (11), 67 (15), 55 (11), 40 (16). HRMS ($C_{16}H_{22}O$): calc. 246.1620, found 246.1627.

4-Methylene-2-oxabicyclo[4.3.0]nonane 9d.

Prepared by reaction of **1a** with **3d** followed by Pd(0)-catalyzed cyclization (yield: 79 % [GLC]). Conditions of ring closure: 65 ^{o}C, 24 h. ^{1}H NMR (400 MHz): (1) 4.84 (m, 1H, $=CH_2$), (2) 4.80 (m, 1H, $=CH_2$), (3) 4.23 (A part of AB system, dd, J(AB) = 12.5 Hz, ^{4}J = 1.6 Hz, 1H, H(3)), (4) 4.03 (B part of AB system, dm, J(BA) = 12.5 Hz, 1H, H(3)), (5) 3.21 (td, ^{3}J = 10.3 Hz and 7.1 Hz, 1H, H(1)), (6) 2.58 (ddd, ^{2}J = 13.1 Hz, ^{3}J(5,6) = 3.9 Hz, ^{4}J = 1.6 Hz, 1H, H(5)), (7) 1.97 (m, 1H, H(5)), (8) 1.93 (m, 1H, H(9)), (9) 1.74 (m, 2H, H(7,8)), (10) 1.64 (m, 1H, H(8)), (11) 1.48 (m, 1H, H(6)), (12) 1.45 (m, 1H, H(9)), (13) 1.17 (m, 1H, H(7)). 2D COSY NMR (400 MHz): 1(2,3,4,7), 2(4,6,7), 3(4,5,6,7), 4(6,7), 5(8,11,12), 6(7,11), 7(11), 8(9,10,12,13), 9(10,11,12,13), 10(12,13), 11(13), 12(13). 2D NOESY NMR (400 MHz, τ_m = 1.0 s or 3.0 s): 1(2,3,4^{W},7^{W}), 2(3,4^{W},6,7^{W}), 3(4,5^{W}), 4(5, 7), 5(7,8,10^{W}), 6(7), 7(13^{W}), 8(9^{W},10^{W},11^{W},12,13^{W}), 9(10,11^{W},12^{W},13), 10(11,12,13^{W}). ^{13}C NMR (63 MHz): 143.7 (s, C(4)), 110.4 (tquintet, $^{1}J(CH)$ = 156 Hz, $^{3}J(CH)$ = 5 Hz, $=CH_2$), 83.9 (d, $^{1}J(CH)$ = 138 Hz, C(1)), 73.1 (t, $^{1}J(CH)$ = 140 Hz, C(3)), 45.1 (d, $^{1}J(CH)$ = 125 Hz, C(6)), 38.1 (t, $^{1}J(CH)$ = 130 Hz, C(5)), 28.3 (t, $^{1}J(CH)$ = 128 Hz, C(7*)), 26.8 (t, $^{1}J(CH)$ = 126 Hz, C(9*)), 19.6 (t, $^{1}J(CH)$ = 135 Hz, C(8*)). MS: 138 (21, $M^{+\cdot}$), 123 (2), 120 (25), 109 (17), 97 (13), 94 (39), 91 (18), 82 (30), 79 (41), 77 (10), 70 (9), 67 (100), 57 (15), 55 (29). HRMS ($C_9H_{14}O$): calc. 138.1045, found 138.1054.

2-(2-(Benzyloxymethyl)-2-propenyl)cyclohexanol 8e.

Prepared by reaction of **1a** with **3e** followed by hydrolysis (yield: 93 % [GLC]). ^{1}H NMR (250 MHz): 7.40-7.26 (m, 5H, C_6H_5), 5.13 (m, 1H, $=CH_2$), 4.99 (s, 1H, $=CH_2$), 4.52 (AB system, δ(A) = 4.55, J(AB) = 11.9 Hz, 1H, $OCH_2C_6H_5$, δ(B) = 4.50, J(BA) = 11.9 Hz, 1H, $OCH_2C_6H_5$), 4.00 (s, 2H, $C(2')CH_2O$), 3.24 (td, ^{3}J = 9.4 Hz and 4.4 Hz, 1H, H(1)), 2.57 (dd, J = 14.0 Hz and 4.6 Hz, 1H, H(1')), 2.02-0.81 (m, 11H, H(2,3,4,5,6, 1'), OH).

4-Methylene-2-oxabicyclo[4.4.0]decane 9e.

Prepared by reaction of **1a** with **3e** followed by Pd(0)-catalyzed cyclization (yield: 85 % [GLC]). Conditions of ring closure: 65 °C, 24 h. ^{1}H NMR (250 MHz): 4.82-4.74 (m, 2H, $=CH_2$), 4.09 (AB system, δ(A) = 4.19, dd, J(AB) = 12.2 Hz, ^{4}J = 1.8 Hz, 1H, H(3), δ(B) = 3.99, J(BA) = 12.2 Hz, 1H, H(3)), 3.02 (td, ^{3}J = 9.8 Hz and 4.2 Hz, 1H, H(1)), 2.33 (ddd, ^{2}J = 13.3 Hz, J = 3.9 Hz, J = 1.8 Hz, 1H, H(5)), 2.00-1.60, 1.45-0.94 (m, 10H, H(5,6,7,8,9,10)). MS: 152 (78, $M^{+\cdot}$), 137 (4), 134 (4), 123 (8), 121 (6), 119 (7), 108 (25), 105 (6), 95 (27), 82 (68), 67 (100), 55 (41). HRMS ($C_{10}H_{16}O$): calc. 152.1201, found 152.1200.

General procedure for the preparation of 3-methylenetetrahydropyrans 9 by uncatalyzed reaction of 1b with epoxides 3 followed by $Pd(OAc)_2/(i\text{-}PrO)_3P$-catalyzed cyclization (Table 2).

To a magnetically stirred solution of **1b** in THF (1.3-1.6 M, 1.2 equiv.), cooled at 0 °C, was added dropwise epoxide **3** (2-10 mmol) and, if necessary (Table 2), *c*-octane (1 mmol) as internal standard. Stirring was continued for 0.5 h at 0 °C and, subsequently, for 4 h at room temperature. To the mixture was added $(i\text{-PrO})_3P$ (30 mol%) and $Pd(OAc)_2$ (5 mol%) whereafter it was heated at 70-80 °C (reflux temperature of the reaction mixture) for 24-48 h. Work-up was carried out as described above. The crude reaction product was analyzed by GLC, GCMS and NMR, or alternatively, it was purified by evaporative distillation. Yields are based on epoxide **3**.

2-Methyl-5-methyleneoxane 9a.

Prepared by reaction of **1b** with **3a** followed by Pd(0)-catalyzed cyclization (yield: 83 % [GLC]).

3-Methylene-1-oxaspiro[5.5]undecane 9b.

Prepared by reaction of **1b** with **3b** followed by Pd(0)-catalyzed cyclization. Evaporative distillation (100-150 °C, 16 Torr) gave **9b** in 94 % yield. In another experiment, the yield was determined by GLC (87 %).

Reaction of 1b with 3c.

Evaporative distillation (100-150 °C, 16 Torr) gave a mixture of **9c**, **9c'** and **9c''** (yield: 70 %; ratio: 15:71:14).

2-Phenyl-5-methyleneoxane 9c.

^{1}H NMR (250 MHz): 7.38-7.21 (m, 5H, C_6H_5), 4.95-4.83 (m, 2H, $=CH_2$), 4.48 (dd, ^{3}J(2,3) = 11.2 Hz and 2.3 Hz, 1H, H(2)), 4.28 (AB system, δ(A) = 4.37, dd, J(AB) = 12.4 Hz, ^{4}J = 1.3 Hz, 1H, H(6), δ(B) = 4.18, J(BA) = 12.4 Hz, 1H, H(6)), 2.67 (dm, ^{2}J = 14.3 Hz, 1H, H(4)), 2.58-2.43 (m, 1H, H(4)), 2.06-1.92 (m, 1H, H(3)), 1.85-1.68 (m, 1H, H(3)). MS: 174 (15, $M^{+\cdot}$), 156 (3), 145 (4), 128 (8), 117 (13), 104 (100), 91 (25), 77 (29), 67 (58), 51 (25).

3-Methylene-5-phenyloxane 9c'.

^{1}H NMR (250 MHz): 7.38-7.21 (m, 5H, C_6H_5), 4.95-4.83 (m, 2H, $=CH_2$), 4.14 (AB system, δ(A) = 4.25, J(AB) = 12.3 Hz, 1H, H(2), δ(B) = 4.02, J(BA) = 12.3 Hz, 1H, H(2)), 4.08- 3.97 (m, 1H, H(6)), 3.54 (dd → 3 lines, ^{2}J = 10.8 Hz, ^{3}J(6,5) = 10.8 Hz, 1H, H(6)), 3.00 (tt, ^{3}J(5,6) = 10.8 Hz, ^{3}J = 4.2 Hz, 1H, H(5)), 2.67 (dm, ^{2}J = 14.3 Hz, 1H, H(4)), 2.58-2.43 (m, 1H, H(4)). MS: 174 (11, $M^{+\cdot}$), 156 (11), 143 (25), 129 (65), 115 (19), 104 (100), 91 (50), 83 (50), 78 (32), 65 (15), 51 (25).

2,3-Dihydro-4*H*-3-methyl-5-phenylpyran 9c''.

^{1}H NMR (250 MHz): 7.38-7.21 (m, 5H, C_6H_5), 6.32 (m, 1H, H(2)), 4.12-3.97 (m, 1H, H(6)), 3.74 (dd → 3 lines, ^{3}J(6,5) = 10.2

Hz, 1H, H(6)), 3.17-3.08 (m, 1H, H(5)), 2.34-2.08 (m, 2H, H(4)), 1.64 (bs, 3H, CH_3).

4-Methylene-2-oxabicyclo[4.3.0]nonane 9d.

Prepared by reaction of **1b** with **3d** followed by Pd(0)-catalyzed cyclization. Evaporative distillation (100-150 °C, 16 Torr) gave **9d** in 85 % yield.

4-Methylene-2-oxabicyclo[4.4.0]decane 9e.

Prepared by reaction of **1b** with **3e** followed by Pd(0)-catalyzed cyclization. Evaporative distillation (100-150 °C, 16 Torr) gave **9e** in 69 % yield.

10-Methylene-8-oxabicyclo[5.4.0]undecane 9f.

Prepared by reaction of **1b** with **3f** followed by Pd(0)-catalyzed cyclization. Evaporative distillation (100-150 °C, 16 Torr) gave **9f** in 76 % yield. ^{1}H NMR (250 MHz): 4.76 (m, 2H, $=CH_2$), 4.04 (AB system, δ(A) = 4.16, dd, J(AB) = 12.2 Hz, ^{4}J = 1.8 Hz, 1H, H(9), δ(B) = 3.92, dd, J(BA) = 12.2 Hz, ^{4}J = 0.6 Hz, 1H, H(9)), 3.07 (td, ^{3}J = 8.9 Hz and 3.8 Hz, 1H, H(7)), 2.34 (ddd, ^{2}J = 13.5 Hz, ^{3}J(11,1) = 3.8 Hz, ^{4}J = 1.8 Hz, 1H, H(11)), 2.04-1.87 (m, 2H), 1.80-1.36 (m, 9H), 1.32-1.13 (m, 1H). MS: 166 (41, $M^{+\cdot}$), 148 (11), 135 (6), 122 (21), 109 (48), 96 (100), 81 (93), 67 (84), 55 (85). HRMS ($C_{11}H_{18}O$): calc. 166.1358, found 166.1366.

2-(Diethoxymethyl)-5-methyleneoxane 9h.

Prepared by reaction of **1b** with **3h** followed by Pd(0)-catalyzed cyclization (yield: 68 % [GLC]). Cyclization was effected by using 60 mol% $(i\text{-PrO})_3$P and 10 mol% $Pd(OAc)_2$. ^{1}H NMR (250 MHz): 4.79 (m, 2H, $=CH_2$), 4.36 (d, ^{3}J = 5.8 Hz, 1H, $CH(OC_2H_5)_2$), 4.11 (AB system, δ(A) = 4.24, dd, J(AB) = 12.4 Hz, ^{4}J = 1.6 Hz, 1H, H(6), δ(B) = 3.98, J(BA) = 12.4 Hz, 1H, H(6)), 3.80-3.46 (m, 5H, H(2), OCH_2CH_3), 2.46 (dm, ^{2}J = 14.5 Hz, 1H, H(4)), 2.35-2.17 (m, 1H, H(4)), 1.96-1.85 (m, 1H, H(3)), 1.50 (ddd, ^{2}J = 26.1 Hz, ^{3}J(3,2) = 11.2 Hz, ^{3}J(3,4) = 4.8 Hz, 1H, H(3)), 1.24, 1.21 (2 x t → q, ^{3}J = 7.1 Hz, 6H, OCH_2CH_3). MS: 163 (2), 155 (1), 136 (29), 109 (8), 103 (100), 97 (5), 81 (9), 75 (52), 69 (17), 57 (6), 53 (18).

10,10-Ethylenedioxy-4-methylene-2-oxabicyclo[4.4.0]decane 9i.

Prepared by reaction of **1b** with **3i** followed by Pd(0)-catalyzed cyclization (yield: 23 % [GLC]). During ring opening **7i** precipitated from the reaction mixture and was dissolved again by addition of DMF (0.3 ml/mmol **3i**). ^{1}H NMR (250 MHz): 4.78 (m, 2H, $=CH_2$), 4.28 (A part of AB system, dd, J(AB) = 12.3 Hz, ^{4}J = 1.7 Hz, 1H, H(3)), 4.18-3.89 (m, 5H, H(3), OCH_2CH_2O), 3.18 (d, ^{3}J(1,6) = 10.1 Hz, 1H, H(1)), 2.42 (ddd, ^{2}J = 13.1 Hz, ^{3}J(5,6) = 3.8 Hz, ^{4}J = 1.8 Hz, 1H, H(5)), 2.02-1.87 (m, 1H, H(5)), 1.84-1.43 (m, 6H), 1.18-0.98 (m, 1H). MS: 210 (6, $M^{+\cdot}$), 148 (45), 139 (2), 122 (3), 109 (5), 99 (100), 95 (3), 86 (4), 79 (4), 73 (2), 69 (11), 67 (8). HRMS ($C_{12}H_{18}O_3$): calc. 210.1256, found 210.1235.

8,8-Ethylenedioxy-4-methylene-2-oxabicyclo[4.4.0]decane 9j.

Prepared by reaction of **1b** with **3j** followed by Pd(0)-catalyzed cyclization (yield: 53 % [GLC]). Cyclization was performed by using 138 mol% $(i\text{-PrO})_3$P and 23 mol% $Pd(OAc)_2$. ^{1}H NMR (400 MHz): (1) 4.81 (quintet, ^{4}J = 1.7 Hz, 1H, $=CH_2$), (2) 4.78 (m, 1H, $=CH_2$), (3) 4.18 (A part of AB system, dd, J(AB) = 12.3 Hz, ^{4}J = 1.8 Hz, 1H, H(3)), (4) 4.10-3.95 (B part of AB system, m, 1H, H(3)), (5) 3.96 (m, 4H, OCH_2CH_2O), (6) 3.25 (ddd, ^{3}J = 11.8 Hz, 9.4 Hz and 4.4 Hz, 1H, H(1)), (7) 2.40 (ddd, ^{2}J = 13.3 Hz, ^{3}J(5a,6) = 3.6 Hz, ^{4}J = 1.9 Hz, 1H, H(5a)), (8) 2.07 (ddd, J = 12.3 Hz, J = 4.4 Hz, J = 2.6 Hz, 1H, H(10a)), (9) 1.95 (tm, J = 11.9 Hz, 1H, H(5b)), (10) 1.73 (dm, J = 9.4 Hz, 1H, H(9a)), (11) 1.63 (m, 2H, H(7a,b)), (12) 1.59 (m, 1H, H(10b)), (13) 1.35 (m, 1H, H(6)), (14) 1.30 (m, 1H, H(9b)). 2D COSY NMR (400 MHz): 1(2,3,4,9), 2(4,9), 3(4,7), 4(9), 6(8,12,13), 7(9,13), 8(10,12), 10(12,14), 11(13), 12(14). 2D NOESY NMR (400 MHz, τ_m = 1.0 s): 1(2,3^W,4^W), 2(7^W), 3(4), 5(6,8,10,11,12), 6(8,9,12^W,13), 7(9,11,13), 8(12), 9(13), 10(12,13), 11(12,13,14), 12(13^W). MS: 210 (11, $M^{+\cdot}$), 182 (3), 141 (3), 122 (2), 115 (25), 99 (100), 95 (4), 86 (87), 79 (3), 69 (11), 53 (35). HRMS ($C_{12}H_{18}O_3$): calc. 210.1256, found 210.1247.

General procedure for the preparation of 3-methylenetetrahydropyrans 13 and 14 by Cu(I)-promoted reaction of 1c with epoxides 3d and 3e followed by [$Pd(PPh_3)_4$]- or $Pd(OAc)_2$/(i-PrO)$_3$P-catalyzed cyclization (Table 4, entries 3,4,7,8).

To a magnetically stirred solution of **1c** in THF (0.60 M, 2.4 mmol), cooled at -30 °C, was added CuI (38 mg, 0.20 mmol). After stirring for 10 minutes, the epoxide **3** (2.0 mmol) was added dropwise. *c*-Octane (1 mmol) was added as internal standard. Stirring was continued while the reaction mixture was kept at -30 °C for 4 h and then allowed to warm-up to room temperature overnight. To the mixture was added [$Pd(PPh_3)_4$] (5-10 mol%) or, alternatively, (i-PrO)$_3$P (30-60 mol%) and $Pd(OAc)_2$ (5-10 mol%) whereafter it was heated at 65 °C for 40 h. Work-up was carried out as described before. The crude reaction product was analyzed by GLC, GCMS and NMR or, alternatively, purified by column chromatography (3 % diethyl ether/97 % pentane). Yields are based on epoxide **3**.

General procedure for the preparation of 3-methylenetetrahydropyrans 11, 13 and 14 by uncatalyzed reaction of 1c or 1d with epoxides 3d and 3e followed by $Pd(OAc)_2$/(i-PrO)$_3$P-catalyzed cyclization (Table 4, entries 1,2,5,6).

To a magnetically stirred solution of **1c** or **1d** in THF (0.80 M, 1.2 equiv.), cooled at 0 °C, was added dropwise epoxide **3** (2-10 mmol) and, as internal standard, *c*-octane (1 mmol). Stirring was continued for 1 h at 0 °C and, subsequently, for 23 h at room temperature. To the mixture was added (i-PrO)$_3$P (30-60 mol%) and $Pd(OAc)_2$ (5-10 mol%) whereafter it was heated at 65 °C for 40 h. Work-up was carried out as described before. The crude reaction product was analyzed by GLC, GCMS and NMR. Yields are based on epoxide **3**.

In this way were prepared (for reaction conditions and yields, see Table 4):

5α-Ethyl-4-methylene-2-oxabicyclo[4.3.0]nonane 5α-11a.

^{1}H NMR (400 MHz): (1) 4.97 (q, ^{4}J = 1.4 Hz, 1H, =CH_2), (2) 4.85 (t, ^{4}J = 1.7 Hz, 1H, =CH_2), (3) 4.25 (A part of AB system, J(AB) = 12.2 Hz, 1H, H(3)), (4) 4.05 (B part of AB system, J(BA) = 12.2 Hz, 1H, H(3)), (5) 3.35 (td, ^{3}J = 10.4 Hz and 7.1 Hz, 1H, H(1)), 1.99-1.15 (m, 10H, H(5,6,7,8,9), CH_2CH_3) [in which: (6) 1.94 (m, 2H, H(5,9)), (7) 1.62 (m, 2H, CH_2CH_3), (8) 1.48 (m, 1H, H(6)), (9) 1.31 (m, 1H, H(9))], (10) 0.97 (t, ^{3}J = 7.4 Hz, 3H, CH_2CH_3). 2D COSY NMR (400 MHz): 1(2,3,4,6), 2(4,6), 3(4), 4(6), 5(6,8,9), 7(10). 2D NOESY NMR (400 MHz, τ_m = 1.0 s or 3.0 s): 1(2,3,4,7^W,10), 2(7,10), 3(4,10), 4(5), 6(10), 7(10). MS: 166 (5, $M^{+\cdot}$), 151 (1), 137 (22), 122 (8), 119 (8), 109 (26), 95 (26), 81 (52), 67 (100), 55 (45). HRMS (mixture of both 5α-**11a** and 5β-**11a**, $C_{11}H_{18}O$): calc. 166.1358, found 166.1356.

***5β-Ethyl-4-methylene-2-oxabicyclo[4.3.0]nonane* 5β-11a.**

^{1}H NMR (400 MHz): (1) 4.92 (t, ^{4}J = 1.8 Hz, 1H, =CH_2), (2) 4.81 (d, ^{4}J = 2.1 Hz, 1H, =CH_2), (3) 4.12 (A part of AB system, dd, J(AB) = 12.6 Hz, ^{4}J = 1.4 Hz, 1H, H(3)), (4) 4.06 (B part of AB system, J(BA) = 12.6 Hz, 1H, H(3)), (5) 3.57 (td, ^{3}J = 10.3 Hz and 7.4 Hz, 1H, H(1)), (6) 2.40 (dt, ^{3}J = 10.9 Hz and 4.5 Hz, 1H, H(5)), 1.99-1.15 (m, 9H, H(6,7,8,9), CH_2CH_3) [in which: (7) 1.94 (m, 1H, H(9)), (8) 1.81 (m, 1H, H(6)), (9) 1.62-1.33 (m, 2H, CH_2CH_3), (10) 1.44 (m, 1H, H(9))], (11) 0.84 (t, ^{3}J = 7.4 Hz, 3H, CH_2CH_3). 2D COSY NMR (400 MHz): 1(2,3,4), 2(3,6), 3(4), 4(6), 5(7,8,10), 6(8,9), 7(11), 9(11). 2D NOESY NMR (400 MHz, τ_m = 1.0 s or 3.0 s): 1(2,3,4), 2(3^W,4^W,6^W), 3(5), 6(11), 9(11). MS: 166 (2, $M^{+\cdot}$), 148 (2), 137 (23), 122 (10), 119 (8), 109 (25), 81 (47), 95 (25), 67 (100), 55 (47). HRMS (mixture of both 5α-**11a** and 5β-**11a**, $C_{11}H_{18}O$): calc. 166.1358, found 166.1356.

(*E*)-4-Propylidene-2-oxabicyclo[4.3.0]nonane (*E*)-13a.

^{1}H NMR (250 MHz): 5.34 (t, ^{3}J = 7.0 Hz, 1H, =$CHCH_2CH_3$), 4.10 (AB system, δ(A) = 4.14, J(AB) = 12.5 Hz, 1H, H(3), δ(B) = 4.06, dt, J(BA) = 12.5 Hz, ^{4}J = 1.2 Hz, 1H, H(3)), 3.25 (dt, ^{3}J = 10.2 Hz and 7.1 Hz, 1H, H(1)), 2.86 (ddd, ^{2}J = 13.2 Hz, ^{3}J(5,6) = 3.5 Hz, ^{4}J = 1.0 Hz, 1H, H(5)), 2.17-1.86, 1.84-1.58, 1.58-1.31, 1.28-1.08 (m, 10H), 0.97 (t, ^{3}J = 7.6 Hz, 3H, CH_2CH_3). MS (mixture of both (*E*)-**13a** and (*Z*)-**13a**): 166 (17, $M^{+\cdot}$), 137 (50), 119 (22), 109 (8), 91 (31), 81 (27), 79 (27), 67 (100), 55 (33).

(*Z*)-4-Propylidene-2-oxabicyclo[4.3.0]nonane (*Z*)-13a.
^{1}H NMR (250 MHz): 5.24 (t, ^{3}J = 7.3 Hz, 1H, =C*H*CH_2CH_3), 4.25 (AB system, δ(A) = 4.68, dd, J(AB) = 12.8 Hz, ^{4}J = 1.4 Hz, 1H, H(3), δ(B) = 3.81, J(BA) = 12.8 Hz, 1H, H(3)), 3.21 (td, ^{3}J = 10.3 Hz and 7.0 Hz, 1H, H(1)), 2.46 (ddm, ^{2}J = 12.9 Hz, ^{3}J = 3.4 Hz, 1H, H(5)), 2.17-1.86, 1.84-1.58, 1.58-1.31, 1.28-1.08 (m, 10H), 0.97 (t, ^{3}J = 7.6 Hz, 3H, CH_2CH_3). MS (mixture of both (*E*)-**13a** and (*Z*)-**13a**): 166 (17, $M^{+\cdot}$), 137 (50), 119 (22), 109 (8), 91 (31), 81 (27), 79 (27), 67 (100), 55 (33).

3α-Ethyl-4-methylene-2-oxabicyclo[4.3.0]nonane 3α-14a.
^{1}H NMR (250 MHz): 4.85 (m, 2H, $=CH_2$), 3.69 (dd, ^{3}J = 6.8 Hz and 5.3 Hz, 1H, H(3)), 3.30 (td, ^{3}J = 10.3 Hz and 7.1 Hz, 1H, H(1)), 2.59 (dd, ^{2}J = 12.8 Hz, ^{3}J(5,6) = 3.8 Hz, 1H, H(5)), 2.07-1.11 (m, 10H, H(5,6,7,8,9), CH_2CH_3), 0.91 (t, ^{3}J = 7.4 Hz, 3H, CH_2CH_3). MS (mixture of both 3α-**14a** and 3β-**14a**): 166 (6, $M^{+\cdot}$), 137 (68), 119 (26), 109 (15), 93 (26), 91 (41), 85 (21), 79 (41), 67 (100), 57 (41), 55 (33).

3β-Ethyl-4-methylene-2-oxabicyclo[4.3.0]nonane 3β-14a.
^{1}H NMR (250 MHz): 4.81 (t, ^{4}J = 2.0 Hz, 1H, $=CH_2$), 4.78 (t, ^{4}J = 1.5 Hz, 1H, $=CH_2$), 4.10 (t, ^{3}J = 7.9 Hz, 1H, H(3)), 3.47 (td, ^{3}J = 10.5 Hz and 7.2 Hz, 1H, H(1)), 2.44 (dd, ^{2}J = 13.2 Hz, ^{3}J(5,6) = 4.0 Hz, 1H, H(5)), 2.17-1.11 (m, 10H, H(5,6,7,8,9), CH_2CH_3), 1.04 (t, ^{3}J = 7.4 Hz, 3H, CH_2CH_3). MS (mixture of both 3α-**14a** and 3β-**14a**): 166 (6, $M^{+\cdot}$), 137 (68), 119 (26), 109 (15), 93 (26), 91 (41), 85 (21), 79 (41), 67 (100), 57 (41), 55 (33).

5α-Ethyl-4-methylene-2-oxabicyclo[4.4.0]decane 5α-11b.
^{1}H NMR (400 MHz): (1) 4.92 (q, ^{4}J = 1.4 Hz, 1H, $=CH_2$), (2) 4.80 (t, ^{4}J = 1.7 Hz, 1H, $=CH_2$), (3) 4.20 (A part of AB system, J(AB) = 11.9 Hz, 1H, H(3)), (4) 4.98 (B part of AB system, J(BA) = 11.9 Hz, 1H, H(3)), (5) 3.10 (td, ^{3}J = 9.8 Hz and 4.1 Hz, 1H, H(1)), 2.06-1.07 (m, 12H, H(5,6,7,8,9,10), CH_2CH_3) [in which: (6) 1.95 (m, 1H, H(10)), (7) 1.86 (m, 1H, H(5)), (8) 1.74 (m, 1H, CH_2CH_3), (9) 1.57 (m, 1H, CH_2CH_3), (10) 1.29 (m, 1H, H(10)), (11) 1.14 (m, 1H, H(6))], (12) 0.92 (t, ^{3}J = 7.4 Hz, 3H, CH_2CH_3). 2D COSY NMR (400 MHz): 1(2,3,4,7), 2(3^W,4^W,7,12^W), 3(4), 4(7), 5(6,8^W,10,11), 6(8,10,11,12), 7(8,9,11), 8(12), 9(12), 11(12). 2D NOESY NMR (400 MHz, τ_m = 2.0 s): 1(2,3), 2(8,9,12), 3(4), 4(5,7^W), 5(7^W), 8(9,12), 9(12), 11(12). MS: 180 (8, $M^{+\cdot}$), 151 (37), 137 (6), 133 (4), 124 (9), 109 (9), 95 (43), 91 (15), 82 (51), 67 (100), 55 (50).

5β-Ethyl-4-methylene-2-oxabicyclo[4.4.0]decane 5β-11b.
^{1}H NMR (400 MHz): (1) 4.86 (t, ^{4}J = 1.8 Hz, 1H, $=CH_2$), (2) 4.74 (d, ^{4}J = 2.1 Hz, 1H, $=CH_2$), (3) 4.08 (A part of AB system, dd, J(AB) = 12.3 Hz, ^{4}J = 1.4 Hz, 1H, H(3)), (4) 4.00 (B part of AB system, J(BA) = 12.3 Hz, 1H, H(3)), (5) 3.35 (td, ^{3}J = 10.1 Hz and 4.4 Hz, 1H, H(1)), (6) 2.13 (dt, ^{3}J = 11.4 Hz and 4.7 Hz, 1H, H(5)), 2.06-1.07 (m, 11H, H(6,7,8,9,10), CH_2CH_3) [in which: (7) 1.95 (m, 1H, H(10)), (8) 1.56 (m, 1H, H(6)), (9) 1.48 (m, 2H, CH_2CH_3), (10) 1.23 (m, 1H, H(10))], (11) 0.80 (t, ^{3}J = 7.3 Hz, 3H, CH_2CH_3). 2D COSY NMR (400 MHz): 1(2,3,4), 2(3,4,6), 3(4,6), 4(6), 5(7,8,10), 6(8,9,10), 9(11). 2D NOESY NMR (400 MHz, τ_m = 2.0 s): 1(2,3^W,4), 2(6,11), 3(4,5,9,11), 4(11), 6(9,11), 9(11). MS: 180 (7, $M^{+\cdot}$), 151 (73), 137 (9), 133 (7), 123 (10), 109 (14), 95 (44), 91 (17), 81 (55), 67 (100), 55 (56).

(*E*)-4-Propylidene-2-oxabicyclo[4.4.0]decane (*E*)-13b.
^{1}H NMR (250 MHz): 5.27 (t, ^{3}J = 7.2 Hz, 1H, =C*H*CH_2CH_3), 4.04 (AB system, δ(A) = 4.08, dd, J(AB) = 12.0 Hz, ^{4}J = 1.6 Hz, 1H, H(3), δ(B) = 3.99, dquintet, J(BA) = 12.0 Hz, ^{4}J = 1.2 Hz, 1H, H(3)), 3.04 (td, ^{3}J = 9.9 Hz and 4.2 Hz, 1H, H(1)), 2.58 (ddd, ^{2}J = 13.5 Hz, ^{3}J = 3.7 Hz, ^{4}J = 1.7 Hz, 1H, H(5)), 2.15-1.99 (m, 2H, CH_2CH_3), 1.99-1.56, 1.44-0.92 (m, 10H), 0.96 (t, ^{3}J = 7.5 Hz, 3H, CH_2CH_3). MS (mixture of both (*E*)-**13b** and (*Z*)-**13b**): 180 (16, $M^{+\cdot}$), 151 (35), 133 (29), 107 (14), 95 (18), 91 (21), 81 (43), 67 (100), 55 (50).

(*Z*)-4-Propylidene-2-oxabicyclo[4.4.0]decane (*Z*)-13b.
^{1}H NMR (250 MHz): 5.19 (t, ^{3}J = 7.2 Hz, 1H, =C*H*CH_2CH_3), 4.20 (AB system, δ(A) = 4.62, dd, J(AB) = 12.4 Hz, ^{4}J = 1.7 Hz,

1H, H(3), δ(B) = 3.77, J(BA) = 12.4 Hz, 1H, H(3)), 3.04 (td, ^{3}J = 9.9 Hz and 4.2 Hz, 1H, H(1)), 2.19 (ddd, ^{2}J = 12.9 Hz, ^{3}J = 3.7 Hz, ^{4}J = 2.5 Hz, 1H, H(5)), 2.15-1.99 (m, 2H, CH_2CH_3), 1.99-1.56, 1.44-0.92 (m, 10H), 0.96 (t, ^{3}J = 7.5 Hz, 3H, CH_2CH_3). MS (mixture of both (*E*)-**13b** and (*Z*)-**13b**): 180 (16, $M^{+\cdot}$), 151 (35), 133 (29), 107 (14), 95 (18), 91 (21), 81 (43), 67 (100), 55 (50).

3α-Ethyl-4-methylene-2-oxabicyclo[4.4.0]decane 3α-14b.
^{1}H NMR (400 MHz): (1) 4.77 (t, ^{4}J = 1.5 Hz, 2H, $=CH_2$), (2) 3.61 (dd, ^{3}J = 7.1 Hz and 4.5 Hz, 1H, H(3)), (3) 3.07 (td, ^{3}J = 10.4 Hz and 4.1 Hz, 1H, H(1)), (4) 2.33 (dd, ^{2}J = 13.2 Hz, ^{3}J(5,6) = 4.0 Hz, 1H, H(5)), (5) 2.08-1.74, (6) 1.74-1.53, (7) 1.40-1.15 (m, 12H, H(5,6,7,8, 9,10), CH_2CH_3), (8) 1.03 (t, ^{3}J = 7.4 Hz, 3H, CH_2CH_3). 2D NOESY NMR (400 MHz, τ_m = 2.5 s): 2(3). MS: 180 (15, $M^{+\cdot}$), 151 (58), 133 (47), 123 (8), 107 (29), 99 (17), 91 (33), 85 (13), 81 (50), 79 (50), 67 (100), 57 (100), 55 (56).

3β-Ethyl-4-methylene-2-oxabicyclo[4.4.0]decane 3β-14b.
^{1}H NMR (400 MHz): (1) 4.74 (t, ^{4}J = 2.1 Hz, 1H, $=CH_2$), (2) 4.72 (t, ^{4}J = 1.9 Hz, 1H, $=CH_2$), (3) 4.04 (t, ^{3}J = 7.9 Hz, 1H, H(3)), (4) 3.26 (td, ^{3}J = 10.1 Hz and 4.2 Hz, 1H, H(1)), (5) 2.16 (dd, ^{2}J = 13.3 Hz, ^{3}J(5,6) = 3.9 Hz, 1H, H(5)), (6) 2.08-1.74, (7) 1.74-1.53, (8) 1.40-1.15 (m, 12H, H(5,6,7,8,9,10), CH_2CH_3), (9) 0.90 (t, ^{3}J = 7.4 Hz, 3H, CH_2CH_3). 2D NOESY NMR (400 MHz, τ_m = 2.5 s): 3(-). MS: 180 (12, $M^{+\cdot}$), 151 (100), 133 (86), 123 (4), 107 (56), 91 (86), 81 (56), 79 (56), 67 (75), 55 (57).

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