Solvent effects on the steric course of the solvolysis of tertiary acyclic derivatives

Paul Müller * and Jean-Claude Rossier

Department of Organic Chemistry, University of Geneva, 30, Quai Ernest Ansermet, CH-1211 Geneva 4, Switzerland

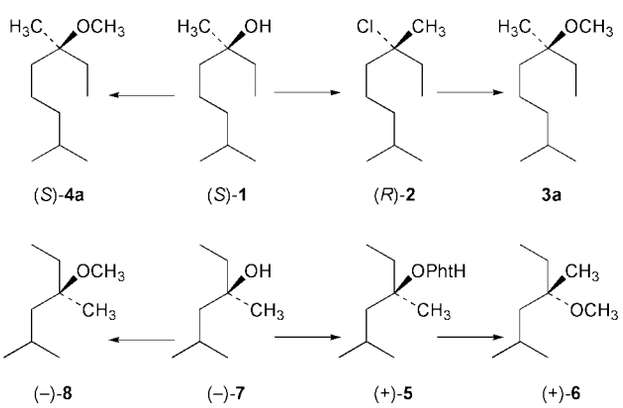
Received (in Cambridge, UK) 19th June 2000, Accepted 30th August 2000
First published as an Advance Article on the web 18th October 2000

The solvolysis of (*R*)-3-chloro-3,7-dimethyloctane (**2**), of the corresponding hydrogen phthalate (*S*)-**4g**, and of the *p*-nitrobenzoate (*S*)-**4h** proceeds with up to 87% inversion of configuration in solvents such as methanol or ethanol. The degree of inversion decreases in more dissociating solvents. In 2,2,2-trifluoroethanol (TFE), up to 40% retention of configuration occurs.

Introduction

The nucleophilic substitution at saturated carbon is traditionally interpreted in terms of two distinct mechanisms, S_N1 and S_N2. The S_N2 pathway exhibits second order kinetics, and is characterized by inversion of configuration at the reacting centre. The stereochemical criterion is unambiguous. In contrast, S_N1 reactions proceed *via* carbenium ions or ion pairs and total or partial loss of stereochemical integrity is observed. Tertiary aliphatic derivatives are generally believed to react by an S_N1 mechanism. A typical textbook example for an S_N1 reaction is the solvolysis of optically active 3-bromo-3-methylhexane in water, which is traditionally believed to proceed with total racemization. This is consistent with a planar carbenium ion as reactive intermediate.[1] However, the experimental evidence reported in the literature does not support this hypothesis.

The steric course of tertiary aliphatic hydrolysis has been investigated in the past by two groups: Ingold and co-workers[2] prepared optically active (*R*)-3-chloro-3,7-dimethyloctane ((*R*)-**2**) from (*S*)-tetrahydrolinalool† (**1**, Scheme 1) and investigated



Scheme 1

its methanolysis at 60 °C. The absolute configuration of **1** was unknown at that time, but has been established since.[3] The reaction afforded the methyl ether **3a** having 34% of the optical activity of the ether **4a** prepared directly *via* methylation of the original alcohol (*S*)-**1**. It was concluded that the reaction proceeded at least with 34% of non-racemizing alcoholysis. The work of Ingold was severely criticized by Doering and Zeiss,[4] because the optical purity of the original chloride was unknown. Doering and Zeiss, in turn, solvolyzed optically active (+)-hydrogen 2,4-dimethyl-4-hexyl phthalate (**5**) of unknown absolute configuration[5] in refluxing MeOH. The reaction proceeded to the corresponding ether (**6**) in 35% yield with 54% inversion of configuration and 46% racemization (equivalent to 77% inversion and 23% retention). The results of both investigations are clearly inconsistent with a free carbenium ion intermediate.

The credibility of both investigations suffers from the inadequate methods available at the time when the experiments were carried out. The enantiomer composition of the solvolysis products was determined from the optical rotations. Unfortunately, the $[a]_D$ values were very low in both experiments: Ingold's chloride **2** had $[a]_D = -0.52$; the rotation of the corresponding methyl ether (*S*)-**4a**, obtained *via* methylation of (*S*)-tetrahydrolinalool, was $[a]_D = -2.03$. The ether **3a** isolated upon methanolysis of **1**, in turn, had $[a]_D = -0.70$. The optical rotation of methyl ether **8** obtained by Doering and Zeiss *via* direct synthesis from optically pure 2,4-dimethylhexan-4-ol (**7**) was −5.85 (calculated from compounds of lower optical purity) and that of the methanolysis product **6** was +2.53. It is nowadays recognized that the determination of optical rotations is not trivial, particularly if the values are small. The results depend critically upon the purity of the samples and upon the experimental conditions.[6] Indeed, the compounds of Ingold and Doering were liquids, and no gas chromatography was available to check their purity. It is not surprising, therefore, that their results met only limited acceptance. The attitude of undergraduate textbooks is typical: some authors accept them fully,[7] while others prefer to simply ignore them.[1] Mechanistic chemists, however, are used to the idea that tertiary aliphatic solvolysis does not proceed *via* free carbenium ions.[8]

We have recently reinvestigated the methanolysis of (*R*)-3-chloro-3,7-dimethyloctane (**2**) at 25 °C using gas chromatography with chiral columns for the determination of the enantiomer composition of the products. Under our conditions, the reaction proceeded with 78% inversion of configuration and 22% racemization, thereby confirming the principal conclusions of the previous investigations.[9] The same methodology has now been extended to reactions of the corresponding hydrogen phthalate (*S*)-**4g** and the *p*-nitrobenzoate (*S*)-**4h**, in solvents of different ionizing power and nucleophilicity.

† The IUPAC name for linalool is 3,7-dimethylocta-4,6-dien-3-ol.

 DOI: 10.1039/b004884o

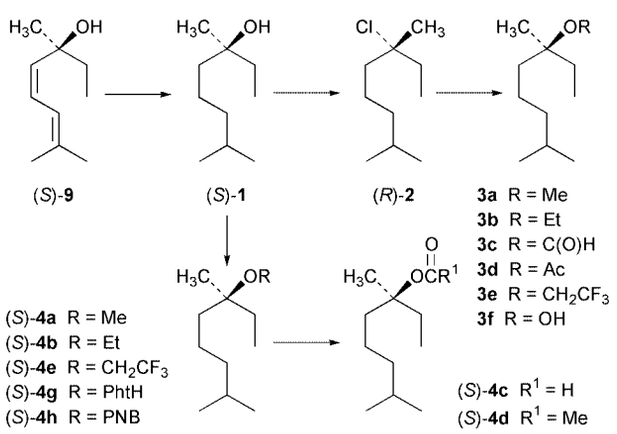
Table 1 Stereochemistry of the solvolysis of (*R*)-3-chloro-3,7-dimethyloctane ((*R*)-**2**, 77.4% ee)

Solvent	Temp./°C (time)	Olefins (%)	Unreacted R–Cl (**2**) (%)	R–X	Yield (%)	[*S*]:[*R*][a]	Ee (%)	Inversion (%)
MeOH, DTBP[b]	25 (3 d)	50	10	**3a**, RO–Me[c]	40	80.1:19.9	60.2	78
EtOH, DTBP[b]	40 (1 d)	30	50	**3b**, RO–Et[d]	20	71.4:28.6	42.8	55
HCOOH, DTBP[b]	0 (1.5 h)	27	30	**3c**, RO–C(O)H	43	66.1:33.9	32.2[f]	42
HCOOH, HCOONa[e]	0 (1.0 h)	20	38	**3c**, RO–C(O)H	41	67.7:32.3	35.4[f]	46
AcOH, DTBP[b]	25 (10 d)	60	32	**3d**, RO–Ac[f]	5	74.0:26.0	48.0	62
TFE, DTBP[b]	25 (4 d)	77	—	**3e**, RO–CH_2CF_3	23	45.7:54.3	−8.6[h]	−13[h]
TFE, RCOONa[g]	25 (5 h)	75	5	**3e**, RO–CH_2CF_3	19	42.5:57.5	−15.0[h]	−22[h]
HFIP, CH_3COONa, 2.0 equiv.	0 (1.0 h)	100	0	RO–$CH(CF_3)_2$	0	—	—	—
t-BuOH (80%), DTBP[b]	25 (4 d)	20	50	**3f**, R–OH	30	68.8:31.2	37.6	49
1,4-Dioxane (80%), DTBP[b]	25 (4 d)	14	50	**3f**, R–OH	36	88.1:11.9	76.2	98

[a] Corrected by response factor of racemic compound (see Table 4). [b] 2.0 Equiv. of 2,6-di-*tert*-butylpyridine added. [c] Enantiomer separation *via* formate. [d] Enantiomer separation *via* acetate. [e] 2.0 Equiv. of HCOONa added. [f] Slow racemization of formate. [g] 2.0 Equiv. of sodium *p*-nitrobenzoate added. [h] R–Cl with 68% ee.

Results

(*R*)-3-Chloro-3,7-dimethyloctane (**2**) was synthesized according to Ingold and co-workers[2] from commercially available linalool (**9**) of 81.2% ee (Scheme 2). Catalytic hydrogenation afforded



Scheme 2

(*S*)-tetrahydrolinalool (**1**)[10] having 78.8% ee. The alcohol was converted to the chloride **2** (77.4% ee) with $SOCl_2$ in the presence of Et_3N.[11] The chloride **2** was configurationally stable at room temperature, but racemized upon exposure to traces of acid. The absolute configuration was determined to be (*R*) on the grounds of the optical rotation {$[\alpha]_D^{20} = -0.49$ (neat, for 77% ee); lit.: $[\alpha]_D^{17} = -0.52$ (neat)[2]}, and from the conversion of a sample of **2** with 65.0% ee back to (*S*)-configured alcohol **1** (44.0% ee) upon exposure to slightly alkaline ($NaHCO_3$) aqueous MeOH. Reference compounds were synthesized starting from racemic and optically enriched alcohol **1** by means of conventional procedures (see the Experimental section). Alkylation of **1** with MeI and EtI produced (*S*)-configured ethers **4a** and **4b**, respectively, which were oxidized with RuO_4[12] to the formate (*S*)-**4c** and acetate (*S*)-**4d**. The (*S*)-configured trifluoroethyl ether R–OCH_2CF_3 (**4e**), in turn, was synthesized *via* attack by the OH of **1** on CF_3CHN_2.[13] The hydrogen phthalate (*S*)-**4g** and the *p*-nitrobenzoate (*S*)-**4h**[14] were synthesized by conventional procedures. The enantiomer composition of **4g** was determined *via* its LAH reduction back to (*S*)-**1** of 76.8% ee. The enantiomers of **4h** were separable by HPLC.

The solvolysis reactions of the chloride (*R*)-**2** were carried out on a 20 mg scale in 1.0–2.0 mL of solvent containing 2.0 equiv. of 2,6-di-*tert*-butylpyridine (DTBP) or, in the case of HCOOH and TFE, 2.0 equiv. of HCOONa or sodium *p*-nitrobenzoate (NaOPNB), respectively. The reactions were allowed to proceed to 50–100% completion. The amount of unreacted **2** is indicated in Table 1 (column 4). Racemization of **2** was negligible under the conditions of the reactions. The reaction mixtures were analysed by GC, and the products **3a**–**f** were identified by comparison of their retention times with those of independently prepared samples. GC-MS analysis of all runs revealed the presence of four isomeric olefins in approximately constant proportions which were not further analysed (column 3). The solvolysis products were configurationally stable under the conditions of solvolysis of the chloride, except the formate ester **3c** which racemized slowly at 0 °C, and totally at 25 °C in formic acid within 1 h. The possibility of partial racemization of the solvolysis products **3** occurring *via* solvent addition to putative intermediate olefins was tested by exposing the mixture of olefins, obtained *via* dehydrohalogenation of **2**, to the reaction conditions. The product composition underwent no change, and no addition products were observed.

The enantiomers of the substitution products **3c**–**f** were separated by GC, and those of **3a**,**b** were separated after conversion to **3c**,**d** with RuO_4. Enantiomer separation was reproducible to *ca*. 2%, except with the acetate **3d**, where the estimated error was *ca*. 5%. The absolute configuration of the major enantiomer of the solvolysis products **3** was (*S*), identical with that of the reference compounds **4**, except in the case of **3e** where the major enantiomer had (*R*)-configuration. In all of the solvents investigated, except TFE, the reaction proceeded with a substantial degree of inversion of configuration. In the nucleophilic solvents such as MeOH and EtOH inversion reached 78 and 55%, respectively. In the mixed solvents inversion of the isolated alcohol **3f** was 38% in 80% *tert*-BuOH and 98% in 80% 1,4-dioxane. In this latter solvent, initial nucleophilic attack by 1,4-dioxane and subsequent reaction of the intermediate oxonium ion with water would result in overall retention of configuration,[15] but no evidence for this competing double displacement was found. No substitution products were observed in the more dissociating and still less nucleophilic solvent, 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP) where, depending upon the reaction conditions, **2** underwent racemization or reacted exclusively by elimination. In 2,2,2-trifluoroethanol (TFE) we observed a small and variable amount, depending upon the reaction conditions, of 11 to 18% of retention of configuration with **2**.

The solvolysis reactions of **4g** and **4h** were effected in a similar way to those of **2** and the same control experiments were carried out. Samples of **4h** with ee values in the range of 74–92% were used. Reactions in low-boiling solvents (MeOH, EtOH) were carried out in sealed ampoules. The results are summarized in Tables 2 and 3. In MeOH, EtOH and AcOH the main enantiomer of the substitution product **3** had (*R*)-

Table 2 Solvolysis of hydrogen (*S*)-3,7-dimethyl-3-octyl phthalate ((*S*)-**4g**, 76.8% ee)

Solvent	Temp./°C (time)	Olefins (%)	ROPtH, **4g** (%)	R–X	Yield (%)	[*S*]:[*R*][a]	Ee (*R*) (%)	Inversion (%)
MeOH	65 (5 d)	57	29	**3a**, R–OMe[c]	14	16.6:83.4	66.8	87
MeOH/Ph(COONa)$_2$[b]	65 (5 d)	56	26	**3a**, R–OMe[c]	18	17.3:82.7	65.4	85
EtOH/Ph(COONa)$_2$[b]	80 (5 d)	51	28	**3b**, RO–Et[d]	21	17.8:82.2	64.4	83
HCOOH, DTBP[e]	25 (2 h)	20	20	**3c**, R–OC(O)H	48	49.8:50.2	0.4[f]	—
HCOOH, Ph(COONa)$_2$[b]	25 (24 h)	22	—	**3c**, R–OC(O)H	63	48.4:51.6	3.2[f]	—
AcOH, DTBP[e]	60 (24 h)	52	40	**3d**, R–OAc	8	35.6:64.4	28.8	38
AcOH, Ph(COONa)$_2$[b]	60 (24 h)	57	29	**3d**, R–OAc	16	33.1:66.9	33.8	44
TFE, DTBP[e]	73 (24 h)	88	—	**3e**, R–OCH$_2$CF$_3$	12	55.0:45.0	−10.0	−13
TFE, Ph(COONa)$_2$[b]	73 (24 h)	81	—	**3e**, R–OCH$_2$CF$_3$	21	56.8:43.2	−12.6	−16

[a] Corrected by response factor of racemic compound (see Table 4). [b] 2.0 Equiv. of Ph(COONa)$_2$ added. [c] Enantiomer separation *via* formate. [d] Enantiomer separation *via* acetate. [e] 2.0 Equiv. of 2,6-di-*tert*-butylpyridine added. [f] Slow racemization of formate.

Table 3 Solvolysis of (*S*)-3,7-dimethyl-3-octyl *p*-nitrobenzoate (*S*)-**4h**

Ee **4h** (%)	Solvent	Temp./°C (time)	Olefins (%)	ROPNB **4h** (%)	R–X	Yield (%)	[*S*]:[*R*][a]	Ee (*R*) (%)	Inversion (%)
85	MeOH, DTBP[b]	85 (10 d)	60	21	**3a**, R–OMe[c]	19	17.5:82.5	65.0	76
85	MeOH, *p*-NO$_2$C$_6$H$_4$COONa[d]	85 (6 d)	39	40	**3a**, R–OMe[c]	21	20.0:80.0	60.0	71
85	EtOH, DTBP[b]	80 (10 d)	28	63	**3b**, R–OEt[e]	9	16.6:83.4	66.8	79
85	HCOOH, DTBP[b]	25 (24 h)	27	—	**3c**, RO–C(O)H	65	50.8:49.2	−2.0[f]	−2
92	HCOOH, *p*-NO$_2$C$_6$H$_4$COONa[d]	25 (24 h)	31	—	**3c**, RO–C(O)H	60	49.5:50.5	1.0[f]	1
85	AcOH, DTBP[b]	70 (20 h)	52	42	**3d**, RO–Ac	6	44.5:55.5	12.9	15
85	AcOH, *p*-NO$_2$C$_6$H$_4$COONa[d]	70 (20 h)	39	52	**3d**, RO–Ac	9	44.8:55.2	10.4	12
74	TFE, DTBP[b]	73 (3 d)	66	—	**3e**, RO–CH$_2$CF$_3$	34	35.0:65.0	−30.0	−40
74	TFE, *p*-NO$_2$C$_6$H$_4$COONa[d]	73 (4 d)	76	—	**3e**, RO–CH$_2$CF$_3$	24	39.3:60.7	−21.4	−29

[a] Corrected by response factor of racemic compound (see Table 4). [b] 2.0 Equiv. of 2,6-di-*tert*-butylpyridine added. [c] Enantiomer separation *via* formate. [d] 2.0 Equiv. NaOPNB added. [e] Enantiomer separation *via* acetate. [f] Slow racemization of formate.

configuration. Inversion of more than 80% was observed with **4g**, while reactions of the OPNB derivative **4h** gave somewhat lower selectivity. Total racemization occurred in formic acid with both leaving groups. However, this observation is not conclusive, since formate racemization was faster than the solvolysis reaction. Partial racemization in slightly different proportions occurred in AcOH. Retention of configuration in TFE increased to *ca*. 15% with the hydrogen phthalate **4g** and to 30–40% with the OPNB derivative **4h**.

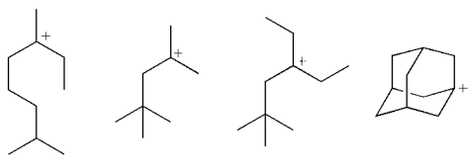
Discussion

The observation of 78% inversion of configuration upon methanolysis of the chloride (*R*)-**2** in MeOH at 25 °C differs somewhat from the 34% reported by Ingold[2] (at 60 °C). The 86% inversion observed upon methanolysis of **4g** is also higher than the 54% determined for hydrogen 3,5-dimethyl-3-hexyl phthalate (**5**) under comparable conditions. The discrepancy in the case of **2** may be ascribed to the differences of reaction temperature and to experimental uncertainties in the determination of the optical rotation of the samples. In the case of the **4g** it may be due, in addition, to its lower degree of steric hindrance owing to the larger distance of the methyl group at C(7) from the reacting carbon atom in comparison to that in **5**. Despite these discrepancies, our overall results are consistent with those of the previous authors. Although we have been critical of the methods they used, we confirm their conclusion that the solvolysis of tertiary aliphatic derivatives does not proceed with total racemization to free carbenium ions in conventional solvents. These reactions do not meet the traditional criteria for simple S_N1 processes.[8]

The degree of inversion of configuration increases in MeOH and EtOH in going from the chloride **2** to the hydrogen phthalate **4g**, but comparison with the data obtained for the OPNB derivative **4h** does not reveal a clear trend. The fraction of inversion decreases in the less nucleophilic solvents for the chloride **2**, but only a very crude correlation is obtained between the degree of inversion and the solvent nucleophilicity parameter *N*.[16] In the case of **4g** and **4h** we observe a sharp increase of racemization in AcOH and total racemization in HCOOH.

The occurrence of inversion of configuration during aliphatic nucleophilic substitution may be ascribed either to solvent attack on the substrate or to attack on an intermediate intimate ion pair.[17] Solvent attack on the substrate is an S_N2 reaction and should result in rate enhancement owing to nucleophilic solvent participation (NSP).[18] NSP should also be observable if solvent attack on the ion pair occurs in the rate-controlling step, but the observation of configurational inversion does not necessarily imply NSP. The possible involvement of NSP in the solvolysis of **2** may be assessed from data in the literature: the rate constant for unassisted solvolysis of tertiary derivatives is extrapolated from the correlation between rates of solvolysis of bridgehead derivatives (under standard conditions) and the stability of bridgehead carbenium ions in the gas phase, which has been reported recently (log $k = 0.441\Delta G^\circ + 0.50$).[19] Rate data for the solvolysis of **2** have been determined in 80% aq. acetone ($k = 1.58 \times 10^{-4}$ s^{-1}, 60 °C) and MeOH ($k = 2.74 \times 10^{-4}$ s^{-1}, 60 °C). Extrapolation to standard conditions (80% EtOH, 70 °C) gives a rate of log $k = 3.2$ relative to that of 1-chloroadamantane (see the Experimental section). This extrapolated value appears plausible in the light of log $k = 3.58$ for solvolysis of 3-methyl-3-pentyl and log $k = 3.37$ for 2-methyl-2-butyl halides under standard conditions (relative to 1-adamantyl).[19] The stability of the 2,6-dimethyl-6-octyl cation **10** is not known, but can be extrapolated from the data for similar ions **11** and **12**, respectively, which may be considered the next higher and next lower homologues of **10** and are 4.9 and 7.6 kcal mol^{-1} more stable than the adamantyl cation (**13**) according to eqn. (1).[20]

$$R^+(g) + Ad\text{–}Cl(g) \longrightarrow R\text{–}Cl(g) + Ad^+(g) \qquad (1)$$



rel. stability	**10**	**11**	**12**	**13**
kcal mol^{-1}	–6.3	–4.9	–7.6	0.0

Fig. 1

To a first approximation, the stability of cations having common structural features is a linear function of the logarithm of the number of atoms.[21] Accordingly, by extrapolation the stability of **10** is −6.3 kcal mol^{-1} (Fig. 1).

With these data the calculated rate for unassisted solvolysis of **2** is 3.3, even higher than the experimental (although extrapolated) rate constant of 3.2. Therefore, these data provide no support for NSP in the solvolysis of **2**. Unfortunately, the present considerations are subject to considerable uncertainties owing to the various approximations and extrapolations required for generation of the data. They are, however, consistent with recent kinetic studies of Takeuchi and others on tertiary aliphatic solvolysis:[20,22] NSP vanishes in extremely congested systems and in systems where positive charge at the reacting centre is stabilized. The neutral precursors of **11** and **12** are only marginally accelerated by NSP in comparison to *tert*-butyl, and the same should apply to **2**. However, since a rate enhancement by a factor of 10 due to NSP may already produce 90% inversion of configuration, the present data do not allow a final conclusion as to whether inversion of configuration upon solvolysis of **2** is due to solvent attack on **2** itself, or on the intimate ion pair. In the light of the results of Takeuchi, **2** is not an ideal substrate and the stereochemical course of its solvolysis should be compared with a substrate for which NSP is clearly established. Investigations in this direction are currently in progress in our laboratory.

Retention of configuration may be caused by electrophilic solvent catalysis.[23] The departure of the leaving group may be assisted by hydrogen bonding to the solvent, and this will result in an ion pair having a solvent molecule in close proximity to the leaving group. Breakdown of this intermediate may occur with preferential incorporation of this solvent molecule rather than of bulk solvent. The fraction of retention of **2** and **4g** is similar, but increases to 30–40% with the OPNB derivative **4h**. Apparently, electrophilic catalysis by the solvent is more important for the less reactive OPNB leaving group than for Cl. In the case of **4g**, however, the carboxylic acid may participate in intramolecular electrophilic catalysis, and thereby, provide a competitive pathway to solvent catalysis. Retentive solvolysis of tertiary aliphatic derivatives in phenol and phenol–benzene mixtures has been ascribed to a 4-centre mechanism involving a solvent molecule attached to the leaving group by hydrogen bonding.[24]

Experimental

General

For general procedures see ref. 25.

Synthesis of 3,7-dimethyl-3-octyl derivatives

Tetrahydrolinalool (*S*)-1.[10] Commercial (*R*)-(−)-linalool (**9**) (Fluka, $[a]_D^{20} = -16.3$ (neat, for 81.2% ee) (10.0 g, 65 mmol)) in EtOH (120 mL) was hydrogenated in the presence of Pd/C (10%, 200 mg) at room temperature and ambient pressure for 3 h. The mixture was then filtered through Celite and the solvent was evaporated. The crude product was distilled (92 °C/15 Torr) to afford (*S*)-**1** (8.70 g, 85%). $[a]_D^{20} = -0.6$ (neat, for 78.8% ee); lit.:[26] $[a]_D^{27} = -0.59$ (neat). IR ($CHCl_3$): 3603s, 2953s, 1460s, 1379s cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 1.55–1.15 (m, 10H), 1.14 (s, 3H), 0.89 (t, $J = 7.2$, 3H), 0.87 (d, $J = 6.8$, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): 72.9 (s), 41.6 (t), 39.6 (t), 34.2 (t), 27.9 (d), 26.3 (q), 22.6 (q), 12.6 (t), 8.1 (q). MS: 158 (absent, M^+) , 129 (26), 111 (23), 73 (100), 69 (88%).

(*R*)-3-Chloro-3,7-dimethyloctane [(*R*)-2]. To (*S*)-tetrahydrolinalool (**1**, 2.50 g, 12.6 mmol) in CH_2Cl_2 (30 mL) containing Et_3N (8.0 mL, 114 mmol) was added at −78 °C and under Ar, $SOCl_2$ (3.0 mL, 41 mmol) dropwise. The mixture was allowed to reach room temperature within 2 h, and stirring was continued for 3 h. The solvent was evaporated at 50 Torr, the residue dissolved in pentane, filtered and the solvent was evaporated. The crude product (1.4 g) was purified by bulb-to-bulb distillation (100 °C/15 Torr) to afford 1.20 g (54%) of **2**, $[a]_D = -0.5$ ($c = 41.8$, hexane, for 77.4% ee). Lit.:[2] $[a]_D^{17} = -0.52$ (neat); lit.:[3b] $[a]_D^{23} = -0.42$ (neat). IR ($CHCl_3$): 2947s, 1460s, 1379s cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 1.81–1.18 (m, 9H), 1.51 (s, 3H), 1.20 (t, $J = 14.8$, 3H), 0.90 (d, $J = 6.8$, 6H). ^{13}C NMR ($CDCl_3$): 75.6 (s), 43.9 (t), 39.1 (t), 36.8 (t), 29.3 (d), 27.9 (q), 22.6 (q), 22.5 (t), 9.1 (q). MS: 178 (absent, M^+), 140 (12), 111 (31), 91 (28), 70 (100), 55 (92).

(*S*)-3-Methoxy-3,7-dimethyloctane (4a). To NaH (400 mg, 10 mmol) in dry THF (20 mL) was added (*S*)-**1** (1.0 g, 6.3 mmol) in MeI (0.26 mL, 4.2 mmol) dropwise under Ar.[26] After 16 h stirring at 25 °C, the mixture was decomposed with H_2O (20 mL), saturated NaCl (20 mL) and ether (40 mL). The layers were separated, and the solvent was dried ($MgSO_4$) and evaporated. The crude product was purified by bulb-tube distillation (70 °C/10 Torr). Yield of **4a**, 685 mg (63%). $[a]_D^{20} = -2.7$ ($c = 56.6$, $CHCl_3$ for 78% ee); lit.:[10] $[a]_D^{23} = -1.72$ (neat). IR ($CHCl_3$): 2928s, 1480s cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 3.15 (s, 3H), 1.55–1.15 (m, 9H), 1.08 (s, 3H), 0.88 (d, $J = 6.4$, 6H), 0.84 (t, $J = 7.4$, 3H). ^{13}C NMR (100 MHz): 48.7 (q), 39.7 (t), 37.3 (t), 29.8 (t), 28.0 (d), 22.6 (q), 22.2 (q), 21.3 (t), 7.9 (q). MS: 172 (absent, M^+), 125 (17), 123 (13), 111 (33), 97 (53), 57 (100).

(*S*)-3-Ethoxy-3,7-dimethyloctane (4b). Compound **4b** was prepared by the procedure described for **4a** from **1** and EtI.[26] Yield 47%. $[a]_D^{20} = -1.6$ ($c = 25$, $CHCl_3$ for 80.0% ee). IR ($CHCl_3$): 2971s, 1460s, 1067s cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 3.33 (q, $J = 7.9$, 2H), 1.57–1.14 (m, 9H), 1.10 (s, 3H), 0.88 (d, $J = 6.6$, 6H), 0.85 (t, $J = 7.2$, 3H). ^{13}C NMR (100 MHz): 55.6 (t), 39.6 (t), 37.7 (t), 30.2 (t), 27.8 (d), 22.8 (q), 22.6 (q), 21.2 (t), 16.0 (q), 7.8 (q). MS: 186 (absent, M^+), 171 (1), 143 (5), 111 (2), 71 (100). HRMS: 171.1748 ($C_1H_{23}O^{+\bullet}$; calc. 171.1749); 157.1606 ($C_{11}H_{21}O^{+\bullet}$; calc. 157.1592); 143.1441 ($C_9H_{19}O^{+\bullet}$; calc. 143.1436).

(*S*)-3,7-Dimethyl-3-octyl formate (4c). To **4a** (86 mg, 0.5 mmol) in CCl_4 (1.0 mL), CH_3CN (1.0 mL) and H_2O (1.5 mL) was added $RuCl_3 \cdot xH_2O$ (5.0 mg, 0.01 mmol) followed by $NaIO_4$ (214 mg, 1 mmol) in portions in 2 h.[12] The mixture was stirred for 24 h. H_2O (10 mL) and CH_2Cl_2 (20 mL each) were added; the layers were separated, and the solvent was dried and evaporated *in vacuo*. Flash chromatography (SiO_2, petroleum ether–EtOAc 19:1) afforded **4c** (43 mg, 46%). $[a]_D^{20} = -4.5$ ($c = 4.4$, hexane for 83.6% ee). IR ($CHCl_3$): 2955s, 1711s cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): 8.06 (s, 1H), 1.85–1.07 (m, 9H), 1.44 (s, 3H), 0.90 (t, $J = 7.2$, 3H), 0.88 (d, $J = 6.6$, 6H). ^{13}C NMR (100 MHz): 160.5 (d), 86.6 (s), 39.2 (t), 38.5 (t), 31.3 (t), 27.9 (d), 23.6 (q), 22.6 (q), 21.3 (q), 7.9 (q). MS: 186 (absent, M^+), 157 (1), 141 (6), 140 (24), 111 (39), 70 (80), 55 (100). HRMS: 140.1559 ($C_1H_{20}^{+\bullet}$; calc. 140.1565).

(*S*)-3,7-Dimethyl-3-octyl acetate (4d). The oxidation procedure described for **4c** was applied to **4b** (150 mg) and afforded

Table 4 Separation and correlation of reference compounds

No.	Compound	Source	Separation	Retention time (*S*)/min	Retention time (*R*)/min	[*S*]/[*R*]	Ee
rac-**1**	*rac*-R–OH	*rac*-Linalool (**9**)	A[a]	16.52	16.88	49.9 : 50.1	
(*S*)-**1**	(*S*)-R–OH	(*R*)-Linalool (**9**)	A[a]	16.51	16.88	89.4 : 10.6[b]	78.8
(*S*)-**1**	(*S*)-R–OH	(*S*)-R–OPNB (**4h**)	A[a]	16.45	16.96	88.7 : 11.3[b]	77.4
(*S*)-**1**	(*S*)-R–OH	(*S*)-R–OPhtH (**4g**)	A[a]	16.53	16.91	88.4 : 11.6[b]	76.8
rac-**2**	*rac*-R–Cl	*rac*-R–OH (**1**)	B[c]	29.88	29.66	50.4 : 49.6	
(*R*)-**2**	(*R*)-R–Cl	(*S*)-R–OH (**1**)	B[c]	29.95	29.71	11.3 : 88.7[b]	−77.4
rac-**4c**	*rac*-R–OC(O)H	*rac*-R–OMe (**4a**)	A[a]	19.44	19.62	49.1 : 50.9	
(*S*)-**4c**	(*S*)-R–OC(O)H[d]	(*S*)-R–OMe (**4a**)	A[a]	19.48	19.96	90.0 : 10.0[b]	80.0
rac-**4d**	*rac*-R–OAc	*rac*-R–OH (**1**)	A[a]	19.86	19.48	52.1 : 47.9	
rac-**4d**	*rac*-R–OAc	*rac*-R–OEt (**4b**)	A[a]	19.88	19.48	52.1 : 47.9	
(*S*)-**4d**	(*S*)-R–OAc[d]	(*S*)-R–OEt (**4b**)	A[a]	19.65	19.49	92.4 : 07.6[b]	83.6
rac-**4e**	*rac*-R–OCH_2CF_3	*rac*-R–OH (**1**)	A[a]	9.97	10.16	51.4 : 48.6	
(*S*)-**4e**	(*S*)-R–OCH_2CF_3[e]	(*S*)-R–OH (**1**)	A[a]	9.97	10.17	90.0 : 10.0	80.0
rac-**4h**	*rac*-R–OPNB	*rac*-R–OH (**1**)	C[f]	24.87	21.13	49.1 : 50.9	
(*S*)-**4h**	(*S*)-R–OPNB	(*S*)-R–OH (**1**)	C[f]	24.87	21.13	88.9 : 11.1[b]	77.8
(*R*)-**9**	(*R*)-Linalool	Fluka	D[g]	20.74	22.68	0.94 : 90.6	81.2

[a] GC; Betadex 120; 5 min at 80 °C, then 1 °C min^{-1} to 180 °C. [b] Corrected by response factor of racemic compound. [c] GC; Gammadex 120; 20 min at 60 °C, then 1 °C min^{-1} to 180 °C. [d] *Via* oxidation. [e] *Via* carbenoid insertion. [f] HPLC; CHIRACEL OJ, hexane–propan-2-ol 99 : 1; 0.5 mL min^{-1}. [g] HPLC, CHIRAPAK AD, hexane–propan-2-ol 99 : 1.

4d (84 mg, 50%). $[\alpha]_D^{20} = -3.5$ ($c = 4.4$, hexane, for 83.6% ee). IR ($CHCl_3$): 2955s, 1716s, 1456s, 1363s, 1260s cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): 1.98 (s, 3H), 1.84–1.06 (m, 9H), 1.38 (s, 3H), 0.87 (d, $J = 5.6$, 6H), 0.86 (t, $J = 7.6$, 3H). ^{13}C NMR (125 MHz):[27] 170.4 (s), 85.2 (s), 39.2 (t), 38.3 (t), 30.8 (t), 27.8 (d), 23.3 (q), 22.6 (q), 22.4 (q), 21.3 (t), 8.0 (q). MS: 200 (absent, M^+), 185 (17), 149 (26), 140 (3), 111 (15), 57 (100), 55 (44). HRMS: 185.1587 ($C_{11}H_{21}O_2^{+\bullet}$; calc. 185.1542).

(*S*)-3-(2,2,2-Trifluoroethoxy)-3,7-dimethyloctane (4e). $NaNO_2$ (0.60 g, 8.7 mmol) in H_2O (3.0 mL) was added dropwise to $CF_3CH_2NH_2 \cdot HCl$ (1.0 g, 7.4 mmol). The resulting gaseous CF_3CN_2[13] was transferred by means of a gas inlet to a flask containing **1** (100 mg, 0.63 mmol), $Rh_2(OAc)_4$ (25 mg, 0.056 mmol) and 4 Å molecular sieves (100 mg) in CH_2Cl_2 under Ar. After 16 h stirring, the mixture was filtered, and the filtrate was concentrated. Flash chromatography (SiO_2, petroleum ether–EtOAc 10 : 1) afforded 39 mg (26%) of **4e**. $[\alpha]_D^{20} = -1.4$ ($c = 1.0$, $CHCl_3$ for 80.0% ee). IR ($CHCl_3$): 2953s, 1746m, 1278s, 1175s cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): 3.67 (q, $J = 8.8$, 2H), 1.57–1.14 (m, 9H), 1.14 (s, 3H), 0.88 (d, $J = 6.6$, 6H), 0.87 (t, $J = 7.6$, 3H). ^{13}C NMR (125 MHz): 78.8 (s), 59.9 (t), 39.5 (t), 37.5 (t), 30.2 (t), 27.9 (d), 22.6 (q), 22.3 (q), 21.1 (t), 7.7 (q). ^{19}F NMR (375 MHz): 89.35 (t, $J = 6.4$). MS: 240 (absent, M^+), 225 (2), 211 (10), 155 (100), 111 (13), 69 (68), 55 (34). HRMS: 225.1468 ($C_{11}H_{20}OF_3^{+\bullet}$; calc. 225.1466); 211.1307 ($C_1H_{18}OF_3^{+\bullet}$; calc. 211.1310); 155.0676 ($C_9H_9F_2^{+\bullet}$; calc. 155.0672).

(*S*)-3,7-Dimethyl-3-octyl hydrogen phthalate (4g). To **1** (5.00 g, 31.6 mmol) in toluene (100 mL) was added potassium (1.23 g, 31.6 mmol). The mixture was heated at 100 °C (2 h) until the potassium was consumed.[28] Phthalic anhydride (4.80 g, 32.4 mmol) was added in portions at 100 °C in 10 min. After 16 h the mixture was cooled, poured on ice, and the layers were separated. The organic phase was extracted with saturated $NaHCO_3$, the extract treated with conc. HCl and reextracted with ether. After the usual work-up, the crude product was purified by flash chromatography (SiO_2, petroleum ether–EtOAc 7 : 3) and yielded 7.9 g (82%) of **4g** as a colourless oil. $[\alpha]_D^{20} = 2.0$ ($c = 2.9$, $CHCl_3$ for 76.8% ee). IR ($CHCl_3$): 3500s, 2956s, 1701s, 1298s cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): 7.87 (dd, $J = 7.4$, 1.6, 1H), 7.70 (dd, $J = 7.5$, 1.3, 1H), 7.56–7.52 (m, 2H), 2.01–1.15 (m, 9H), 1.57 (s, 3H), 0.94 (t, $J = 7.6$, 3H), 0.86 (d, $J = 6.6$, 6H). ^{13}C NMR (125 MHz): 172.7 (s), 166.9 (s), 134.4 (s), 131.8 (d), 130.5 (d), 130.2 (s), 129.7 (d), 128.9 (d), 88.0 (s), 39.20 (t), 39.9 (t), 30.9 (t), 27.8 (s), 22.9 (q), 22.6 (q), 21.4 (t), 8.1 (q). MS: 306 (absent, M^+), 167 (9), 149 (35), 140 (51), 111 (18), 83 (53), 70 (100), 55 (97). HRMS: 221.0799 ($C_{12}H_{13}O_4^{+\bullet}$; calc. 221.0814); 167.0337 ($C_8H_7O_4^{+\bullet}$; calc. 167.0344); 140.1564 ($C_{10}H_{20}^{+\bullet}$; calc. 140.1565).

(*S*)-3,7-Dimethyl-3-octyl *p*-nitrobenzoate (4h). To the alcohol **1** (3.00 g, 18.9 mmol) in pyridine (30 mL) was added *p*-nitrobenzoyl chloride (4.00 g, 22 mmol) in portions within 1 h. The mixture was stirred for 3 d at room temperature, then poured into water (100 mL) and extracted with CH_2Cl_2 (2 × 50 mL). The solvent was washed with saturated $NaHCO_3$, dried ($MgSO_4$) and evaporated. Purification by flash chromatography (SiO_2, petroleum ether–EtOAc 4 : 1) afforded 5.1 g (88%) of **4h** with 78% ee. Three recrystallizations (petroleum ether, −25 °C) afforded **4h** with 92% ee, mp 40 °C. $[\alpha]_D^{20} = -0.7$ ($c = 11.6$, $CHCl_3$ for 92% ee). IR ($CHCl_3$): 2945s, 1711s, 1608s, 1525s, 1460s, 1348s, 1284s cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): 8.27 (d, $J = 9.9$, 2H), 8.14 (d, $J = 8.2$, 2H), 2.07–1.20 (m, 9H), 1.57 (s, 3H), 0.92 (t, $J = 7.4$, 3H), 0.86 (d, $J = 5.7$, 6H). ^{13}C NMR (125 MHz): 163.5 (s), 150.2 (s), 137.4 (s), 130.4 (d), 123.4 (d), 87.7 (s), 39.2 (t), 38.0 (t), 31.0 (t), 27.7 (d), 23.3 (q), 22.5 (q), 21.4 (t), 8.1 (q). MS: 307 (absent, M^+), 222 (6), 150 (100), 140 (27), 111 (14), 70 (59), 55 (45). HRMS: 278.1391 ($C_{15}H_{20},O_4N^{+\bullet}$; calc. 278.1392); 222.0763 ($C_{11}H_{12}O_4N^{+\bullet}$; calc. 222.0766).

Solvolysis of (*R*)-3-chloro-3,7-dimethyloctane [(*R*)-2]

The chloride **2** (17.6 mg, 0.10 mmol) was added to the appropriate solvent (1.00 mL) containing 2,6-di-*tert*-butylpyridine (45 µl, 0.20 mmol) at room temperature under Ar. After the appropriate time, the solvent was evaporated at 50 Torr, the residue was diluted to 5.0 mL with CH_2Cl_2 and the product mixture was analysed by GC with an external standard. When formic acid or acetic acid was used as solvent, the reaction mixture was neutralized with $NaHCO_3$ and extracted with CH_2Cl_2. The product mixtures containing the ethers **3a** and **3b**, respectively, were evaporated and subjected to bulb-to-bulb distillation (100 °C/15 Torr). The distillate was oxidized with RuO_4 to **3c** and **3d**, respectively, as described above. For results of chloride solvolysis, see Table 1. Details of the separation of the reaction products **3** and reference compounds **4**, as well as response factors, are summarized in Table 4.

Solvolysis of hydrogen (*S*)-3,7-dimethyl-3-octyl phthalate (4g)

The hydrogen phthalate (30 mg, 0.10 mmol) was stirred under Ar in the appropriate solvent as indicated in Table 2. After the reaction, the mixture was diluted to 5.0 mL, and the product composition was determined by GC with an external standard. Unreacted **4g** was isolated after evaporation of the volatiles and chromatography. The ee of the ethers **3a** and **3b** was determined after their oxidation to **4c** and **4d**, respectively.

Solvolysis of (*S*)-3,7-dimethyl-3-octyl *p*-nitrobenzoate (4h)

The procedure was identical to that used for **4g**. The reactions in MeOH at 85 °C were carried out in sealed tubes confined in an autoclave.

Test for solvent addition to intermediate olefins

The chloride **2** (90 mg) was dehydrohalogenated by heating in AcOH (0.5 mL) at 80 °C for 3 d. A mixture of 4 isomeric olefins ($C_{10}H_{20}$) in a ratio of 27 : 18 : 24 : 31 was isolated in 75% yield. This mixture was exposed to AcOH buffered with NaOAc (65 °C, 24 h), HCOOH buffered with HCOONa (25 °C, 24 h), and TFE buffered with NaOPNB (65 °C, 24 h). GC analysis of the reaction mixture revealed no addition products, and the isomer composition was unchanged. Similarily, no addition products were formed upon exposure of 2-methylpent-2-ene to MeOH (85 °C, 24 h) and EtOH (reflux, 24 h).

Extrapolation of rate constants

The rate constant for solvolysis of **2** in 80% acetone at 60 °C is $k = 1.58 \times 10^{-4}$ s^{-1} and in MeOH is $k = 2.74 \times 10^{-4}$ s^{-1}. The rate constant for solvolysis of 1-chloroadamantane in 80% EtOH at 60 °C (log $k = -6.0$) was obtained by means of the Arrhenius equation from data at other temperatures.[18b] Application of a correction for solvent change to MeOH ($Y_{Cl} = -1.2$, 25 °C) and 80% acetone ($Y_{Cl} = -0.8$, 25 °C), respectively, gives −7.1 and −6.7. Thus the relative rate constant of **2** is log $k = 3.7$ in MeOH, and log $k = 2.9$ in 80% acetone with an average value of log $k = 3.3$. Extrapolation to 70 °C affords a relative rate of log $k = 3.2$.

Acknowledgements

This work was supported by the Swiss National Science Foundation (Grants Nos. 20-52581.97 and 2027-048156) and by the University of Geneva. The authors are indebted to Professors Ken'ichi Takeuchi and J.-L. M. Abboud, for communication of their results prior to publication.

References

1 (*a*) K. P. C Vollhardt and N. E. Schore, *Organic Chemistry*, 3rd edn., W. H. Freeman, New York, 1998; (*b*) H. Hart and J.-M. Conia, *Introduction à la Chimie Organique*, Masson, Paris, 1997.
2 E. D. Hughes, C. K. Ingold, R. J. L. Martin and D. F. Meigh, *Nature*, 1950, **166**, 679.
3 (*a*) G. Ohloff and R. Klein, *Tetrahedron*, 1962, **18**, 37; (*b*) P. E. Verkade, K. S. de Vries and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, 1964, **83**, 367.
4 W. v. E. Doering and H. H. Zeiss, *J. Am. Chem. Soc.*, 1953, **75**, 4733.
5 W. v. E. Doering and H. H. Zeiss, *J. Am. Chem. Soc.*, 1948, **70**, 3966; W. v. E. Doering and H. H. Zeiss, *J. Am. Chem. Soc.*, 1950, **72**, 147.
6 E. L. Eliel and S. H. Wilen, *Stereochemistry of Organic Compounds*, J. Wiley and Sons, New York, 1993; G. Helmchen, R. W. Hofmann, J. Mulzer and E. Schaumann, in *Houben-Weyl*, *Methods of Organic Chemistry*, Thieme, Stuttgart, 1995, vol. 21a, ch. A3.
7 G. M. Louden, *Organic Chemistry*, 2nd edn., Benjamin/Cummings Publishing Company, Menlo Park, CA, USA, 1988.
8 (*a*) T. W. Lowry and K. Schueller Richardson, *Mechanism and Theory in Organic Chemistry*, 3rd edn., Harper Collins Publishers, New York, 1987; (*b*) R. A. Y. Jones, *Physical and Mechanistic Chemistry*, 2nd edn., Cambridge University Press, Cambridge, 1984.
9 P. Müller, J.-C. Rossier and J.-L. M. Abboud, *J. Phys. Org. Chem.*, 2000, **13**, in the press.
10 D. B. Denney and R. R. DiLeone, *J. Am. Chem. Soc.*, 1962, **84**, 4737.
11 P. G. Stevens and N. L. McNiven, *J. Am. Chem. Soc.*, 1939, **61**, 1296.
12 P. H. J. Carlsen, T. Katsuki, V. S. Martin and K. B. Sharpless, *J. Org. Chem.*, 1981, **46**, 3936.
13 K. L. Koller and H. C. Dorn, *Anal. Chem.*, 1982, **54**, 529.
14 K. Okamoto and T. Kinoshita, *Bull. Chem. Soc. Jpn.*, 1972, **45**, 2802.
15 H. Weiner and R. A. Sneen, *J. Am. Chem. Soc.*, 1965, **87**, 287.
16 F. L. Schadt, T. W. Bentley and P. v. R. Schleyer, *J. Am. Chem. Soc.*, 1976, **98**, 7667; T. W. Bentley, *Nucleophilicity*, eds. J. M. Harris and S. P. McManus, ACS Advances in Chemistry Series, Washington, D.C., 1987; T. W. Bentley and G. E. Carter, *J. Org. Chem.*, 1983, **48**, 579.
17 (*a*) S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck and G. C. Robinson, *J. Am. Chem. Soc.*, 1956, **78**, 328; (*b*) V. J. Shiner and R. D. Fisher, *J. Am. Chem. Soc.*, 1971, **93**, 2553.
18 (*a*) T. W. Bentley, C. T. Bowen, D. H. Morten and P. v. R. Schleyer, *J. Am. Chem. Soc.*, 1981, **103**, 5466; (*b*) T. W. Bentley and G. E. Carter, *J. Am. Chem. Soc.*, 1982, **104**, 5741; (*c*) T. W. Bentley, C. T. Bowen, W. Parker and C. I. F. Watt, *J. Am. Chem. Soc.*, 1979, **101**, 2486; (*d*) T. W. Bentley, C. T. Bowen, W. Parker and C. I. F. Watt, *J. Chem. Soc.*, *Perkin Trans. 2*, 1980, 1244.
19 P. Müller, J. Mareda and D. Milin, *J. Phys. Org. Chem.*, 1995, **8**, 507; J.-L. M. Abboud, M. Herreros, R. Notario, J. S. Lomas, J. Mareda, P. Müller and J.-C. Rossier, *J. Org. Chem.*, 1999, **64**, 6401; J.-L. M. Abboud, O. Castaño, E. W. Della, M. Herreros, P. Müller, R. Notario and J.-C. Rossier, *J. Am. Chem. Soc.*, 1997, **119**, 2262.
20 K. Takeuchi, M. Takasuka, E. Shiba, T. Kinoshita, T. Okazaki, J.-L. Abboud, R. Notario and O. Castaño, *J. Am. Chem. Soc.*, 2000, **122**, 7351.
21 F. P. Lossing and J. L. Holmes, *J. Am. Chem. Soc.*, 1984, **106**, 6917.
22 (*a*) K. Takeuchi, Y. Ohga, T. Ushino and M. Takasuka, *J. Phys. Org. Chem.*, 1997, **10**, 717; (*b*) K. Takeuchi, Y. Ohga, T. Ushino and M. Takasuka, *J. Org. Chem.*, 1997, **62**, 4904; (*c*) K.-T. Liu, S.-J. Hou and M.-L. Tsao, *J. Org. Chem.*, 1998, **63**, 1360; (*d*) T. W. Bentley, G. Llewellyn and Z. H. Ryn, *J. Org. Chem.*, 1998, **63**, 4654.
23 T. W. Bentley and K. Roberts, *J. Org. Chem.*, 1985, **50**, 4821.
24 K. Okamoto, T. Kinoshita, T. Oshida, T. Yamamoto, Y. Ito and M. Dohi, *J. Chem. Soc.*, *Perkin Trans. 2*, 1976, 1617; K. Okamoto and T. Kinoshita, *Chem. Lett.*, 1974, 1037; K. Okamoto, *Pure Appl. Chem.*, 1984, **56**, 1797.
25 M. P. Doyle, W. R. Winchester, M. N. Protopopova, P. Müller, G. Bernardineli, D. Ene and S. Motallebi, *Helv. Chim. Acta*, 1993, **76**, 2227.
26 C. A. Brown and D. Barton, *Synthesis*, 1974, 434.
27 F. Bohlmann and R. Zeisberg, *Org. Magn. Reson.*, 1975, **7**, 426.
28 A. F. Fuller and J. Kenyon, *J. Chem. Soc.*, 1924, 2304.