93. Synthesis of Optically Pure Compounds by Enantiotopically Differentiating Monoacetalization of Prochiral Diketones. Part II. Fragmentation of β-Keto-Acetals[1])

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Summary

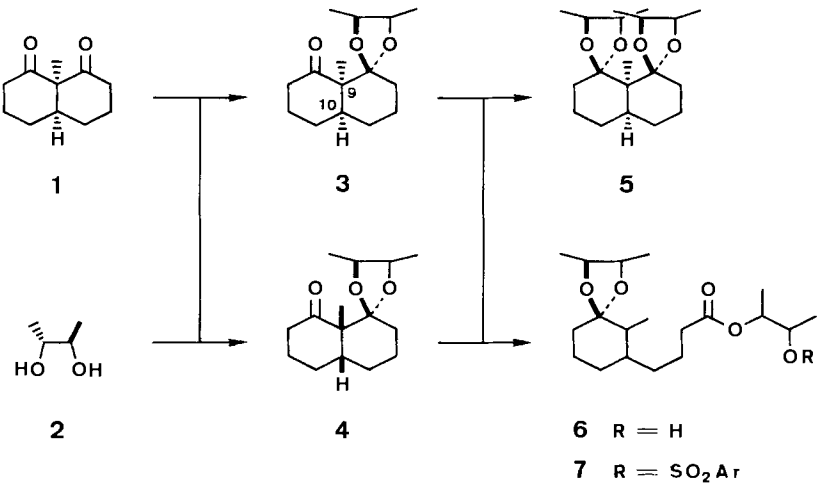
Treatment of β-keto-acetals, derived from non-enolisable β-diketones, with sulfonic acids in boiling benzene results in a smooth *retro-Claisen*-type fragmentation. The acetal-C-atom is thereby transformed into a carboxylic ester *via* a dialkoxycarbenium ion, which is dealkylated by the sulfonate counter-ion. Application of this reaction to the diastereomeric monoacetals **3** and **4**, derived from *cis*-9-methyl-decalin-1,8-dione (**1**), followed by transesterification with CH_3OH, yields optically pure 4-(2′-methyl-3′-oxocyclohexyl)butyrate **9** ((+)-**9** from **3**, (−)-**9** from **4**) and the monosulfonate of *meso*-2,3-butanediol (−)-**13** *(Scheme 2)*. Unexpectedly, this cleavage proceeds as well with monoacetal **26**, obtained by acetalization of *trans*-9-methyl-decalin-1,8-dione (**27**) with 2,2-dimethyl-1,3-propanediol *(Scheme 7)*. Some attempts, aiming at an isomerization of the *cis*- and *trans*-decalin derivatives **3** and **24**, or **25** and **26**, *via* the postulated carboxonium intermediate, were not successful.

1. Introduction. – In [1] we have presented a new access to optically pure compounds by monoacetalization of prochiral diketones with a chiral diol, separation of the two diastereomeric monoacetals, and further chemical transformation involving the unprotected keto function followed by acetal cleavage. This method was especially effective with *cis*-9-methyl-decalin-1,8-dione (**1**), which, upon acetalization with (2*R*,3*R*)-2,3-butanediol (**2**), gave the separable monoacetals **3** and **4** in high yield (85–90%) and with high enantiotopical differentiation. The major product, monoacetal **3** with (9*S*,10*R*)-configuration, formed in 70–80% excess (**3**/**4** ≤ 9:1), could thereby be isolated in 76% yield. By-products of this derivatization were the bis-acetal **5** (*ca.* 5%) and variable amounts of the esters **6** and **7** *(Scheme 1)*.

For two reasons the monocyclic products **6** and **7** are of special interest: *1*) the formation of the sulfonate **7** is responsible for the consumption of the sulfonic acid, which catalyzes the acetalization; although the enantiotopic differentiation is enhanced

[1]) Part I: [1]. These results, which have been presented in part at the 'Herbstversammlung der Schweizerischen Chemischen Gesellschaft', October 16, 1981, in Bern, are comprised in the Ph. D. thesis of *P.M.* [2]. The nomenclature and classification of stereodifferentiating reactions proposed by *Izumi & Tai* [3] are used in this communication.

Scheme 1



by lowering the amount of catalyst, the acetalization is stopped before completion with 5 mol-% of acid [1]; *2*) if the monoacetals **3** and **4** could be cleaved to chiral cyclohexanones like **6** and **7** without loss of optical purity, the margin of optically pure compounds obtainable *via* monoacetalization of prochiral β-diketones would be considerably extended. It was therefore decided to investigate the reaction path leading to **6** and **7**, a transformation resembling the *retro-Claisen* reaction of β-dicarbonyls.

2. Fragmentation of Monoacetals 3 and 4. – Treatment of (9*S*,10*R*)-monoacetal **3** with CH_3SO_3H (1.2 equiv.) in boiling benzene for 1 h resulted in a high-yield (90%) cleavage to the cyclohexanone derivative **8**[2])[3]). Transesterification with CH_3OH catalyzed by CH_3ONa gave the methyl ester (+)-**9**[2])[4]) in 93% yield. The structure of (+)-**9** followed from spectral comparison with (±)-**9**, obtained from dione **1** by base-catalyzed methanolysis [1]. The absolute configuration was deduced by CD. The spectrum of *trans*-(+)-**9**[4]) exhibited a negative minimum ($\Delta\varepsilon = -1.29$) at 289 nm, corresponding to the n→π* transition of the cyclohexanone (+)-**9** with (1′*R*)-configuration. The optical purity of (+)-**9** was better than 99%, determined by acetalization with (2*R*,3*R*)-2,3-butanediol (**2**) and GC analysis of the acetal **10**[2]), obtained in 94% yield[5]). The

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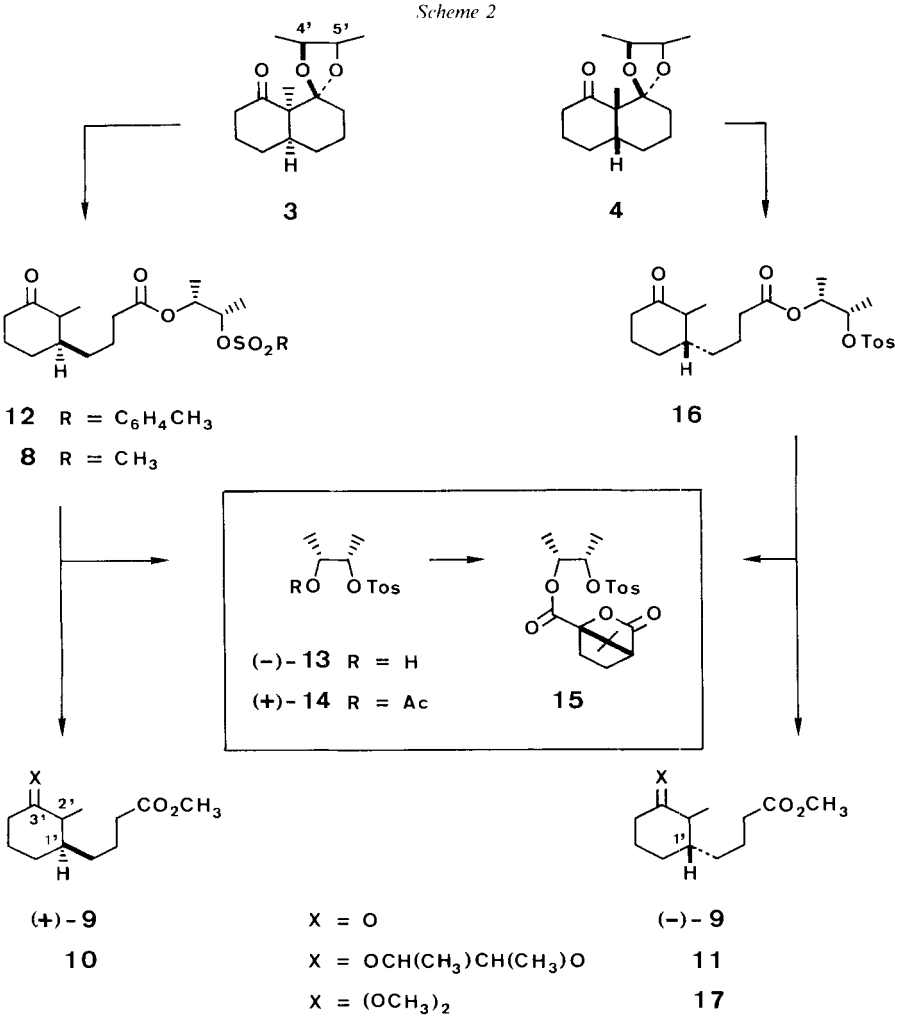
[2]) Mixture of epimers at C(2′). The *cis*/*trans*-ratio was determined either by ^{1}H-NMR or GC (see *Exper. Part*). A single compound number is given to all 4-(2′-methyl-3′-oxocyclohexyl)butyric acid derivatives, which are generally 1′,2′-epimer mixtures. Such mixtures, which, referring to C(1′), are enantiomerically pure, are characterized by the sign of $[\alpha]_D$.

[3]) The acetals **6** and **7** isolated from the acetalization of dione **1** [1] are therefore formed by cleavage of the monoacetals **3** and **4** followed by acetalization with excess diol **2**.

[4]) A partial separation of the epimers giving pure *trans*-(+)-**9** was achieved by chromatography.

[5]) Acetalization of (±)-**9** with diol **2** afforded a 1:1 mixture of the diastereomeric acetals **10** ((1′*R*)-configuration) and **11** ((1′*S*)-configuration) as *cis*/*trans*-epimers. Analysis of this four-component mixture by capillary GC showed 3 peaks: a small peak (25%), which was tentatively assigned to the non-separated *trans*-isomers of **10** and **11**, and two larger peaks (35% and 40%), separated by 0.1 min, corresponding to *cis*-**10** (shorter t_R) and *cis*-**11**. The chromatograms of the acetal mixtures obtained from optically pure (+)-**9** and (−)-**9** exhibited only one of the two larger peaks (*ca.* 75%). Although the *trans*-isomer of the free ketone **9** is expected to be thermodynamically favored, the *cis*-isomers of the acetals **10** and **11** are probably more stable or the kinetically favored products of the acetalization of **9** (see *below*[7])[8])).

Scheme 2

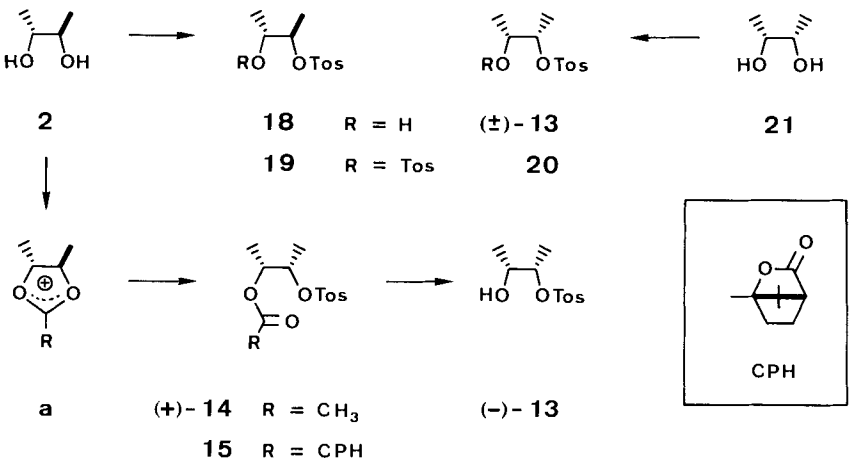


fragmentation of the (9*S*,10*R*)-monoacetal **3** proceeded therefore with complete retention of the configuration of C(10) *(Scheme 2)*.

A somewhat slower cleavage of monoacetal **3** was observed with TosOH. The tosylate **12** was, however, isolated in good yield (90% based on converted **3**). To evaluate the configuration of the ester side chain of **12**, the methanolysis was carried out under acidic conditions[6]). Treatment of **12** with CH_3SO_3H in CH_3OH afforded the methyl ester (+)-**9** and the tosylate (–)-**13** *(Scheme 2)*. The relative and absolute configuration of the *meso*-2,3-butanediol derivative (–)-**13** was determined by comparison of physical and spectral data of (–)-**13**, its acetate (+)-**14**, and camphanate **15** with independently prepared reference compounds (see *below*). It was found to be diastereomerically and optically pure with (1*S*,2*R*)-configuration. The configuration of either C(4') or C(5')

[6]) Strong base leads to destruction of the α-hydroxy-sulfonates.

Scheme 3



was therefore inverted in the course of the fragmentation of monoacetal **3**. Analysis of the methyl ester (+)-**9** obtained *via* **12** showed, that the 1′,2′-*cis*-isomer predominated (*ca.* 60%)[7]). The normal *trans*/*cis*-ratio (4:1) was obtained by equilibration with CH_3ONa/CH_3OH. The optical purity of (+)-**9** determined *via* acetal **10**, was again better than 99%, with none of the diastereomer **11** detectable[5]).

The fragmentation of the (9*R*,10*S*)-monoacetal **4** with TosOH proceeded equally well, yielding the ester **16**. Acidic methanolysis of **16** afforded the methyl ester (−)-**9**, the tosylate (−)-**13**, and some dimethylacetal **17** (34%)[8]). The butanediol derivative (−)-**13** was again characterized as camphanate **15** and found diastereomerically and optically pure. As above, the methyl ester (−)-**9** (*cis*/*trans* 63:37) was epimerized with CH_3ONa/CH_3OH (→*cis*/*trans* 22:78). Acetalization with diol **2** gave the derivative **11** in 98% yield, containing, according to GC analysis[5]), about 2% of diastereomer **10**. The optical purity of (−)-**9** was therefore better than 95% *(Scheme 2)*[9]). *The stereochemical course of the sulfonic-acid-mediated fragmentation of the diastereomeric monoacetals* **3** *and* **4** *is therefore well-defined, consistent for both cases, and clean.*

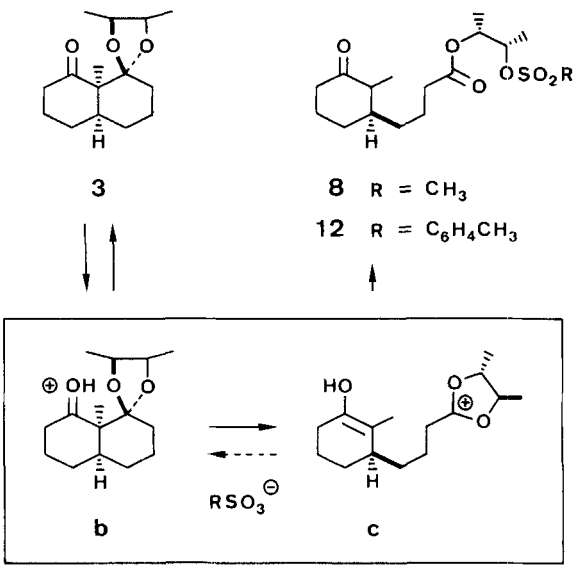
3. Preparation of 2,3-Butanediol Derivatives. – Treatment of the monoacetals **3** and **4** with TosOH followed by transesterification gave the methylester (+)-**9** from **3** and (−)-**9** from **4** together with the 2,3-butanediol-monotosylate (−)-**13** *(Scheme 2)*.

[7]) In CH_3OH/CH_3SO_3H the keto function of **12** and **9** is masked to some extent as hemiacetal or acetal (see *below*). The steric interaction of the geminal oxygen-substituents at C(3′) of such a derivative with the CH_3-group at C(2′) is expected to shift the thermodynamic equilibrium in favor of the (1′,2′)-*cis*-epimer with axial C(2′)-methyl-group. Provided, that the thermodynamic equilibrium of the *cis*/*trans*-epimers of ketone **9**, which is regenerated during workup, is not reached, this would be a rationalization for the predominance of the *cis*-epimer found after acid-catalyzed methanolysis.

[8]) The acetal **17** was most probably the 1′,2′-*cis*-epimer, since deprotection with wet silica gel according to *Conia et al.* [4] gave (−)-*cis*-**9** containing traces of the *trans*-epimer (2%).

[9]) The somewhat lower optical purity of (−)-**9** obtained from **4** compared to (+)-**9** derived from **3** is most likely due to contamination of monoacetal **4** with *ca.* 2% of isomer **3** and not to a loss of optical purity in the course of the fragmentation.

Scheme 4

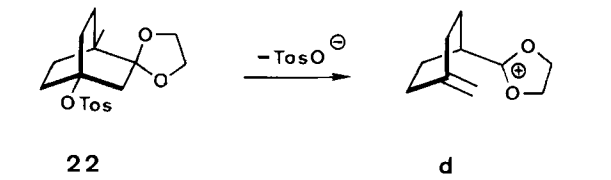


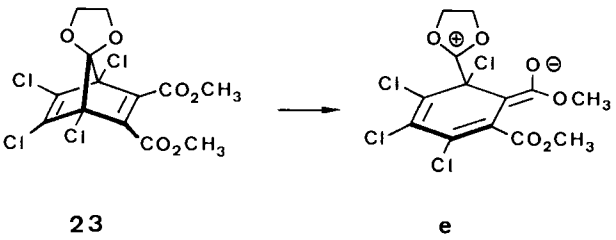
Spectral comparison of (−)-**13** with the reference compounds **18** and (±)-**13**, obtained together with the ditosylates **19** and **20** by tosylation of diols **2** and **21**, clearly showed, that (−)-**13**, obtained from the fragmentation reactions, was a derivative of *meso*-diol **21**[10]). Optically pure (1*S*,2*R*)-2-hydroxy-1-methylpropyl *p*-toluenesulfonate (**13**) was obtained from (2*R*,3*R*)-butanediol **2** by treatment with AcOH/TosOH in benzene according to *Auteri et al.* [5], followed by hydrolysis of the acetate (+)-**14**. The stereochemical outcome of this transformation follows from the well-documented mechanism [6–9], involving a S_N2-dealkylation of the intermediate dioxolanylium ion **a** by the sulfonate counter ion, affording (+)-**14** with inverted configuration of the sulfonylated center. Analogous reaction of **2** with camphanic acid/TosOH gave a single camphanate with structure **15** *(Scheme 3)*.

4. Mechanistic Discussion. – The sulfonic-acid-mediated fragmentation of β-keto-acetals **3** and **4**, proceeding with retention of the configuration at C(10) and inversion at one of the dioxolane-C-atoms *(Scheme 2)*, can be rationalized by the mechanism depicted in *Scheme 4*. The key-step of this transformation is the *retro-Claisen* reaction of a species **b**, protonated at the carbonyl-O-atom, affording the dioxolanylium ion **c**. Dealkylation of **c** by the sulfonate counter-ion finally gives the product **8** (R = CH_3) or **12** (R = $C_6H_4CH_3$). The last step of the proposed mechanism is a thoroughly studied process [5–9], and the inverted configuration at C(2″) of **8** and **12** can be considered as strong support for the dioxolanylium intermediate **c**. No precedent example, on the

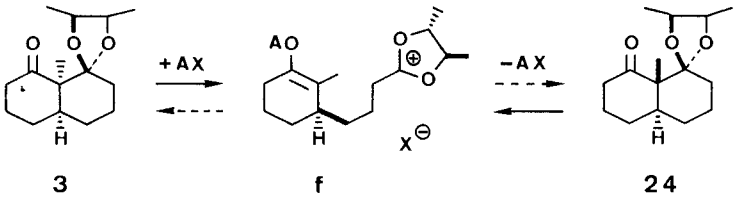
[10]) Pronounced differences are found in the ^{1}H-NMR spectra of **13** and **18**: the chemical shifts of the H–C(1)- and H–C(2)-resonances are 4.55 and 3.86 ppm for **13**, and 4.46 and 3.70 ppm for **18**; the coupling constant between H–C(1) and H–C(2) is 3 Hz in the case of **13** and 6 Hz for **18** (see *Exper. Part*).

Scheme 5





Scheme 6



other hand, could be found for the β-keto-acetal cleavage (**b**→**c**, *Scheme 4*)[11])[12]). Related, however, is the fragmentation of acetal-protected β-keto-sulfonates (*e.g.* **22**→**d**, *Scheme 5*) [14] [15], and some similar reactions of halogenides [16], alcohols [16d], and epoxides [17]. A closer analogy to the cleavage **b**→**c** *(Scheme 4)* can be seen in the spontaneous aromatization of *Diels-Alder* adduct **23** *via* dioxolanylium ion **e** *(Scheme 5)* [18].

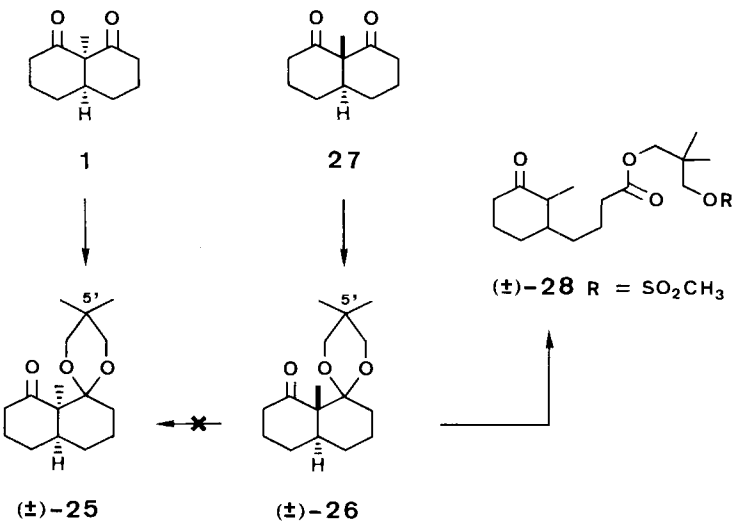
5. Attempts to Epimerize β-Keto-Acetals. – Although the monoacetal **3** is easily obtainable from the prochiral dione **1** in good yield, this is not the case for the *trans*-isomer **24** [1]. This valuable compound could, however, be accessible by epimerization of **3** *via* the dioxolanylium ion **f** *(Scheme 6)*, provided that the *retro-Claisen* step of the monoacetal cleavage is reversible[13]). Competing side reactions of the intermediate **f**,

[11]) This statement relies on several review articles [8–13] and on a *CAS-on-line* search (November 1983), using combinations of the key-words *diketone, acetal, ketal, retro, Claisen, fragmentation, cleavage,* and *cleaving.*

[12]) For a discussion of the reverse process (**c**→**b**) see *below.*

[13]) Contrarily to the cleavage **b**→**c** *(Scheme 4)* [11]), there are reports on the reverse process: *e.g.* the formylation of silylenolethers by orthoformates, catalyzed either by *Lewis* acids [19] or trimethylsilyltriflate [20], the acylation of lithium-enolates [21] or activated aromatic compounds by dioxolanylium ions [11], and analogous reactions with sulfur-stabilized carbenium ions [22].

Scheme 7



that ought to be suppressed, are the keto-enol tautomerization (**f**, A = H) and dealkylation of the dioxolanylium ion by the counter-ion X. No epimerization to **24** could, however, be observed, when monoacetal **3** was treated with $BF_3 \cdot Et_2O$ in Et_2O at r.t., with trimethylsilyltriflate in CCl_4 at r.t., or with *Nafion-H* in boiling benzene. The starting material **3** was thereby recovered in yields of 94%, 73%, and 45%, respectively[14]).

Next, the racemic monoacetals **25** and **26** were prepared in high yield by acetalization of dione **1** and *trans*-dione **27**, respectively, with 2,2-dimethyl-1,3-propanediol *(Scheme 7)*. It was assumed, that the geminal methyl substituents of C(5') should thwart the dealkylation of the dioxolanylium intermediate, obtained by cleavage of **25** or **26**, and that an equilibration of **25** and **26** should therefore have a better chance. Quite unexpectedly, however, treatment of monoacetal **26** with CH_3SO_3H resulted in the formation of the monocyclic ester **28**, isolated in 70% yield *(Scheme 7)*[15]). Thus, the fragmentation of *β*-keto-acetals seems to be quite a general process, not restricted to derivatives of *cis*-dione **1**[16]). Finally, treatment of mono-acetal **26** with $BF_3 \cdot Et_2O$ in Et_2O at r.t. or with CF_3SO_3H in DMF at 80° gave again no detectable isomerization (→**25**) *(Scheme 7)*. Isolated was the starting material **26**, 88% with $BF_3 \cdot Et_2O$, 44% (together with 38% of dione **27**) with CF_3SO_3H[14])[17]).

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[14]) For an experimental description of these results, see [2].

[15]) This result throws some doubt on the proposed mechanism of the monoacetal fragmentation *(Scheme 4)*, since it contrasts the finding, that the carboxonium ion obtained from trineopentyl orthoformate is not dealkylated by chloride ion [23].

[16]) The base-catalyzed *retro-Claisen* reaction was found to proceed under much milder conditions for *cis*-dione **1** than for the *trans*-isomer **27** [1].

[17]) The *trans*-epimer **26** was chosen for these experiments, since it was found, that *Friedel-Crafts*-type cyclization of 4-(2'-methyl-3'-oxocyclohexyl)butyric acid leads exclusively to the *cis*-dione **1** [2] [24]. If the formation of *β*-keto-acetals from carboxonium ions would be kinetically controlled, an epimerization would only be possible from the *trans*-monoacetal **26**.

Conclusion. – The experiments of this report describe a clean regiospecific *retro-Claisen* type cleavage of β-keto-acetals derived from non-enolisable β-diketones. The stereochemical outcome of this transformation, proceeding with the incorporation of a sulfonic-acid molecule, can be reasonably explained involving a dialkoxy-carbenium-ion intermediate, which is dealkylated by the sulfonate counter-ion *(Scheme 4)*. The synthetically valuable specificity of this novel transformation[11]) relies on the regioselectivity of the monoacetalization. Compared to the direct regioselective *retro-Claisen* reaction, this two-step variant has the advantage, that the unwanted monoacetal can be recycled to the starting diketone more easily than the product of the unwanted β-diketone cleavage. It has further to be noted that the sense and degree of the regioselectivity is not necessarily the same for the two variants, despite the fact that the same hemiacetal intermediate is involved. While the rates of the *retro-Claisen* reaction are strongly influenced by steric factors of the addition to the carbonyl group [25], the rate-limiting step of the acetalization is the loss of water from the hemiacetal intermediate.

The preparative potential of this transformation is exemplified by the facile access to both enantiomers of the 2,3-disubstituted cyclohexanone **9** from the bicyclic prochiral diketone **1** *via* the diastereomeric monoacetals **3** and **4** *(Schemes 1* and *2)*. Optically active 2,3-disubstituted cycloalkanones and aliphatic ketones have been obtained by enantioface [26] or diastereoface [27] differentiating *Michael* additions to enones, by cyclization of allylesters using a chiral Pd-catalyst [28], or by Rh-catalyzed cyclization of 2-diazo-3-oxocarboxylates with a chiral ester group [29].

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Experimental Part

General Remarks. See [1]. In the *^1H- and ^{13}C-NMR spectra* of epimer mixtures the signals, which correspond to the major component, are marked with an asterisk. For *gas-liquid-chromatographic* analyses of product ratios the following columns have been used: *UCON 50 HB 5100* coated on a 25-m column (*Pyrex*, 0.36 mm diameter), *SE-52 coated* on a 25-m column (*Pyrex*, 0.32 mm diameter).

1. *Fragmentation of Monoacetal* **3** *with CH_3SO_3H.* – 1.1. *(1R,2S)2-Mesyloxy-1-methylpropyl 4-[(1'R)-2'-Methyl-3'-oxocyclohexyl]butyrate* (**8**). A solution of **3** (163 mg, 0.647 mmol) and CH_3SO_3H (50 µl, 0.77 mmol) in dry benzene (10 ml) was boiled under reflux for 1 h (Ar). The mixture was quenched by addition to 30 ml of sat. $NaHCO_3$-solution and worked up by extraction with Et_2O. Chromatography on silica gel (Et_2O/hexane 3:1) gave 202 mg (90%) of **8**, mixture of epimers: 2'R*(trans)*/2'S*(cis)* 3:1, according to ^{1}H-NMR. $[\alpha]_D = +31.0°$ ($c = 2.42$, $CHCl_3$). IR ($CHCl_3$): 2970*m*, 2940*m*, 2865*m*, 1727*s*, 1701*s*, 1445*w*, 1345 br. *s*, 1172*s*, 1100*m*, 967*m*, 916*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.01 and 1.05* (2*d*, $J = 6.5$, CH_3–C(2')); 1.26, 1.27*, 1.40, and 1.41* (4*d*, $J = 6.5$, CH_3–C(1''), 3H–C(3'')); 1.16–2.66 (*m*, 14H); 3.04 (*s*, CH_3–SO_3); 4.88 and 5.01* (2*dq*, J = 3.3 and 6.5) and 4.97–5.05 (*m*) (H–C(1''), H–C(2'')). MS: 270 (1, $M^+ - 78$), 252 (4), 234 (3), 197 (4), 181 (12), 163 (8), 140 (15), 135 (37), 132 (11), 127 (27), 114 (23), *111* (100), 93 (9), 81 (12), 73 (24), 69 (11), 67 (11), 55 (58), 45 (15), 43 (25), 41 (28), 39 (10).

1.2. *(+)-Methyl 4-[(1'R)-2'-Methyl-3'-oxocyclohexyl]butyrate* (**9**). To a solution of CH_3ONa in CH_3OH, prepared by the addition of Na (15 mg, 0.65 mg-at) to CH_3OH (2 ml), butyrate **8** (157 mg, 0.451 mmol), dissolved in CH_3OH (4 ml), was added. After stirring for 3.5 h at r.t. (Ar), the mixture was diluted with H_2O and worked up with Et_2O. Chromatography (silica gel, hexane/Et_2O 2:1) gave 89 mg (93%) of (+)-**9**, mixture of

epimers: *2'R(trans)*/*2'S(cis)* 81:19, according to GC (*UCON*, 160°, 0.35 kg/cm^2): t_R 5.6 min (*2'S*), t_R 6.0 min (*2'R*). $[\alpha]_D = +33.2°$ ($c = 2.16$, $CHCl_3$). IR, ^{1}H-NMR, and MS of (±)-**9** see [1]. Pure *(+)-methyl 4-[(1'R,2'R)-2'-methyl-3'-oxocyclohexyl]butyrate* (**9**) was obtained by rechromatography (silica gel, hexane/Et_2O 5:1) from the first fractions of (+)-**9**. $[\alpha]_D = +27.8°$ ($c = 0.64$, $CHCl_3$). UV(EtOH): 284 ($\varepsilon = 25$). CD(EtOH): 289 ($\Delta\varepsilon = -1.29$). IR ($CCl_4$): 2970*m*, 2950*m*, 2935*m*, 2865*m*, 1740*s*, 1711*s*, 1455*m*, 1446*m*, 1435*m*, 1380*w*, 1358*w*, 1316*w*, 1249*m*, 1217*m*, 1197*m*, 1176*m*, 1154*m*, 1093*w*, 1057*w*, 988*w*, 960*w*, 883*w*, 850*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.05 (*d*, $J = 6.5$, CH_3–C(2')); 1.14–1.84 (*m*, 7H); 1.88–2.46 (*m*, 7H); 3.68 (*s*, CH_3O–C(1)). MS: 212 (5, M^+), 197 (2), 194 (3), 181 (3), 165 (2), 163 (2), 151 (5), 135 (9), 124 (4), 123 (5), *111* (100), 109 (5), 97 (5), 95 (7), 93 (5), 87 (4), 83 (11), 82 (11), 81 (13), 74 (15), 69 (11), 67 (12), 59 (14), 55 (44), 43 (11), 42 (14), 41 (35), 39 (16).

1.3. *Methyl 4-[(2'R,3'R,7'R)-2',3',6'-Trimethyl-1',4'-dioxaspiro[4.5]dec-7-yl]butyrate* (**10**). A mixture of (+)-**9** (26 mg, 0.123 mmol), (2*R*,3*R*)-2,3-butanediol (**2**) (14 mg, 0.15 mmol), and TosOH·H_2O (3 mg) in benzene (10 ml) was boiled under reflux at a *Dean-Stark* trap for 4 h (Ar). After quenching with sat. $NaHCO_3$-solution, the mixture was worked up with Et_2O. Chromatography (silica gel, hexane/Et_2O 5:1) gave 33 mg (94%) of acetal **10**, mixture of epimers: *6'S(cis)*/*6'R(trans)* 77:23[5])[7])[8]), according to GC (*SE-52*, 160°, 0.40 kg/cm^2): t_R 7.8 min (*6'R*), t_R 8.7 min (*6'S*), no *cis*-**11** ((*7'S*,*6'R*), t_R 8.8 min) detectable. $[\alpha]_D = +22.7°$ ($c = 1.74$, $CHCl_3$). IR (CCl_4): 2975*s*, 2935*s*, 2865*m*, 1741*s*, 1454*m*, 1437*m*, 1377*m*, 1362*w*, 1340*w*, 1330*w*, 1290*w*, 1240*w*, 1195*m*, 1178*m*, 1167*m*, 1144*m*, 1098*s*, 1025*w*, 978*w*, 950*m*, 921*w*, 878*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.84 (*d*, $J = 7$) and 0.88* (*d*, $J = 6$) (CH_3–C(6')); 1.20–1.25 (*m*) and 1.21* and 1.24* (2*d*, $J = 6$) (CH_3–C(2'), CH_3–C(3')), 0.85–1.85 (*m*, 12H); 2.20–2.40 (*m*, 2H–C(2)); 3.66 (*s*, CH_3O–C(1)); 3.50–3.70 (*m*, H–C(2'), H–C(3')). MS: 284 (9, M^+), 269 (1), 255 (5), 253 (4), 241 (30), 211 (6), 197 (4), 183 (35), 141 (12), 139 (17), 135 (6), 128 (21), *127* (100), 114 (29), 111 (10), 95 (8), 83 (8), 81 (11), 79 (7), 69 (9), 67 (11), 59 (10), 55 (51), 43 (15), 41 (23).

2. *Fragmentation of* **3** *with TosOH*. – 2.1. *(1R,2S)-1-Methyl-2-tosyloxypropyl 4-[(1'R)-2'-Methyl-3'-oxocyclohexyl]butyrate* (**12**). A suspension of TosOH·H_2O (122 mg, 0.64 mmol) and molecular sieves (m.s., 5 Å, 515 mg) in dry benzene (5 ml) was boiled for 15 min under reflux (Ar). After the addition of monoacetal **3** (144 mg, 0.572 mol), dissolved in benzene (5 ml), the mixture was boiled under reflux for 1.5 h, cooled, filtered, and quenched by the addition to 50 ml of sat. $NaHCO_3$-solution. Workup with Et_2O and chromatography (silica gel, hexane/Et_2O 1:1) gave 29 mg (20%) of starting material **3** and 177 mg (73%) of ester **12**, mixture of epimers: *2'R(trans)*/*2'S(cis)* 3:1, according to ^{1}H-NMR. $[\alpha]_D = +22.6°$ ($c = 2.36$, $CHCl_3$). IR ($CHCl_3$): 2970*m*, 2940*m*, 2870*m*, 1728*s*, 1705*s*, 1600*w*, 1494*w*, 1449*m*, 1368*s*, 1309*m*, 1292*w*, 1187*m*, 1176*s*, 1132*w*, 1106*m*, 1093*m*, 1075*m*, 1030*w*, 1021*w*, 1000*w*, 983*m*, 962*w*, 917*s*, 886*w*, 836*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.01 (*d*, $J = 7$) and 1.04* (*d*, $J = 6.5$) (CH_3–C(2')); 1,17, 1.18*, and 1.24 (3*d*, $J = 6.5$, CH_3–C(1''), 3H–C(3'')); 0.95–2.70 (*m*, 14H); 2.45 (*s*, $CH_3C_6H_4SO_3$); 4.65–4.75 (*m*), 4.67* (*dq*, $J = 3$ and 6.5), 4.81–4.90 (*m*), and 4.86* (*dq*, $J = 3$ and 6.5) (H–C(1''), H–C(2'')); 7.32–7.36 and 7.77–7.81 (2*m*, *AA'BB'-system*, $J_{AB} \approx 8$, $CH_3C_6H_4SO_3$). MS(di.): 424 (0.1, M^+), 409 (0.1), 406 (0.1), 279 (2), 252 (7), 228 (6), 200 (3), 172 (14), 167 (5), 164 (6), 156 (32), 155 (44), 141 (13), 140 (54), 127 (73), 114 (83), 111 (42), 108 (13), 107 (13), 95 (9), *91* (100), 83 (10), 82 (11), 81 (15), 79 (14), 77 (11), 73 (15), 69 (12), 67 (15), 65 (29), 57 (13), 55 (59), 53 (11), 45 (29), 43 (41), 41 (39), 39 (22).

2.2. *Acid-Catalyzed Methanolysis of* **12**. A solution of **12** (170 mg, 0.401 mmol) and CH_3SO_3H (130 µl, 2.01 mmol) in CH_3OH (3 ml) was stirred for 12 h at r.t. (Ar). The mixture was poured into 50 ml of sat. $NaHCO_3$-solution and worked up with Et_2O. Chromatography (silica gel, hexane/Et_2O 1:1) of the product mixture gave 70 mg (82%) of (+)-**9**, mixture of epimers: 2'R*(trans)*/2'S*(cis)* 39:61, according to GC (see *1.2*), $[\alpha]_D = +42.2°$ ($c = 1.94$, $CHCl_3$), and 77 mg (78%) of *(−)-(1S,2R)-2-Hydroxy-1-methylpropyl* p-*Toluenesulfonate* (**13**). $[\alpha]_D = -10.4°$ ($c = 1.69$, $CHCl_3$). IR ($CHCl_3$): 3600*w*, 3560–3330*w*, 2990*w*, 2940*w*, 1600*w*, 1492*w*, 1448*w*, 1363*m*, 1309*w*, 1292*w*, 1189*m*, 1176*s*, 1101*m*, 1082*m*, 1020*m*, 1009*m*, 978*m*, 920*m*, 904*s*. ^{1}H-NMR (100 MHz, $CDCl_3$): 1.10 and 1.19 (2*d*, $J = 8.5$, CH_3–C(1), 3H–C(3)); 2.01 (*s*, *exchangeable with* D_2O, OH); 2.42 (*s*, $CH_3C_6H_4SO_3$); 3.86 (*dq*, J = 3 and 8.5, H–C(2)); 4.55 (*dq*, J = 3 and 8.5, H–C(1)); 7.20–7.42 and 7.66–7.88 (2*m*, *AA'BB'-system*, $J_{AB} \approx 8$, $CH_3C_6H_4SO_3$). MS(*di.*) 245 (1, $M^+ + 1$), 229 (1), 227 (0.5), 200 (19), 172 (4), 157 (9), 156 (48), 155 (70), 139 (3), 108 (7), 107 (8), 92 (56), *91* (100), 77 (4), 65 (27), 45 (28), 43 (23), 39 (9).

2.3. *Analysis of Methyl Ester* (+)-**9**. – A solution of the (39:61)-epimer mixture of (+)-**9** (40 mg, 0.189 mmol) in CH_3OH (3 ml) was added to CH_3ONa/CH_3OH, prepared by the addition of Na (20 mg, 0.87 mg-at) to 2 ml of CH_3OH. After stirring at r.t. for 3 h (Ar), the reaction mixture was poured to ice/H_2O and worked up with Et_2O. Chromatography (silica gel, hexane/Et_2O 2:1) yielded 38 mg (95%) of (+)-**9**, mixture of epimers: *2'R(trans)*/*2'S(cis)* 78:22 (GC, see *1.2*), $[\alpha]_D = +34.7°$ ($c = 2.18$, $CHCl_3$). A solution of this epimer mixture of (+)-**9** (34 mg, 0.16 mmol), **2** (18 mg, 0.20 mmol), and TosOH (4 mg) in benzene (10 ml) was boiled under reflux for 5 h at a *Dean-Stark* trap. Usual workup and chromatography (silica gel, hexane/Et_2O 5:1) gave 45 mg

(98%) of acetal **10**, mixture of epimers: *6'S(cis)*/*6'R(trans)* 72:28[5])[7])[8]), with no *cis*-**11** (*7'S,6'R*) detectable (GC, see *1.3*). $[\alpha]_D = +22.5°$ ($c = 1.90$, $CHCl_3$).

2.4. *(+)-(1S,2R)-2-Acetoxy-1-methylpropyl* p-*Toluenesulfonate* (**14**). A solution of (−)-**13** (27 mg, 0.11 mmol) in Ac_2O/pyridine (0.1 ml of each) was kept at r.t. for 20 h. The mixture was worked up with Et_2O, the org. layers were washed with 1N HCl, H_2O, and sat. NaCl-solution. Chromatography (silica gel, hexane/Et_2O 1:1) gave 30 mg (94%) of **14**. M.p. 43° (Et_2O/pentane). $[\alpha]_D = +21.2°$ ($c = 1.13$, $CHCl_3$). IR ($CHCl_3$): 2990*w*, 2945*w*, 1730*s*, 1600*w*, 1446*w*, 1370*s*, 1308*w*, 1290*w*, 1245*s*, 1189*s*, 1175*s*, 1106*m*, 1093*m*, 1075*m*, 1027*m*, 1020*m*, 984*m*, 953*w*, 918*s*, 870*m*, 833*w*. ^{1}H-NMR (100 MHz, $CDCl_3$): 1.16 (*d*, $J = 6$) and 1.24 (*d*, $J = 6.5$) (CH_3–C(1), 3H–C(3)); 1.88 (*s*, CH_3COO); 2.41 (*s*, $CH_3C_6H_4SO_3$); 4.65 (*dq*, $J = 3$ and 6.5) and 4.75 (*dq*, $J = 3$ and 6) (H–C(1), H–C(2)); 7.20–7.44 and 7.66–7.86 (2*m*, *AA'BB'-system*, $J_{AB} \approx 8$, $CH_3C_6H_4SO_3$). MS: 286 (0.2, M^+), 271 (0.3), 242 (2), 229 (0.5), 226 (1), 199 (7), 198 (2), 156 (3), 155 (20), 150 (6), 130 (1), 119 (3), 115 (5), 114 (3), 92 (3), 91 (20), 89 (5), 88 (7), 87 (8), 73 (5), 72 (7), 65 (7), 55 (6), 45 (18), 44 (5), *43* (100), 42 (6), 39 (5). Anal. calc. for $C_{13}H_{18}O_5S$ (286.35): C 54.53, H 6.34, S 11.20; found: C 54.56, H 6.38, S 11.22.

2.5. *(1R, 2S)-1-Methyl-2-tosyloxypropyl (1S,4R)-7,7-Dimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxylate* (**15**). A solution of (−)-**13** (27 mg, 0.11 mmol), camphanic chloride (120 mg, 0.554 mmol), and 4-(dimethylamino)pyridine (10 mg) in pyridine (2 ml) was stirred for 20 h at r.t. (Ar). The mixture was worked up with Et_2O, the org. phases were washed with 1N HCl, H_2O, and sat. NaCl-solution. Chromatography (silica gel, pentane/CH_2Cl_2/Et_2O 20:20:3) gave 42 mg (89%) of camphanate **15**. $[\alpha]_D = -17.1°$ ($c = 1.49$, $CHCl_3$). M.p. 106° (Et_2O). IR ($CHCl_3$): 2980*m*, 2940*w*, 2880*w*, 1786*s*, 1743*m*, 1600*w*, 1448*w*, 1398*w*, 1367*m*, 1341*m*, 1315*m*, 1273*m*, 1190*m*, 1175*s*, 1102*m*, 1060*m*, 1016*w*, 990*w*, 956*w*, 920*m*, 883*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.94, 1.04, and 1.11 (3*s*, 3 CH_3); 1,25 and 1,252 (2*d*, $J = 6.5$, CH_3–C(1'), 3H–C(3')); 1.64 (*ddd*, $J = 13$, 9, and 4, 1H), 1.86–2.06 (*m*, 2H), and 2.445 (*ddd*, $J = 14$, 10.5, and 4, 1H) (CH_2–CH_2); 2.45 (*s*, $CH_3C_6H_4SO_3$); 4.74 and 5.12 (2*dq*, $J = 3$ and 6.5, H–C(1'), H–C(2')); 7.32–7.42 and 7.70–7.84 (2*m*, *AA'BB'-system*, $J_{AB} \approx 8$, $CH_3C_6H_4SO_3$). MS(*di.*): 424 (7, M^+), 396 (3), 378 (6), 288 (6), 253 (27), 226 (6), 206 (4), 199 (4), 181 (14), 173 (7), 172 (6), 164 (10), 155 (55), 153 (30), 136 (60), 134 (34), 125 (70), 124 (21), 121 (19), 109 (83), 107 (22), 97 (35), *91* (100), 83 (88), 73 (10), 69 (12), 67 (15), 65 (21), 55 (47), 43 (15), 41 (30), 39 (10). Anal. calc. for $C_{21}H_{28}O_7S$ (424.52): C 59.42, H 6.65, S 7.55; found: C 59.24, H 6.62, S 7.52.

3. *Fragmentation of Monoacetal* **4** *with TosOH.* – 3.1. *(1R,2S)-1-Methyl-2-tosyloxypropyl 4-[(1'S)-2'-Methyl-3'-oxocyclohexyl]butyrate* (**16**). A suspension of $TosOH \cdot H_2O$ (85 mg, 0.447 mmol) and m.s. 5 Å (500 mg) in dry benzene (5 ml) was boiled 15 min under reflux before monoacetal **4** (92 mg, 0.365 mmol), dissolved in benzene (5 ml), was added. After boiling for 3 h under reflux (Ar), the mixture was worked up as above (*2.1*), and the crude product mixture was purified by chromatography (silica gel, hexane/Et_2O 1:1) yielding 14 mg (15%) of starting material **4** and 117 mg (75%) of ester **16**, mixture of epimers: *2'S(trans)*/*2'R(cis)* 3:1, according to ^{1}H-NMR. $[\alpha]_D = -11.9$ ($c = 1.85$, $CHCl_3$). IR ($CHCl_3$): 2935*m*, 2865*m*, 1725*s*, 1702*s*, 1597*m*, 1445*m*, 1363*s*, 1307*w*, 1288*w*, 1172*s*, 1133*w*, 1102*m*, 1090*m*, 1074*m*, 1018*w*, 997*w*, 980*m*, 959*w*, 913*s*, 886*w*, 832*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.01 (*d*, $J = 7$) and 1.04* (*d*, $J = 6.5$) (CH_3–C(2')); 1.17, 1.18*, and 1.24 (3*d*, $J = 6.5$, CH_3–C(1''), 3H–C(3'')); 1.0–2.7 (*m*, 14H); 2.45 (*s*, $CH_3C_6H_4SO_3$); 4.65–4.75 (*m*), 4.70* (*dq*, $J = 3$ and 6.5), 4.82–4.91 (*m*), and 4.86* (*dq*, $J = 3$ and 6.5) (H–C(1''), H–C(2'')); 7.3–7.4 and 7.74–7.86 (2*m*, *AA'BB'-system*, $J_{AB} \approx 8$, $CH_3C_6H_4SO_3$). MS(*di.*): 424 (0.2, M^+), 409 (0.1), 406 (0.1), 286 (0.3), 252 (2), 181 (5), 172 (19), 155 (9), 140 (50), 135 (31), 127 (69), 114 (92), 111 (81), 107 (27), 91 (96), 65 (27), *55* (100), 41 (36).

3.2. *Acid-Catalyzed Methanolysis of* **16**. A solution of **16** (109 mg, 0.257 mmol) and CH_3SO_3H (84 µl, 1.296 mmol) in CH_3OH (2 ml) was stirred for 16 h at r.t. (Ar). After quenching with 50 ml of sat. $NaHCO_3$-solution, the mixture was worked up with Et_2O. Chromatographic separation (silica gel, hexane/Et_2O 1:1) gave 23 mg (34%) of acetal (+)-**17**, 29 mg (53%) of (−)-**9**, mixture of epimers: *2'S(trans)*/*2'R(cis)* 37:63, according to GC (see *1.2*), $[\alpha]_D = -41.9°$ ($c = 1.36$, $CHCl_3$), and 53 mg (84%) of (−)-**13**, $[\alpha]_D = -11.0°$ ($c = 1.36$, $CHCl_3$).

Methyl (+)-4-[(1'S,2'R)-2'-Methyl-3',3'-dimethoxycyclohexyl]butyrate (**17**). $[\alpha]_D = +8.3°$ ($c = 0.963$, $CHCl_3$). IR (CCl_4): 2950*s*, 2860*m*, 2830*m*, 1740*s*, 1462*m*, 1445*m*, 1435*m*, 1420*w*, 1380*w*, 1360*m*, 1346*w*, 1307*w*, 1278*w*, 1240*m*, 1195*m*, 1176*m*, 1170*m*, 1158*m*, 1104*m*, 1087*m*, 1062*m*, 1051*s*, 980*w*, 934*m*, 900*w*, 874*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 0.78 (*d*, $J = 7$, CH_3–C(2')); 0.8–2.3 (*m*, 12H); 2.15–2.45 (*m*, *3 main signals*, 2H–C(2)); 3.14 (*s*, 2 CH_3O); 3.66 (*s*, CH_3OCO). MS: 226 (9, $M^+ - 32$), 211 (2), 195 (4), 194 (1), 183 (4), 151 (2), 140 (6), *125* (100), 119 (3), 111 (6), 105 (3), 98 (12), 93 (14), 86 (21), 79 (6), 67 (8), 55 (8), 45 (5), 41 (9).

3.3. *Hydrolysis of Acetal (+)-***17**. To a stirred suspension of silica gel (1 g) in 2 ml of CH_2Cl_2 H_2O (0.1 ml) was added. After 10 min acetal **17** (21 mg, 0.071 mmol) was added, dissolved in CH_2Cl_2 (2 ml), and stirring was continued for 23 h. Filtration *(Celite)*, evaporation of the filtrate, and chromatography (silica gel, hexane/Et_2O 1:1) of the residue gave 15 mg (87%) of ketone (−)-**9**: *2'S(trans)*/*2'R(cis)* 2:98, according to GC (see *1.2*). $[\alpha]_D = -52.4°$ ($c = 1.078$, $CHCl_3$).

3.4. *Analysis of Ester (−)-***9**. A solution of (−)-**9** (25 mg, 0.118 mmol, 37:63 epimer mixture) in CH_3OH (3 ml) was added to CH_3ONa/CH_3OH, obtained by reaction of Na (15 mg) with CH_3OH (2 ml). After stirring for 3 h at r.t. (Ar), the mixture was worked up with Et_2O. Chromatography (silica gel, hexane/Et_2O 2:1) gave 24 mg (96%) of (−)-**9**, mixture of epimers: *2'S(trans)/2'R(cis)* 78:22, according to GC (see *1.2*), $[\alpha]_D = -33.4°$ ($c = 0.84$, $CHCl_3$). A solution of (−)-**9** (22 mg, 0.104 mmol), butanediol **2** (12 µl, 0.132 mmol), and $TosOH \cdot H_2O$ (3 mg) in benzene (10 ml) was boiled under reflux at a *Dean-Stark* trap for 4 h. Usual workup and chromatography (silica gel, hexane/Et_2O 5:1) gave 29 mg (98%) of *methyl-4-[(2'R,3'R,7'R)-2',3',6'-Trimethyl-1',4'-dioxaspiro[4.5]dec-7-yl]butyrate* (**11**) containing *ca.* 2% **10** (see *below*), mixture of epimers: *6'R(cis)/6'S(trans)* 70:30[5])[7])[8]), according to GC (see *1.3*): t_R 7.8 min **11** (*6'S*) and **10** (*6'R*) 30%, t_R 8.7 min **10** (*6'S*) < 2%, t_R 8.8 min **11** (*6'R*) 68%. $[\alpha]_D = -35.4°$ ($c = 1.36$, $CHCl_3$). IR (CCl_4): 2970*m*, 2940*s*, 2930*s*, 2865*m*, 1739*s*, 1452*m*, 1436*m*, 1418*w*, 1375*m*, 1360*w*, 1345*w*, 1327*w*, 1288*m*, 1267*m*, 1250*m*, 1240*m*, 1200*m*, 1180*s*, 1167*s*, 1140*m*, 1096*s*, 1030*w*, 977*w*, 942*m*, 922*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.85 (*d*, $J = 7$) and 0.91* (*d*, $J = 6$) (CH_3–C(6')); 1.21* and 1.25* (*2d*, $J = 6$), 1.22 and 1.225 (*2d*, $J = 5.5$) (CH_3–C(2'), CH_3–C(3')); 0.9–1.88 (*m*, 12H); 2.18–2.40 (*m*, 2H–C(2)); 3.66* and 3.665 (*2s*, CH_3O–C(1)); 3.46–3.78 (*m*, H–C(2'), H–C(3')). MS: 284 (5, M^+), 255 (4), 253 (3), 241 (22), 211 (4), 197 (3), 183 (32), 141 (13), 139 (17), 135 (6), *127* (100), 114 (28), 111 (13), 95 (6), 83 (8), 81 (9), 79 (5), 69 (8), 67 (9), 56 (12), 55 (46), 43 (12), 41 (19).

3.5. *Derivatization of (−)-***13** *with Camphanic Chloride*. A solution of (−)-**13** (22 mg, 0.09 mmol), camphanic chloride (98 mg, 0.452 mmol), and 4-(dimethylamino)pyridine (12 mg) in pyridine (2 ml) was stirred for 22 h at r.t. (Ar). Workup as above (*2.5*) and chromatography (silica gel, pentane/CH_2Cl_2/Et_2O 20:20:3) gave 36 mg (94%) of **15**. $[\alpha]_D = -17.5°$ ($c = 1.36$, $CHCl_3$). IR, ^{1}H-NMR, and MS see *2.5*.

4. *Preparation of Reference Compounds*. – 4.1. *Acetalization of* (±)-**9** *with Butanediol* **2**. A solution of (±)-**9** (77 mg, 0.363 mmol), diol **2** (40 mg, 0.44 mmol), and $TosOH \cdot H_2O$ (5 mg) in benzene (20 ml) was treated as above (*1.3*) giving 98 mg (95%) of a 1:1 mixture of **10** and **11**, mixture of *cis/trans* 75:25, according to GC (see *above 1.3*): t_R 7.8 min (25%) **10** (*7'R,6'R*) and **11** (*7'S,6'S*), t_R 8.7 min (40%) **10** (*7'R,6'S*), and t_R 8.8 min (35%) **11** (*7'S,6'R*). Spectra of **10** (see *1.3*), spectra of **11** (see *3.4*).

4.2. *Tosylation of* meso-*2,3-butanediol* (**21**). TosCl (1.745 g, 9.15 mmol) was added to a cooled (0°) solution of diol **21** (546 mg, 6.06 mmol) in pyridine (20 ml). After stirring for 23 h at r.t. (Ar), the mixture was poured to 100 ml of 1N HCl and worked up with CH_2Cl_2. The org. phases were washed with 1N HCl, sat. $NaHCO_3$- and NaCl-solution. Chromatographic separation (silica gel, Et_2O/hexane 2:1) of the products gave 502 mg (21%) of ditosylate **20** and 898 mg (60%) of monotosylate (±)-**13**, spectra of **13** see *2.2*.

meso-*Dimethylethylene Di-*p-*toluenesulfonate* (**20**). M.p. 96° (Et_2O). IR ($CHCl_3$): 2985*w*, 2930*w*, 2860*w*, 1597*m*, 1492*w*, 1445*w*, 1364*s*, 1306*w*, 1289*w*, 1172*s*, 1086*m*, 1072*m*, 1018*m*, 990*m*, 978*m*, 936*m*, 902*s*, 850*m*. ^{1}H-NMR (100 MHz, $CDCl_3$): 1.21 (*d*, $J = 6$, CH_3–C(1), CH_3–C(2)); 2.42 (*s*, $2CH_3C_6H_4SO_3$); 3.46–3.66 (*m*, H–C(1), H–C(2)); 7.16–7.38 and 7.56–7.78 (*2m*, $2CH_3C_6H_4SO_3$). MS: 398 (4, M^+), 344 (0.7), 326 (0.6), 314 (0.8), 310 (8), 229 (1), 288 (1), 280 (2), 273 (3), 262 (5), 228 (2), 227 (4), 226 (3), 199 (10), 186 (6), 157 (7), 156 (10), *155* (100), 139 (6), 119 (4), 107 (5), 92 (10), 91 (83), 77 (5), 74 (14), 65 (17), 59 (22), 55 (7), 54 (13), 53 (9), 51 (7), 45 (21), 44 (16), 43 (17), 41 (9), 39 (17). Anal. calc. for $C_{18}H_{22}O_6S_2$ (398.50): C 54.25, H 5.56, S 16.09; found: C 54.29, H 5.55, S 15.87.

4.3. *(−)-(1*R,*2*R*)-2-Hydroxy-1-methylpropyl* p-*Toluenesulfonate* (**18**). TosCl (1.192 g, 6.23 mmol) was added to a cooled (0°) solution of diol **2** (374 mg, 4.15 mmol) in pyridine (20 ml). After stirring for 23 h at r.t. (Ar), the mixture was worked up with CH_2Cl_2. The org. layers were washed with 1N HCl (2×), sat. $NaHCO_3$-, and NaCl-solution. Chromatography (silica gel, Et_2O/hexane 2:1) yielded 408 mg (24%) of ditosylate **19** and 559 mg (55%) of (−)-**18**. $[\alpha]_D = -6.6°$ ($c = 2.17$, $CHCl_3$). IR ($CHCl_3$): 3600*m*, 3660–3300*w*, 2990*w*, 2935*w*, 2880*w*, 1600*w*, 1492*w*, 1447*w*, 1360*s*, 1309*w*, 1292*w*, 1190*m*, 1176*s*, 1108*m*, 1098*m*, 1030*m*, 1020*m*, 990*w*, 925*m*, 902*s*, 832*w*, 815*w*. ^{1}H-NMR (100 MHz, $CDCl_3$): 1.12 and 1.23 (*2d*, $J = 6$, CH_3–C(1), 3H–C(3)); 2.12 (br. *s*, $W_{1/2} \approx 3$, *exchangeable with* D_2O, OH); 2.42 (*s*, $CH_3C_6H_4SO_3$); 3.70 (*quint.*, $J = 6$, H–C(2)); 4.46 (*quint.*, $J = 6$, H–C(1)); 7.2–7.44 and 7.65–7.9 (*2m, AA'BB'-system*, $J_{AB} \approx 8$, $CH_3C_6H_4SO_3$). MS (*di.*): 228 (11, $M^+ - 16$), 227 (1), 200 (20), 172 (4), 156 (49), 155 (72), 139 (3), 108 (7), 107 (8), 93 (5), 92 (55), *91* (100), 77 (4), 72 (12), 65 (25), 45 (27), 43 (41), 39 (10).

4.4. *Preparation of (+)-***14**. A mixture of **2** (236 mg, 2.62 mmol), AcOH (171 mg, 2.85 mmol), and $TosOH \cdot H_2O$ (499 mg, 2.62 mmol in benzene (20 ml) was boiled under reflux at a *Dean-Stark* trap for 5 h (Ar). The cooled mixture was added to sat. $NaHCO_3$-solution and worked up with Et_2O. Chromatography (silica gel, hexane/Et_2O 1:1) gave 579 mg (77%) of (+)-**14**. $[\alpha]_D = +21.2°$ ($c = 1.71$, $CHCl_3$). Analytical data see *2.4*.

4.5. *Preparation of (−)-***13**. A solution of acetate (+)-**14** (218 mg, 0.76 mmol) and CH_3SO_3H (0.25 ml, 3.86 mmol) in CH_3OH (5 ml) was stirred for 19 h at r.t. (Ar). The reaction was quenched by the addition to 50 ml of

sat. $NaHCO_3$-solution and worked up with Et_2O. Chromatography (silica gel, Et_2O/hexane 3:1) gave 173 mg (93%) of (−)-**13**. $[\alpha]_D = -11.0°$ ($c = 1.80$, $CHCl_3$). Analytical data see *2.2.*

4.6. *Preparation of Camphanate* **15**. A solution of diol **2** (260 mg, 2.89 mmol), camphanic acid (589 mg, 3.02 mmol), and $TosOH \cdot H_2O$ (536 mg, 2.82 mmol) in benzene (20 ml) was boiled under reflux at a *Dean-Stark* trap for 5 h (Ar). The reaction mixture was poured to sat. $NaHCO_3$-solution and worked up with CH_2Cl_2. Chromatography (silica gel, Et_2O/hexane 2:1) of the crude product (1.088 g) gave 1.015 g (82%) of **15**. $[\alpha]_D = -17.9°$ ($c = 1.60$, $CHCl_3$). Analytical data see *2.5.*

5. *Experiments with 2,2-Dimetylpropylen Acetals.* – 5.1. *(±)-(9-Methyl-*cis*-8-decalone)-1-spiro-2'-(5',5'-dimethyl-1',3'-dioxane)* (**25**). A mixture of dione **1** [1] [24] (173 mg, 0.961 mmol), 2,2-dimethyl-1,3-propanediol (104 mg, 1.0 mmol), $TosOH \cdot H_2O$ (12 mg), and m.s. 5 Å (500 mg) in benzene (5 ml) was stirred for 15 h at r.t. (Ar). After separation of the sieves by filtration *(Celite)*, the reaction mixture was added to sat. $NaHCO_3$-solution and worked up with Et_2O. Chromatography (silica gel, hexane/Et_2O 2:1) yielded 240 mg (93%) of monoacetal (±)-**25**. M.p. 138° (Et_2O/pentane). IR (CCl_4): 2950*s*, 2930*s*, 2860*s*, 1700*s*, 1467*m*, 1445*m*, 1414*w*, 1393*m*, 1377*m*, 1363*m*, 1349*w*, 1336*m*, 1320*m*, 1279*m*, 1271*m*, 1250*w*, 1238*m*, 1216*w*, 1204*w*, 1181*m*, 1161*m*, 1147*m*, 1118*s*, 1105*s*, 1094*s*, 1082*s*, 1061*m*, 1037*w*, 1014*m*, 972*w*, 955*m*, 912*m*, 885*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.69 and 1.05 (2*s*, $(CH_3)_2$–C(5')); 1.35 (*br.*, $W_{1/2} \approx 5$, CH_3–C(9)); 1.2–2.8 (*m*, 13H); 3.28 and 3.36 (2*dd*, $J = 11.5$ and 2.5, H_{eq}–C(4'), H_{eq}–C(6')); 3.63 and 3.70 (2*d*, $J = 11.5$, H_{ax}–C(4'), H_{ax}–C(6')). MS: 266 (14, M^+), 251 (1), 238 (3), 237 (5), 223 (3), 210 (2), 195 (3), 184 (4), 182 (4), 181 (8), 180 (5), 169 (7), 154 (63), 152 (8), 141 (66), *128* (100), 124 (21), 111 (17), 109 (13), 95 (8), 83 (7), 82 (10), 81 (13), 79 (9), 69 (40), 67 (13), 55 (30), 53 (9), 43 (13), 41 (42), 39 (12). Anal. calc. for $C_{16}H_{26}O_3$ (266.37): C 72.14, H 9.84; found: C 72.19, H 9.87.

5.2. *(±)-(9-Methyl-*trans*-8-decalone)-1-spiro-2'-(5',5'-dimethyl-1',3'-dioxane)* (**26**). A mixture of *trans*-dione **27** (296 mg, 1.644 mmol), 2,2-dimethyl-1,3-propanediol (180 mg, 1.728 mmol), $TosOH \cdot H_2O$ (15 mg), and m.s. 5 Å (840 mg) in benzene (5 ml) was stirred for 15 h at r.t. (Ar). The mixture was filtered *(Celite)*, added to sat. $NaHCO_3$-solution, and worked up with Et_2O. Chromatography (silica gel, hexane/Et_2O 2:1) gave 415 mg (94%) of (±)-**26**. IR (CCl_4): 2950*s*, 2930*s*, 2860*s*, 1716*s*, 1470*m*, 1437*m*, 1394*m*, 1365*m*, 1347*w*, 1333*w*, 1313*w*, 1288*m*, 1257*m*, 1217*w*, 1185*m*, 1169*m*, 1136*m*, 1106*s*, 1092*m*, 1071*m*, 1057*w*, 1043*m*, 1021*m*, 1002*w*, 991*m*, 960*w*, 941*w*, 916*m*, 869*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.71 and 1.16 (2*s*, $(CH_3)_2$–C(5')); 1.31 (*s*, CH_3–C(9)); 1.1–1.64 (*m*, 7H); 1.68–1.94 (*m*, 2H); 2.30–2.58 (*m*, 3H); 2.67 (*d*, $J \approx 14$, *additional splitting*, H_{eq}–C(7)); 3.32 and 3.43 (2*dd*, $J = 11.5$ and 2.5, H_{eq}–C(4'), H_{eq}–C(6')); 3.62 and 3.73 (2*d*, $J = 11.5$, H_{ax}–C(4'), H_{ax}–C(6')). MS: 266 (13, M^+), 251 (1), 238 (3), 237 (6), 223 (3), 195 (4), 184 (6), 182 (4), 181 (6), 180 (5), 169 (10), 154 (66), 142 (43), 141 (69), 137 (6), *128* (100), 124 (10), 111 (7), 109 (9), 95 (7), 83 (8), 82 (8), 81 (12), 79 (7), 69 (41), 67 (12), 55 (27), 43 (10), 41 (36), 39 (10). Anal. calc. for $C_{16}H_{26}O_3$ (266.37): C 72.14, H 9.84; found: C 72.03, H 9.82.

5.3. *(±)-3-Mesyloxy-2,2-dimethylpropyl 4-(2'-Methyl-3'-oxocyclohexyl)butyrate* (**28**). A solution of monoacetal **26** (76 mg, 0.285 mmol) and CH_3SO_3H (22 µl, 0.34 mmol), in benzene (5 ml) containing m.s. 5 Å (500 mg) was boiled under reflux for 3 h (Ar). The mixture was added to sat. $NaHCO_3$-solution and worked up with Et_2O. Chromatography (silica gel, Et_2O/hexane 3:1) gave 73 mg (70%) of (±)-**28**, mixture of C(1')/C(2')-epimers. IR ($CHCl_3$): 2935*m*, 2865*m*, 1722*s*, 1700*s*, 1455*m*, 1445*m*, 1355*s*, 1340*s*, 1168*s*, 1085*w*, 978*m*, 956*s*, 827*m*. ^{1}H-NMR (100 MHz, $CDCl_3$): 0.99 (*s*, $(CH_3)_2$–C(2'')); 0.9–1.2 (*signals of* CH_3–C(2')); 0.8–2.6 (*m*, 14H); 2.99 (*s*, CH_3SO_3); 3.90 and 3.99 (2*m*, $W_{1/2} \approx 3$, 2H–C(1''), 2H–C(3'')). MS (*di.*): 362 (1, M^+), 347 (1), 344 (1), 267 (1), 253 (2), 251 (1), 224 (5), 181 (15), 163 (10), 152 (5), 151 (6), 137 (6), 135 (33), 128 (11), 124 (6), 123 (5), *111* (100), 97 (5), 95 (6), 93 (5), 83 (7), 82 (5), 81 (9), 79 (9), 69 (34), 68 (6), 67 (9), 56 (10), 55 (35), 41 (29), 39 (6).

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