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The Zirconium Alkoxide-Catalyzed Aldol-Tishchenko Reaction of Ketone Aldols

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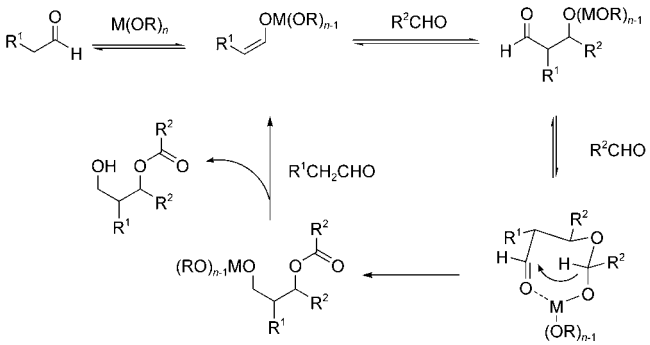
Abstract: The aldol-Tishchenko reaction of ketone aldols as enol equivalents has been developed as an efficient strategy to furnish differentiated 1,3-*anti*-diol monoesters in one step. The thermodynamically unstable ketone aldols undergo a facile retro-aldolization to yield a presumed zirconium enolate in situ, which then undergoes the aldol-Tishchenko reaction in typically high yields and with complete 1,3-*anti* diastereocontrol. Evaluation of a broad range of metal alkoxides as catalysts and optimization of the reaction protocol led to a modified zirconium alkoxide catalyst with attenuated Lewis acidity and dichloromethane as solvent, which resulted in suppression of the undesired acyl migration to a large extent. Various ketone aldols have been prepared and subjected to the general process, giving rise to a broad range of differently substituted 1,3-*anti*-diol monoesters, which may be hydrolyzed to the corresponding 1,3-*anti*-diols.

Keywords: alcohols · aldol reaction · diastereoselectivity · Tishchenko reduction · zirconium

Introduction

Since the pioneering studies of Nord et al.[1] more than six decades ago the aldol-Tishchenko reaction has occupied a prominent position in organic chemistry as a highly effective method to couple unactivated carbonyl compounds giving rise to 1,3-diol monoesters.[2] The classic reaction is composed of a base-induced enolization of one carbonyl compound, typically an aldehyde, and subsequent aldol addition to another aldehyde equivalent, furnishing a metal aldolate, which upon reaction with a third aldehyde equivalent, forms a hemiacetal metal alkoxide. This in turn transfers the hemiacetal hydrogen atom in a cyclic arrangement to the carbonyl moiety, eventually resulting in reduction of the carbonyl group and oxidation of the hemiacetal to the ester moiety (Scheme 1). The rate-determining step of this sequence is believed to be the Tishchenko reduction of the hemiacetal metal alkoxide after a fast and reversible aldolization step.



Scheme 1. Mechanism of the classic aldol-Tishchenko reaction.

This proposal has, however, only been substantiated kinetically for reactions of lithium ketone enolates.[3]

An appealing feature of this transformation is the domino-type[4] reaction pathway with a catalyst that promotes both the aldol reaction through enolization of the carbonyl compound and the Tishchenko reduction of the aldol intermediate. Subsequently, this general scheme has been steadily improved in terms of efficiency and selectivity. Initially, the reaction was mainly restricted to the coupling of three identical aldehydes with either aluminium ate complexes of the general formula $Mg[Al(OR)_4]_2$ or regular magnesium and calcium alkoxides as catalysts in a homo aldol-Tishchenko reaction.[1] Later preformed lithium ketone enolates were shown to add to two equivalents of an aldehyde,

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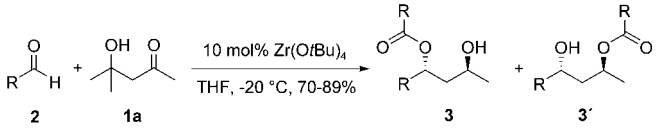
furnishing cross aldol-Tishchenko products with exceptional levels of diastereoselectivity.[5] Mahrwald et al. established a catalytic cross aldol-Tishchenko reaction of unmodified ketones and aldehydes to yield 1,3-diol monoesters with high stereoselecitvity.[6] Additionally, silyl enolates with Lewis acid activation,[7] zinc,[8] and samarium enolates[9] have been employed in stoichiometric cross aldol-Tishchenko reactions. Morken et al. have systematically investigated simple metal alkoxides for a catalytic cross aldol-Tishchenko reaction of unmodified ketones and aldehydes, revealing NaO*t*Bu and LiO*i*Pr as optimal catalysts.[10] Subsequently, the same group showed that a chiral yttrium–salen complex was capable of catalyzing a moderately enantioselective cross aldol-Tishchenko reaction between two different aldehydes.[11] Very recently, Shibasaki and co-workers discovered a chiral lanthanum–lithium–BINOLate complex, which gave rise to a highly enantioselective cross aldol-Tishchenko reaction of aryl alkyl ketones and aldehydes in good yields.[12] Independently, Mlynarski and Mitura reported chiral aldol-Tishchenko reactions between ketones and aldehydes catalyzed by a ytterbium alkoxide.[13]

In 2001, Nevalainen et al.[14] and we[15] independently established cross aldol-Tishchenko reactions of ketone aldols, such as diacetone alcohol (**1a**), and aldehydes **2** with either Al- or Zr-based catalysts, respectively. Zr(O*t*Bu)$_4$ was shown to be the catalyst of choice in our process and catalyzed a rapid retro-aldol cleavage of **1a**, furnishing a ketone enolate in situ, which underwent the aldol-Tishchenko reaction with aliphatic aldehydes. 1,3-*anti*-diol monoesters **3** were obtained in typically good yields and with complete *anti* diastereoselectivity (Scheme 2). Other Ti or Zr alkoxides



2 **1a** **3** **3′**

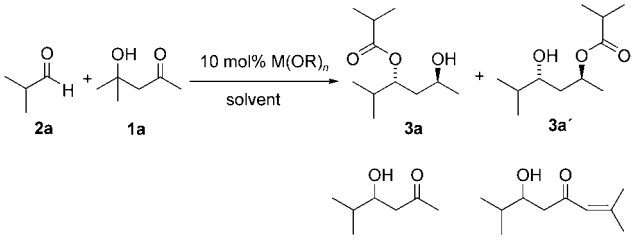
Scheme 2. Zr(O*t*Bu)$_4$-catalyzed aldol-Tishchenko reaction with diacetone alcohol (**1a**) as enol equivalent.

proved less effective in this reaction. Subsequently we reported the first catalytic, enantioselective aldol-Tishchenko reaction according to this general scheme employing Zr–TADDOLates as chiral catalysts.[16] A major drawback of our initial protocol was the undesired acyl migration that took place especially with straight-chain aliphatic aldehydes and furnished regioisomeric mixtures of 1,3-diol monoesters. Herein we present a full account of our work on the Zr-catalyzed aldol-Tishchenko reaction of a broad range of ketone aldols and aldehydes. Among the factors that have been investigated were optimization of catalyst, solvent, temperature, and ketone aldol structure. In particular, a specifically designed Zr alkoxide with attenuated Lewis acidity has been developed as catalyst, which suppressed the undesired acyl migration to a large extent.

Results and Discussion

Survey of metal alkoxides as catalysts: Our initial discovery that Zr(O*t*Bu)$_4$[17] effectively catalyzed the aldol-Tishchenko reaction between diacetone alcohol and a number of aliphatic aldehydes prompted us to test the catalytic activity of a range of metal alkoxides for this process. Thus, we chose the reaction between diacetone alcohol (**1a**) and isobutyraldehyde (**2a**) (3 equiv) as our model reaction to evaluate different metal alkoxides at a 10 mol% level (Table 1).

Table 1. Evaluation of different metal alkoxides for the aldol-Tishchenko reaction of diacetone alcohol (**1a**) and isobutyraldehyde (**2a**).[a]



2a **1a** **3a** **3a′** **4** **5**

Entry	M(OR)$_n$[h]	*T* [°C]	Solvent	*t* [h]	Yield[b,c] **3a**/**3a′** [%]	Yield[c] **4** [%]	Yield[c] **5** [%]
1	Zr(O*t*Bu)$_4$	0	CH_2Cl_2	2	84[e]		
2	Hf(O*t*Bu)$_4$	−20	THF	17	64		
3	Zr(O*i*Pr)$_4$	0	THF	24	5		
4	Ti(O*i*Pr)$_4$	RT	CH_2Cl_2	24	0	12	
5	Ti(O*t*Bu)$_4$	RT	CH_2Cl_2	24	5	14	
6	$Y_5O(OiPr)_{13}$[g]	−20	CH_2Cl_2	1	89[d,f]		
7	Mg*n*Bu$_2$	0	THF	2	68	12	
8	ZnEt$_2$	0	THF	24	9	28	
9	LiO*t*Bu	0	THF	3	2	22	
10	NaO*t*Bu	0	THF	3	0	43	19
11	KO*t*Bu	0	THF	3	0	66	18

[a] Reaction conditions: **1a** (1 equiv), **2a** (3 equiv), and M(OR)$_n$ or MR$_2$ (10 mol%), respectively, in the given solvent (4 mL per mmol of **1a**). [b] Combined yield of **3a** and **3a′**, which were isolated as a mixture, the ratios of regioisomers were not detected unless otherwise noted (entries 1 and 6). [c] Isolated yield of chromatographed and analytically pure compounds. [d] 8% of the *syn*-isomer of **3a** (as a mixture of regioisomers) were isolated additionally. [e] Ratio **3a**/**3a′** = 11:1. [f] Ratio **3a**/**3a′** = 10:1. [g] 2 mol% of $Y_5O(OiPr)_{13}$ was used to achieve a 10 mol% level based on "Y(OR)$_3$". [h] In the case of Mg*n*Bu$_2$ and ZnEt$_2$ (entries 7 and 8), in situ formation of M(OR)$_2$ through reaction with diacetone alcohol is assumed.

The use of Zr(O*t*Bu)$_4$ in dichloromethane at 0°C furnished the desired 1,3-*anti*-diol monoester **3a**/**3a′** in 84% yield as a 11:1 mixture of regioisomers after 2 h (entry 1). Not unexpectedly, Hf(O*t*Bu)$_4$ smoothly catalyzed this transformation too, giving rise to **3a**/**3a′**, albeit only in 64% yield after 17 h at −20°C (entry 2). In contrast, Zr(O*i*Pr)$_4$ gave only 5% of the aldol-Tishchenko product **3a**/**3a′** (entry 3). This discrepancy between the two zirconium alkoxides most probably originates from different aggregation states. Whereas the former tends to form oligomers,[18] the latter is known to exist as a tetrahedral and highly reactive monomer.[19] In the presence of either Ti(O*i*Pr)$_4$ or Ti(O*t*Bu)$_4$, no or only little formation of **3a**/**3a′** could be observed even

after 24 h at room temperature along with small amounts of the intermediate aldol product **4** (entries 4, 5). Apparently Ti^{IV} alkoxides display diminished Brønstedt basicity as well as Lewis acidity relative to Zr^{IV} alkoxides and fail to induce a rapid retro-aldol cleavage of **1a**. Late transition metals such as Zn^{II} also exhibited poor reactivity in this process, as one might have expected on the basis of the known stability of Zn–aldolates in enzymatic as well as chemical processes.[20] $[Y_5O(OiPr)_{13}]$ (2 mol%) proved to be a very potent catalyst furnishing 1,3-*anti*-diol monoester **3a**/**3a**′ (10:1 mixture) in 89% yield after just 1 h at −20°C . However, in this particular case we additionally isolated 8% of the *syn* diastereomers of **3a**/**3a**′ (entry 6). Accordingly, we did not evaluate this catalyst further as a promising alternative for Zr alkoxides.

Alkali metal alkoxides MO*t*Bu (M = Li, Na, K) were able to catalyze the retro-aldol process, but gave only low to moderate yields of aldol product **4**, along with some aldol condensation product **5** (entries 9–11). Only LiO*t*Bu yielded trace amounts of aldol-Tishchenko product **3a**/**3a**′. Finally, Bu_2Mg catalyzed our model aldol-Tishchenko reaction and furnished **3a**/**3a**′ in 68% yield along with 12% of aldol product **4**, indicating an incomplete Tishchenko reduction step in this process (entry 7). Thus, among the examined metal alkoxides $Zr(OtBu)_4$ was identified as the catalyst of choice in terms of yield and selectivity for our process.

Optimization of the solvent: The effect of solvent on the yield and the regioisomeric ratio with $Zr(OtBu)_4$ as catalyst was studied again in our model reaction between diacetone alcohol (**1a**) and isobutyraldehyde (**2a**) (Table 2). Dichloromethane (84% yield, 11:1 ratio of regioisomers) proved to be the solvent of choice (entry 1). Etheral solvents, such as THF and diethyl ether, gave rise to comparable yields, albeit in lower regioisomeric selectivities (entries 2, 3). The same holds true for noncoordinating solvents, such as toluene (entry 4). Among the polar aprotic solvents, DMF furnished the product with very good regioisomeric ratio of 14:1 ratio, but in only moderate yield of 55% (entry 5). Acetonitrile apparently facilitated the acyl migration and gave rise to a 1:1 mixture of regioisomers in good yield (entry 6). Chloroform was not suitable as solvent, due to deprotonation of the acidic proton by the highly basic catalyst. Only trace amounts of product could be isolated in this reaction.

Table 2. Optimization of solvent in reaction **1a** and **2a**.[a]

Entry	Solvent	Yield[b] **3a**/**3a**′ [%]	Ratio[c] **3a**/**3a**′
1	CH_2Cl_2	84	11:1
2	THF	84	5:1
3	Et_2O	90	5:1
4	toluene	87	6:1
5	DMF	55	14:1
6	MeCN	84	1:1
7	$CHCl_3$	trace	–

[a] Reaction conditions: **1a** (1 equiv), **2a** (3 equiv), and $Zr(OtBu)_4$ (10 mol%) in the given solvent (4 mL per mmol of **1a**), 0°C, reaction time 2 h. [b] Combined yield of **3a**/**3a**′, which were isolated as a mixture. [c] Determined by ^{1}H NMR spectroscopy.

Effect of the temperature: In our effort to suppress the undesired acyl migration leading to mixtures of regioisomeric 1,3-*anti*-diol monoesters **3a**/**3a**′, we attempted to gradually decrease the reaction temperature and hoped for a beneficial effect on the regioisomeric ratio (Table 3). Compared to our initial experiment at 0°C (2 h, 84% yield, regioisomeric ratio 11:1), the reaction at −20°C required 4 h for complete conversion and furnished the product **3a**/**3a**′ in comparable yield and regioisomeric ratio (entry 2). Remarkably, the reaction also proceeded at −50°C; however, the rate of the reaction became so slow that the product was obtained in only 55% yield after 24 h (entry 3). Still, the regioisomeric ratio was improved to 16:1. Further decreasing the reaction temperatures to −65 and −78°C resulted in very slow reactions and negligible yields (5% and 0%, respectively) after prolonged reaction times. This indicates a very slow retro-aldol cleavage at these temperatures (entries 4 and 5). In conclusion, best results were obtained at convenient 0°C in short reaction time.

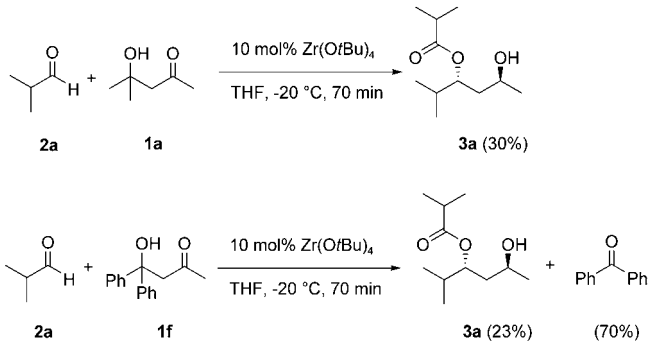
Table 3. Optimization of temperature in reaction **1a** and **2a**.[a]

Entry	*T* [°C]	*t* [h]	Yield **3a**/**3a**′ [%][b]	Ratio[c] **3a**/**3a**′
1	0	2	84	11:1
2	−20	4	87	10:1
3	−50	24	55	16:1
4	−65	40	5	–
5	−78	24	0	–

[a] Reaction conditions: **1a** (1 equiv), **2a** (3 equiv), and $Zr(OtBu)_4$ (10 mol%) in CH_2Cl_2 (4 mL per mmol of **1a**). [b] Combined yield of **3a**/**3a**′ isolated as a mixture. [c] Determined by ^{1}H NMR spectroscopy.

Variation of the ketone aldol structure: In an effort to further speed up the retro-aldol cleavage we prepared the mixed aldol of acetone and benzophenone **1f**[21] and employed it in the reaction with isobutyraldehyde (**2a**) under otherwise identical conditions. We expected a much faster retro-aldol reaction of **1f** on the basis of the highly conjugated byproduct benzophenone and hence reduced reaction times. When the reaction of diacetone alcohol (**1a**) and **2a** was stopped after just 70 min at −20°C, product **3a** was isolated in only 30% yield. On the other hand, the benzophenone-based ketone aldol **1f** was completely consumed in reaction with **2a** after 70 min at −20°C, but yielded only 23% of product **3a** along with minor amounts of aldol product **4**. Interestingly, the byproduct benzophenone was isolated in 70% yield instead (Scheme 3). It appears that retro-aldol cleavage of **1f** is rapid indeed, but this does not give rise to a productive reaction pathway.

Optimization of the alkoxide ligands: Recently, we reported the first enantioselective version of the title reaction using the chiral tartaric acid derived TADDOL **6** (α,α,α′,α′-tetra-



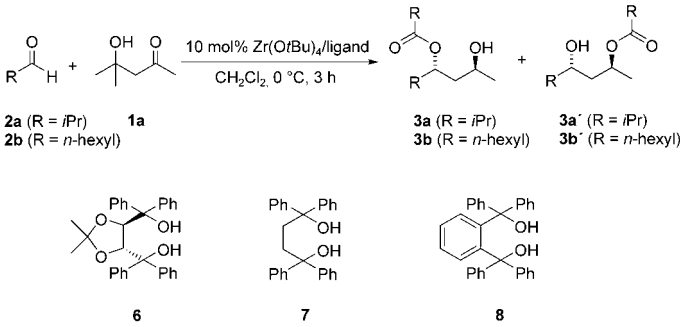
Scheme 3. Variation of ketone aldol structure.

Table 4. Evaluation of alkoxide ligands.[a]

Entry	Ligand	R	Products	Yield[b] [%]	Ratio[c] **3/3′**
1	none	*i*Pr	**3a/3a′**	84	11:1
2	none	*n*-hexyl	**3b/3b′**	72	1:1
3	**7**	*i*Pr	**3a/3a′**	26	20:1
4	**7**	*n*-hexyl	**3b/3b′**	31	20:1
5	**8**	*i*Pr	**3a/3a′**	79	20:1
6	**8**	*n*-hexyl	**3b/3b′**	91	5:1

[a] Reaction conditions: The modified catalyst was prepared by stirring a solution of ligand (0.10 mmol) and $Zr(OtBu)_4$ (0.10 mmol) in CH_2Cl_2 (4 mL) for 0.5 h at RT. To this solution **1a** (1.0 mmol) and **2a** (3.0 mmol) were added at 0 °C. [b] Combined yield of **3/3′** isolated as a mixture. [c] Determined by ^1H NMR spectroscopy.

phenyl-2,2-dimethyl-1,3-dioxolane-4,5-dimethanol) as ligand for Zr.[16] In the course of these studies we found much improved regioisomeric ratios with the chiral Zr–TADDOLates as catalysts, indicating that they exerted attenuated Lewis acidity relative to $Zr(OtBu)_4$ that resulted in suppression of the undesired acyl migration to a large extent. Inspired by these results we decided to prepare simple achiral bulky diols **7** and **8** structurally similar to the TADDOL **6** in order to study their effect on the regioselectivity of the aldol-Tishchenko reaction (Scheme 4).



Scheme 4. Optimization of alkoxide ligands.

The diols **7**[22] and **8**[23] were readily available in one step through Grignard addition of phenyl magnesium bromide to inexpensive succinic acid dimethyl ester and phthalic acid dimethyl ester, respectively. In our preliminary studies we found that the degree of acyl migration was dependent on the steric bulk of the acyl group of the 1,3-diol monoesters **3/3′**, with straight-chain acyl groups being more readily transferred than α-branched acyl groups. Thus, we chose isobutyraldehyde (**2a**) as a representative α-branched aldehyde and *n*-heptanal (**2b**) as a representative straight-chain aldehyde, and conducted aldol-Tishchenko reactions of **1a** with these two aldehydes under two sets of reaction conditions. In the first set, $Zr(OtBu)_4$ and diol **7** (10 mol% each) were dissolved in CH_2Cl_2 at 0 °C and used as catalyst, whereas in the second set $Zr(OtBu)_4$ and diol **8** (10 mol% each) were combined analogously and employed as catalyst. Subsequently, we compared these results with the $Zr(OtBu)_4$-catalyzed reactions (Table 4).

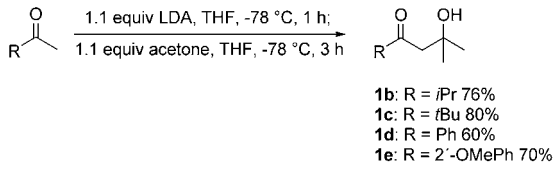
The $Zr(OtBu)_4$-catalyzed reaction of **1a** and **2a** yielded 1,3-*anti*-diol monoester **3a/3a′** in 84% yield as a 11:1 mixture of regioisomers as mentioned above, whereas *n*-heptanal furnished the corresponding product **3b/3b′** in 72% yield as a 1:1 mixture of regioisomers indicating a very rapid acyl migration process in this system (entries 1 and 2). When $Zr(OtBu)_4$ (10 mol%) was stirred with diol **7** (10 mol%) in CH_2Cl_2 for 30 min at room temperature, a presumed complex between $Zr(OtBu)_4$ and diol **7** was formed that gave rise to **3a/3a′** within 3 h at 0 °C in low yield, but excellent regioselectivity of 20:1 (entry 3). An even more striking example constituted the reaction of **1a** and **2b** catalyzed by the same catalyst combination yielding **3b/3b′** in low yield, but drastically improved regioselectivity of again 20:1 (by ^1H NMR spectroscopy; entry 4). We assume that the reason for the low reactivity of the complex formed from $Zr(OtBu)_4$ and diol **7** is the conformational flexibility of the ligand, which is different from the TADDOL-type ligands. Accordingly, we switched to the conformationally more rigid diol **8** and formed the corresponding zirconium complex as described above.

Indeed, aldol-Tishchenko reaction of **1a** and **2a** catalyzed by $Zr(OtBu)_4$/diol **8** (10 mol% each) gave rise to **3a/3a′** in 79% yield and with an excellent regioisomeric ratio of 20:1 (entry 5). In the more difficult conversion of **1a** with *n*-heptanal (**2b**), this modified catalyst led to formation of 1,3-*anti*-diol monoesters **3b/3b′** in 91% yield with an improved regioisomeric ratio of 5:1 (entry 6). Apparently, the $Zr(OtBu)_4$/diol **8** complex retained the high catalytic activity of the parent $Zr(OtBu)_4$ and still suppressed the undesired acyl migration almost completely in reaction with α-branched aldehydes and largely with straight-chain aldehydes.

Thus, we have established a modified protocol for the Zr alkoxide-catalyzed aldol-Tishchenko reaction of ketone aldols, which comprises the use of $Zr(OtBu)_4$ and diol **8** as catalyst (10 mol% each) in CH_2Cl_2 as solvent at 0 °C. This new protocol has now been applied to reactions of different ketone aldols **1** and aldehydes **2** in the synthesis of a broad range of 1,3-*anti*-diol monoesters **3**.

Preparation of ketone aldols 1: The ketone aldols **1b–e** were prepared by enolization of the corresponding methyl ketones pinacolone, isopropyl methyl ketone, acetophenone

and (2′-methoxy)acetophenone, respectively, with LDA at −78 °C and subsequent aldolization with acetone. This procedure gave rise to the ketone aldols **1b–e** in yields between 60 and 80 % (Scheme 5).



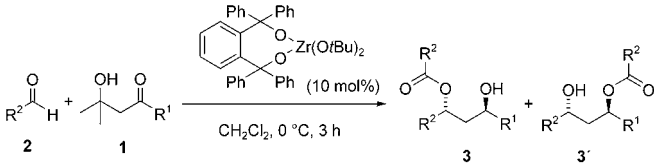
Scheme 5. Preparation of ketone aldols **1b–e**

Scope of the aldol-Tishchenko reaction: According to the optimized reaction conditions discussed above, ketone aldols **1** were treated with aliphatic aldehydes **2** (3 equiv) in dichloromethane at 0 °C for 3 h, giving rise to a broad range of 1,3-*anti* diol monoesters **3**. The results are summarized in Table 5. Generally good to excellent yields were obtained ranging between 70 and 94 %. Straight-chain aldehydes like *n*-heptanal and 3-methyl butyraldehyde, as well as α-branched aldehydes (e.g. isobutyraldehyde, 2-ethyl butyraldehyde) and cyclic aldehydes (cyclohexane carbaldehyde, cyclopropane carbaldehyde) were successfully employed in these transformations. Only pival aldehyde, as a sterically very hindered aliphatic aldehyde, failed to undergo the aldol-Tishchenko reaction, and the reaction stopped at the aldol stage. This same behavior was observed for aromatic and α,β-unsaturated aldehydes, which all gave the intermediate aldol products as major products. Apparently, they are not suitable hydrogen donors in our Zr-catalyzed Tishchenko reduction, which is in contrast to the SmI_2-catalyzed Tishchenko reduction pioneered by Evans et al. in which benzaldehyde is routinely employed as reductant.[24] We found, however, that pinacolone-derived ketone aldol **1c** reacted smoothly with benzaldehyde under these conditions, furnishing 1,3-*anti*-diol monoester **3i** in 86 % yield (entry 9).

The degree of acyl migration clearly depended on the steric demand of the acyl group. For α-branched acyl groups and cyclic acyl groups, respectively, the transesterification process was slow, furnishing the products **3**/**3′** in excellent 20:1 ratio in most cases (entries 1, 3, 4, 5, 9, 10, 11). In reactions with *n*-heptanal as acceptor, the straight-chain acyl group in the products **3**/**3′** was transferred more rapidly leading to regioisomeric mixtures of 5:1 to 15:1 (see entries 2, 12, 14).

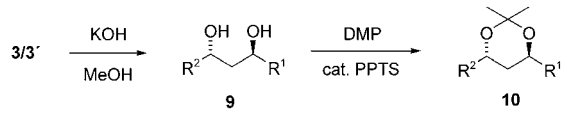
Assignment of relative configuration of aldol-Tishchenko products 3/3′: For the determination of their relative stereochemistry, all products **3**/**3′** were hydrolyzed with KOH in methanol to the corresponding diols **9**, whose ^{1}H NMR and ^{13}C NMR spectra proved their diastereomeric purity (≥97:3). Subsequently, diols **9** were transformed to their corresponding acetonides **10** by acid-catalyzed transacetalization in 2,2-dimethoxypropane. The analysis of the ^{13}C NMR spectra of **10** revealed their 1,3-*anti* stereochemistry according to the method developed by Rychnovsky[25] (Scheme 6). 1,3-*anti*-Diol acetonides adopt twist–boat conformations, in which the two methyl groups at the acetal moiety are in nearly identical environments and thus both have ^{13}C NMR chemical shifts of approximately 25 ppm. In contrast, 1,3-*syn*-diol acetonides prefer chair conformations, in which one of the methyl groups is axial and the other is equatorial; thus the axial methyl group has a chemical shift of about 20 ppm, while the equatorial methyl group has a chemical shift of approximately 30 ppm.

Table 5. Scope of the Zr alkoxide-catalyzed aldol-Tishchenko reaction for the synthesis of 1,3-*anti*-diol monoesters.[a]



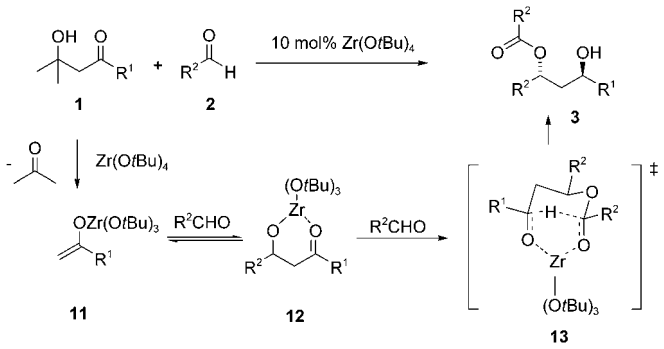
Entry	R^1 (**1**)	R^2 (**2**)	Product	Yield **3**/**3′** [%][b]	Ratio **3**/**3′**[c]
1	Me (**1a**)	*i*Pr (**2a**)	**3a**	79	20:1
2	Me (**1a**)	*n*-C_6H_{13} (**2b**)	**3b**	91	5:1
3	Me (**1a**)	2-methylpropyl (**2c**)	**3c**	87	20:1
4	Me (**1a**)	1-ethylpropyl (**2d**)	**3d**	72	20:1
5	Me (**1a**)	*c*-C_6H_{11} (**2e**)	**3e**	86	20:1
6[d]	*i*Pr (**1b**)	*i*Pr (**2a**)	**3f**	94	–
7	*i*Pr (**1b**)	*n*-C_6H_{13} (**2b**)	**3g**	86	5:1
8	*t*Bu (**1c**)	*i*Pr (**2a**)	**3h**	84	7:1
9	*t*Bu (**1c**)	Ph (**2f**)	**3i**	86	20:1
10	*t*Bu (**1c**)	1-ethylpropyl (**2d**)	**3j**	86	20:1
11	*t*Bu (**1c**)	*c*-C_6H_{11} (**2e**)	**3k**	75	20:1
12	*t*Bu (**1c**)	*n*-C_6H_{13} (**2b**)	**3l**	88	15:1
13	*t*Bu (**1c**)	*c*-C_3H_5 (**2g**)	**3m**	70	13:1
14	Ph (**1d**)	*n*-C_6H_{13} (**2b**)	**3n**	79	10:1
15	Ph (**1d**)	*i*Pr (**2a**)	**3o**	75	14:1
16	2′-MeO-C_6H_4(**1e**)	*i*Pr (**2a**)	**3p**	90	12:1
17	2′-MeO-C_6H_4 (**1e**)	*n*-C_6H_{13} (**2b**)	**3q**	89	12:1

[a] Reaction conditions: A solution of diol **8** (0.10 mmol) and $Zr(OtBu)_4$ (0.10 mmol) in CH_2Cl_2 (4 mL) was stirred for 0.5 h at RT. To this solution **1** (1.0 mmol) and **2** (3.0 mmol) were added at 0 °C. [b] Combined yield of **3**/**3′**, which were isolated as a mixture except for entries 9, 13, 14, 15, 16, 17, in which cases the regioisomeric products were separated by flash chromatography. [c] Determined by ^{1}H NMR or ^{13}C NMR spectroscopy, except for entries 9, 13, 14, 15, 16, 17, in which cases the regioisomeric products were separated by flash chromatography. [d] This reaction was run with $Zr(OtBu)_4$ as catalyst.



Scheme 6. Assignment of relative configuration of aldol-Tishchenko products **3**/**3′**.

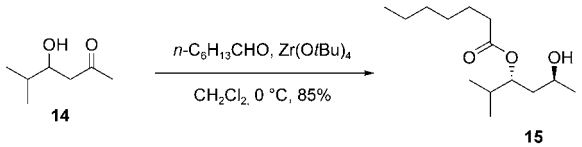
Reaction mechanism: A plausible mechanism for the aldol-Tishchenko reaction is given in Scheme 7. The zirconium alkoxide catalyst initiates a retro-aldol reaction of ketone



Scheme 7. Proposed mechanism for the aldol-Tishchenko reaction.

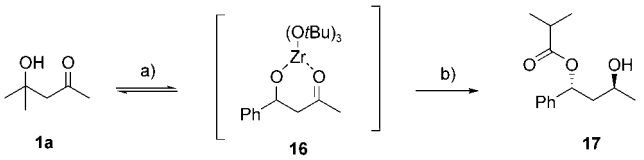
aldol **1** and generates a zirconium enolate **11** in situ under liberation of one molecule of acetone. Enolate **11** undergoes aldolization with the aldehyde under formation of the intermediate zirconium aldolate **12**, which in turn forms a hemiacetal zirconium alkoxide with a second equivalent of aldehyde. The Tishchenko reduction is believed to proceed through the depicted transition structure **13**, in which zirconium atom is chelated by the alkoxide and carbonyl oxygen atoms. The observed high level of *anti* diastereoselectivity may then be explained through intramolecular hydride delivery towards a proaxially oriented carbonyl group.

Control experiments indicate that formation of aldolate **12** is reversible, whereas the subsequent Tishchenko reduction proceeds fast and is irreversible. Thus, when aldol **14** was subjected to $Zr(OtBu)_4$ (10 mol%) and *n*-heptanal (2 equiv), the desired Tishchenko product **15** was obtained without a trace of any scrambling product with exchanged alkyl groups. That means that once the aldol product forms, the Tishchenko reduction withdraws it from the aldol equilibrium (Scheme 8).



Scheme 8. $Zr(OtBu)_4$-catalyzed Tishchenko reduction of aldol product **14**.

Sequential aldol-Tishchenko reaction with two different aldehydes: To probe the versatility of this process we attempted a sequential aldol-Tishchenko reaction with two different aldehydes. Since the second step, the Tishchenko reduction, has been shown to be very fast, we were restricted to the use of an aldehyde as aldol acceptor, which was not successful as a hydride donor. Thus, we employed benzaldehyde as aldol acceptor and isobutyraldehyde as hydrogen donor. Stirring diacetone alcohol (**1a**) and benzaldehyde (**2f**) (2 equiv) in the presence of $Zr(OtBu)_4$ (10 mol%) for 24 h in CH_2Cl_2 at −20 °C led to the formation of cross aldolate adduct **16**, which after addition of isobutyraldehyde (**2a**) (2 equiv) and another $Zr(OtBu)_4$ (10 mol%) was reduced in situ to 1,3-*anti*-diol monoester **17** in 48% overall yield (Scheme 9).



Scheme 9. Sequential aldol-Tishchenko reaction with two different aldehydes. a) 2.0 equiv PhCHO, 10 mol% $Zr(OtBu)_4$, CH_2Cl_2, −20 °C, 24 h; b) 2.0 equiv *i*PrCHO, 10 mol% $Zr(OtBu)_4$, CH_2Cl_2, 30 min, 48%.

Conclusion

The aldol-Tishchenko reaction has been steadily improved in terms of utility and selectivity in recent decades. In the present investigation ketone aldols such as diacetone alcohol have been employed as enol equivalents on the basis of their facile retro-aldolization tendency. Zirconium alkoxides have been shown to catalyze this retro-aldolization and yield zirconium enolates in situ that underwent rapid aldol-Tishchenko reactions with a broad range of aldehydes. Differentiated 1,3-*anti*-diol monoesters were thus obtained in one step, generally with good yields and excellent *anti* diastereocontrol. A modified zirconium alkoxide catalyst with attenuated Lewis acidity has been developed that was capable of suppressing the undesired acyl migration in the 1,3-diol monoesters to a large extent, thereby enhancing the regioisomeric ratio of the products. The present methodology offers a simple yet powerful way to synthesize 1,3-dioxygenated compounds in one step with complete stereocontrol.

Experimental Section

General: All reactions were performed in flame-dried glassware under an atmosphere of dry nitrogen. The following reaction solvents were distilled from the indicated drying agents: dichloromethane (CaH_2), tetrahydrofuran ($LiAlH_4$, triphenylmethane), diethyl ether (Na, benzophenone), toluene (Na, benzophenone), *N*,*N*-dimethylformamide (Acros ACS grade), acetonitrile (Acros ACS grade), chloroform (Acros ACS grade). Diethyl ether and pentane for chromatography were technical grade and distilled from KOH. All reactions were monitored by thin-layer chroma-

tography (TLC) on precoated silica gel SIL G/UV$_{254}$ plates (Machery, Nagel & Co.); spots were visualized by treatment with a solution of vanillin (0.5 g), conc. acetic acid (10 mL), and conc. H_2SO_4 (5 mL) in methanol (90 mL). Flash column chromatography was performed by using Merck silica gel 60 230–400 mesh. Diacetone alcohol (**1a**) and all aldehydes **2** were distilled and kept under N_2 until use. Diisopropylamine was freshly distilled from CaH_2 prior to use. Zr(O*t*Bu)$_4$ was purchased from Strem Chemical Co. as 99.99% PURATREM quality packed in ampules. These ampules were opened in an inert atmosphere glove box when the Zr(O*t*Bu)$_4$ was filled in a septum-sealed flask and kept under Ar until use. Diols **7**[22] and **8**,[23] and ketone aldol **1f**[21] were prepared according to literature procedures. All other chemicals were used as received from commercial suppliers. ^{1}H and ^{13}C NMR spectra were recorded with Varian VXR 200 (200 MHz) or Bruker AMX 300 (300 MHz) spectrometers in $CDCl_3$ at 25 °C with TMS as internal standard. IR spectra of deposited films were recorded with a Bruker IFS 25 FT-IR instrument. UV spectra were obtained with a Perkin–Elmer Lambda 9 spectrometer. Melting points are uncorrected. Mass spectra were measured at 70 eV (EI) or 200 eV (DCI/NH_3) with a Finnigan MAT 95 A spectrometer. High-resolution mass spectra (HRMS; ESI/Na) were measured with a Bruker Daltonics APEX II FT-ICR spectrometer. Microanalyses were carried out at the microanalytical laboratory of the Institut für Organische Chemie der Universität Göttingen.

Preparation of ketone aldols 1 (general procedure 1): A stirred solution of diisopropylamine (15.5 mL, 110 mmol) in diethyl ether (300 mL) was cooled to 0 °C before a solution of *n*-BuLi in hexane (2.5 M, 44 mL, 110 mmol) was added slowly over 5 min. The resulting solution was stirred for 30 min at 0 °C prior to cooling to −78 °C. The appropriate methyl ketone (100 mmol) was then added slowly over 5 min to this solution. The resulting solution was stirred for 1 h at −78 °C prior to slow addition of dry acetone (8.82 mL, 120 mmol). Stirring was continued for 3 h at −78 °C before the reaction was quenched with saturated aqueous ammonium chloride solution. The reaction mixture was allowed to reach room temperature. The layers were separated and the aqueous layer was extracted twice with diethyl ether. The combined organic layers were dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel.

5-Hydroxy-2,5-dimethyl-3-hexanone (1b): Following general procedure 1, isopropyl methyl ketone (10.7 mL, 100 mmol) was converted to its acetone aldol adduct. Flash chromatography (silica gel, diethyl ether/pentane 1:2) of the crude product afforded **1b** as a colorless liquid (10.9 g, 76%). R_f = 0.35 (diethyl ether/pentane 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.90 (brs, 1H; OH), 2.62 (s, 2H; CH_2), 2.55 (sept, J = 7.0 Hz, 1H; C*H*(CH$_3$)$_2$), 1.22 (s, 6H; C(OH)(C*H*$_3$)$_2$), 1.08 ppm (d, J = 7.0 Hz, 6H; CH(C*H*$_3$)$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 217.1, 69.54, 50.42, 41.97, 29.19, 17.77 ppm; IR (film): $\tilde{\nu}$ = 3494, 2973, 2935, 1698, 1467, 1382, 1315, 1153, 1051, 976, 913, 764 cm^{-1}; MS (200 eV, DCI/NH_3): *m*/*z* (%): 306 (15) [2*M*+NH_4]$^+$, 179 (5) [*M*+NH_3+NH_4]$^+$, 162 (100) [*M*+NH_4]$^+$, 145 (13) [*M*+H]$^+$; elemental analysis calcd (%) for $C_8H_{16}O_2$ (144.21): C 66.63, H 11.18; found: C 66.41, H 10.99.

5-Hydroxy-2,2,5-trimethyl-3-hexanone (1c): Following general procedure 1, pinacolone (12.5 mL, 100 mmol) was converted to its acetone aldol adduct. Flash chromatography (silica gel, diethyl ether/pentane 1:2) of the crude product afforded **1c** as a colorless liquid (12.6 g, 80%). R_f = 0.23 (diethyl ether/pentane 1:3); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.40 (brs, 1H; OH), 2.65 (s, 2H; CH_2), 1.24 (s, 6H; CH_3), 1.13 ppm (s, 9H; C(C*H*$_3$)$_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 218.8, 69.65, 46.74, 44.78, 29.26, 25.95 ppm; IR (film): $\tilde{\nu}$ = 3519, 2957, 2930, 2860, 1714, 1467, 1364, 1176, 1101, 1074, 734 cm^{-1}; MS (200 eV, DCI/NH_3): *m*/*z* (%): 193 (12) [*M*+NH_3+NH_4]$^+$, 176 (100) [*M*+NH_4]$^+$, 159 (10) [*M*+H]$^+$; HRMS (ESI): calcd for $C_{18}H_{36}NaO_4$: 339.2506; found: 339.2497 [2*M*+Na]$^+$.

1-Phenyl-3-methyl-3-hydroxy-1-butanone (1d): Following general procedure 1, acetophenone (11.7 mL, 100 mmol) was converted to its acetone aldol adduct. The reaction mixture was quenched with water instead of saturated NH_4Cl solution. Flash chromatography (silica gel, diethyl ether/pentane 1:3) of the crude product afforded **1d** as a colorless liquid (10.7 g, 60%). R_f = 0.25 (diethyl ether/pentane 1:1); ^{1}H NMR(200 MHz, $CDCl_3$): δ = 7.98–7.92 (m, 2H; ArH), 7.44–7.63 (m, 3H; ArH), 4.16 (brs, 1H; OH), 3.15 (s, 2H; CH_2), 1.35 ppm (s, 6H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 201.8, 137.2, 133.6, 128.7, 128.1, 69.89, 48.55, 29.56 ppm; IR (film): $\tilde{\nu}$ = 3519, 2957, 2930, 2860, 1714, 1467, 1364, 1176, 1074, 734 cm^{-1}; UV (CH_3CN): λ_{max} (lg ε) = 204.0 (3.870), 242.0 (4.006), 278.0 nm (2.925); MS (200 eV, DCI/NH_3): *m*/*z* (%): 213 (9) [*M*+NH_3+NH_4]$^+$, 196 (90) [*M*+NH_4]$^+$, 179 (20) [*M*+H]$^+$, 155 (90), 138 (100) [PhCOCH_3+NH_4]$^+$; HRMS (ESI): calcd for $C_{22}H_{28}NaO_4$: 379.1880; found: 379.1877 [2*M*+Na]$^+$.

1-(2′-Methoxyphenyl)-3-methyl-3-hydroxy-1-butanone (1e): Following general procedure 1, (2′-methoxy)acetophenone (13.8 mL, 100 mmol) was converted to its acetone aldol adduct. Flash chromatography (silica gel, diethyl ether/pentane 1:2) of the crude product afforded **1e** as a colorless liquid (14.6 g, 70%). R_f = 0.20 (diethyl ether/pentane 1:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.68 (dd, J = 7.5, 1.5 Hz, 1H; ArH), 7.50 (dt, J = 1.5, 7.5 Hz, 1H; ArH), 7.03 (t, J = 7.5 Hz, 1H; ArH), 6.97 (d, J = 7.5 Hz, 1H; ArH), 4.30 (s, 1H; OH), 3.92 (s, 3H; OCH_3), 3.18 (s, 2H; CH_2), 1.32 ppm (s, 6H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 204.5, 158.5, 133.9, 129.9, 128.6, 120.6, 111.5, 70.12, 55.43, 53.68, 28.37 ppm; IR (film): $\tilde{\nu}$ = 3491 (OH), 2973, 1663, 1598, 1486, 1465, 1377, 1245, 1203, 1023, 975, 910, 758 cm^{-1}; UV (CH_3CN): λ_{max} (lg ε) = 210.0 (4.203), 247.0 (3.863), 303 nm (3.523); MS (70 eV, EI): *m*/*z* (%): 208 (5) [*M*]$^+$, 193 (10) [*M*−CH_3]$^+$, 150 (7) [*M*−acetone]$^+$, 135 (100) [*M*−acetone−CH_3]$^+$; elemental analysis calcd (%) for $C_{12}H_{16}O_3$ (208.26): C 68.93, H 7.53; found: C 69.23, H 7.75.

Zr(O*t*Bu)$_4$/diol 8-catalyzed aldol-Tishchenko reaction of ketone aldols 1 with aldehydes 2 (general procedure 2): Zr(O*t*Bu)$_4$ (39 μL, 0.10 mmol) was added at room temperature to a stirred solution of diol **8** (44 mg, 0.10 mmol) in dichloromethane (4 mL) and stirring was continued for 30 min. The resulting solution was cooled to 0 °C and ketone aldol **1** (1.00 mmol) and aldehyde **2** (3.00 mmol) were added simultaneously. The reaction mixture was stirred for 3 h at 0 °C before addition of 0.5 M aqueous HCl solution (4 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3×15 mL). The combined organic layers were dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography.

1,3-Diol monoester 3a/3a′: Following general procedure 2, compound **1a** (124 μL, 1.00 mmol) was treated with **2a** (274 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:3) of the crude product yielded **3a/3a′** as a colorless oil (160 mg, 79%, 20:1 mixture of regioisomers). Data for **3a**: R_f = 0.39 (diethyl ether/pentane 1:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.88 (ddd, J = 8.5, 5.5, 3.0 Hz, 1H; CHOCOR), 3.58 (m, 1H; C*H*(OH)), 3.02 (brs, 1H; OH), 2.61 (sept, J = 7.0 Hz, 1H; C*H*(CH$_3$)$_2$), 1.81 (m, 1H; C*H*(CH$_3$)$_2$), 1.45–1.69 (m, 2H; CH_2), 1.22 (d, J = 7.0 Hz, 6H; CH(C*H*$_3$)$_2$), 1.19 (d, J = 7.0 Hz, 3H; CH_3), 0.94 ppm (d, J = 7.0 Hz, 6H; CH(C*H*$_3$)$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 178.6, 75.49, 63.25, 41.61, 34.39, 32.16, 22.91, 19.23, 19.14, 18.87, 17.61 ppm; IR (film): $\tilde{\nu}$ = 3452, 2969, 2936, 2878, 1731, 1272, 1202, 1163, 1072 cm^{-1}; MS (200 eV, DCI/NH_3): *m*/*z* (%): 422 (1) [2*M*+NH_4]$^+$, 237 (7) [*M*+$NH_4$$^+$+$NH_3$], 220 (100) [*M*+$NH_4$]$^+$, 203 (13) [*M*+H]$^+$; elemental analysis calcd (%) for $C_{11}H_{22}O_3$ (202.29): C 65.31, H 10.96; found: C 65.22, H 11.02.

1,3-Diol monoester 3b/3b′: Following general procedure 2, **1a** (124 μL, 1.00 mmol) was treated with **2b** (418 μL 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:4) of the crude product yielded **3b/3b′** as a colorless oil (261 mg, 91%, 5:1 mixture of regioisomers). Data for **3b**: R_f = 0.47 (diethyl ether/pentane 1:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.05 (m, 1H; CHOCOR), 3.65 (m, 1H; C*H*OH), 3.13 (brs, 1H; OH), 2.34 (t, J = 7.5 Hz, 2H; CH_2COOR), 1.22–1.70 (m, 20H; CH_2), 1.18 (d, J = 6.3 Hz, 3H; CH_3), 0.84–0.95 ppm (m, 6H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 176.3, 71.63, 63.31, 44.72, 34.89, 34.56, 31.73, 31.46, 29.02, 28.85, 25.49, 25.10, 22.80, 22.57, 22.50, 14.07, 14.03 ppm; IR (film): $\tilde{\nu}$ = 3453, 2930, 2859, 1733, 1460, 1378, 1176, 1102, 1031, 938 cm^{-1}; MS (200 eV, DCI/NH_3): *m*/*z* (%): 590 (2) [2*M*+NH_4]$^+$, 304 (100) [*M*+NH_4]$^+$, 287 (12) [*M*+H]$^+$; elemental analysis calcd (%) for $C_{17}H_{34}O_3$ (286.45): C 71.28, H 11.96; found: C 71.36, H 11.66.

1,3-Diol monoester 3c/3c′: Following general procedure 2 **1a** (124 μL, 1.00 mmol) was treated with **2c** (323 μL, 3.00 mmol). Flash chromatogra-

phy (silica gel, diethyl ether/pentane 1:4) of the crude product yielded **3c/3c′** as a colorless oil (200 mg, 87%, 20:1 mixture of regioisomers). Data for **3c**: R_f=0.46 (diethyl ether/pentane 1:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ=5.16 (m, 1H; CHOCOR), 3.65 (m, 1H; C*H*OH), 3.25 (brs, 1H; OH), 2.00–2.28 (m, 3H; COCH_2CH(CH_3)$_2$, 1.21–1.72 (m, 5H; CH_2, CH(CH_3)$_2$), 1.17 (d, J=6.5 Hz, 3H; CH_3), 0.97 (d, J=6.0 Hz, 6H; CH_3), 0.91 (d, J=6.0 Hz, 3H; CH_3), 0.88 ppm (d, J=6.0 Hz, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=174.7, 69.90, 63.22, 45.24, 43.96, 43.63, 25.68, 24.66, 23.17, 22.72, 22.44, 22.40, 21.86 ppm; IR (film): $\tilde{\nu}$=3453, 2961, 2873, 1732, 1468, 1370, 1295, 1195, 1120, 974, 945 cm^{-1}; MS (200 eV, DCI/NH_3): *m*/*z* (%): 248 (100) [*M*+NH_4]$^+$, 231 (10) [*M*+H]$^+$; elemental analysis calcd (%) for $C_{13}H_{26}O_3$ (230.35): C 67.79, H 11.38; found: C 67.53, H 11.12.

1,3-Diol monoester 3d/3d′: Following general procedure 2, **1a** (124 μL, 1.00 mmol) was treated with **2d** (369 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:4) of the crude product yielded **3d/3d′** as a colorless oil (186 mg, 72%, 20:1 mixture of regioisomers). Data for **3d**: R_f=0.50 (diethyl ether/pentane 1:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ=5.17 (dt, J=11.0, 2.5 Hz, 1H; CHOCOR), 3.64 (ddq, J=4.5, 2.5, 6.0 Hz, 1H; C*H*OH), 2.65 (brs, 1H; OH), 2.24 (tt, J=8.0, 6.0 Hz, 1H; ROOCCH(CH_2CH_3)$_2$), 1.26–1.76 (m, 11H; CH_2, CH), 1.19 (d, J=6.0 Hz, 3H; CH_3CHOH), 0.98–0.85 ppm (m, 12H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=177.7, 72.36, 63.29, 49.26, 45.21, 41.24, 24.90, 22.87, 22.32, 21.97, 11.88, 11.76, 11.73, 11.58 ppm; IR (film): $\tilde{\nu}$=3460, 2965, 2935, 2878, 1710, 1461, 1384, 1270, 1188, 1149, 1085, 982, 951, 815 cm^{-1}; MS (200 eV, DCI/NH_3): *m*/*z* (%): 276 (100) [*M*+NH_4]$^+$, 259 (8) [*M*+H]$^+$; elemental analysis calcd (%) for $C_{15}H_{30}O_3$ (258.40): C 69.72, H 11.70; found: C 69.48, H 11.43.

1,3-Diol monoester 3e/3e′: Following general procedure 2, **1a** (124 μL, 1.00 mmol) was treated with **2e** (361 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:4) of the crude product yielded **3e/3e′** as a colorless oil (243 mg, 86%, 20:1 mixture of regioisomers). Data for **3e**: R_f=0.47 (diethyl ether/pentane 1:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ=4.87 (ddd, J=9.5, 6.0, 4.0 Hz, 1H; CHOCOR), 3.66–3.43 (m, 1H; C*H*OH), 3.22 (brs, 1H; OH), 2.44–2.26 (m, 1H; CHCOOR, 2.04–0.88 (m, 23H; CH_2, CH), 1.17 ppm (d, J=6.0 Hz, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=177.7, 74.82, 63.17, 43.53, 41.90, 41.58, 29.26, 29.24, 29.18, 28.08, 26.33, 26.06, 25.99, 25.69, 25.45, 25.40, 22.79 ppm; IR (film): $\tilde{\nu}$=3445, 2929, 2845, 1729, 1450, 1377, 1175, 1034, 950, 844 cm^{-1}; MS (200 eV, DCI/NH_3): *m*/*z* (%): 582 (2) [2*M*+NH_4]$^+$, 317 (2) [*M*+NH_4+NH_3]$^+$, 300 (100) [*M*+NH_4]$^+$, 283 (12) [*M*+H]$^+$; elemental analysis calcd (%) for $C_{17}H_{30}O_3$ (282.42): C 72.30, H 10.71; found: C 72.49, H 10.37.

1,3-Diol monoester 3f: Zr(O*t*Bu)$_4$ (39 μL, 0.10 mmol) was added to a solution of ketone aldol **1b** (144 mg, 1.00 mmol) and **2a** (274 μL, 3.00 mmol) in CH_2Cl_2 (4 mL) at 0°C. The solution was stirred for 3 h at 0°C before addition of 0.5 M aqueous HCl solution (4 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3×15 mL). The combined organic layers were dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica gel, diethyl ether/pentane 1:3) to yield **3f** as a colorless oil (217 mg, 94%). Data for **3f**: R_f=0.32 (diethyl ether/pentane 1:2); ^{1}H NMR (200 MHz, $CDCl_3$): δ=4.91 (ddd, J=9.0, 5.5, 3.5 Hz, 1H; CHOCOR), 3.11 (ddd, J=9.0, 5.5, 3.5 Hz, 1H; C*H*OH), 2.95 (brs, 1H; OH), 2.60 (sept, J=7.0 Hz, 1H; CH(CH_3)$_2$), 1.48–1.90 (m, 4H; CH_2, CH(CH_3)$_2$), 1.19 (d, J=7.0 Hz, 3H; CH(CH_3)$_2$), 1.18 (d, J=7.0 Hz, 3H; CH(CH_3)$_2$), 0.92 (d, J=7.0 Hz, 6H; CH(CH_3)$_2$), 0.89 ppm (d, J=7.0 Hz, 6H; CH(CH_3)$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=178.5, 75.60, 71.88, 36.50, 34.40, 33.55, 32.32, 19.21, 19.20, 18.94, 18.80, 18.05, 17.64 ppm; IR (film): $\tilde{\nu}$=3516, 2966, 2877, 1714, 1470, 1388, 1269, 1202, 1163, 1075, 1005, 831 cm^{-1}; MS (200 eV, DCI/NH_3): *m*/*z* (%): 248 (100) [*M*+NH_4]$^+$, 231 (10) [*M*+H]$^+$; HRMS (ESI): calcd for $C_{13}H_{26}NaO_3$: 253.1774; found: 253.1775 [*M*+Na]$^+$.

1,3-Diol monoester 3g/3g′: Following general procedure 2, a solution of ketone aldol **1b** (144 mg, 1.00 mmol) in CH_2Cl_2 (0.5 mL) was treated with **2b** (418 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:7) of the crude product yielded **3g/3g′** as a colorless oil (270 mg, 86%, 5:1 mixture of regioisomers). Data for **3g**: R_f=0.42 (diethyl ether/pentane 1:3); ^{1}H NMR (200 MHz, $CDCl_3$): δ=5.09 (m, 1H; CHOCOR), 3.19 (ddd, J=10.0, 5.5, 3.0 Hz, 1H; C*H*OH), 2.80 (brs, 1H; OH), 2.34 (t, J=7.0 Hz, 2H; CH_2COOR), 1.21–1.87 (m, 21H; CH_2, CH-(CH_3)$_2$), 0.82–0.96 ppm (m, 12H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=175.1, 71.69, 39.50, 34.96, 34.49, 33.35, 31.62, 31.36, 28.93, 28.73, 25.41, 25.02, 22.45, 22.40, 18.63, 17.84, 13.95, 13.92 ppm; IR (film): $\tilde{\nu}$=3520, 2958, 2929, 2859, 1715, 1469, 1175, 1103, 1031, 726 cm^{-1}; MS (200 eV, DCI/NH_3): *m*/*z* (%): 646 (35) [2*M*+NH_4]$^+$, 332 (100) [*M*+NH_4]$^+$, 315 (9) [*M*+H]$^+$; HRMS (ESI): calcd for $C_{38}H_{76}NaO_6$: 651.5533; found: 651.5534 [2*M*+Na]$^+$.

1,3-Diol monoester 3h/3h′: Following general procedure 2, a solution of ketone aldol **1c** (158 mg, 1.00 mmol) in CH_2Cl_2 (0.5 mL) was treated with **2a** (274 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:5) of the crude product yielded **3h/3h′** as a colorless oil (205 mg 84%, 7:1 mixture of regioisomers). Data for **3h**: R_f=0.42 (diethyl ether/pentane 1:3); ^{1}H NMR (200 MHz, $CDCl_3$): δ=4.95 (ddd, J=10.5, 5.0, 2.0 Hz, 1H; CHOCOR), 3.00 (dd, J=10.5, 2.0 Hz, 1H; C*H*OH), 2.61 (sept, J=7.0 Hz, 1H; CH(CH_3)$_2$), 2.50 (brs, 1H; OH), 1.95–1.75 (m, 1H; CH(CH_3)$_2$), 1.65 (ddd, J=14.0, 10.5, 2.0 Hz, 1H; CH*H*), 1.47 (ddd, J=14.0, 10.5, 2.0 Hz, 1H; C*H*H), 1.20 (d, J=7.0 Hz, 6H; CH(CH_3)$_2$), 0.93 (d, J=7.0 Hz, 6H; CH(CH_3)$_2$), 0.89 ppm (s, 9H; C-(CH_3)$_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=178.4, 75.81, 74.73, 34.42, 34.41, 33.96, 32.37, 25.94, 19.26, 19.20, 18.97, 17.63 ppm; IR (film): $\tilde{\nu}$=3518, 2967, 2876, 1714, 1389, 1267, 1204, 1163, 1070, 1011 cm^{-1}; MS (200 eV, DCI/NH_3): *m*/*z* (%): 279 (2) [*M*+NH_3+NH_4]$^+$, 262 (100) [*M*+NH_4]$^+$, 245 (5) [*M*+H]$^+$; elemental analysis calcd (%) for $C_{14}H_{28}O_3$ (244.37): C 68.81, H 11.55; found: C 69.08, H 11.29.

1,3-Diol monoester 3i: Following general procedure 2, a solution of ketone aldol **1c** (158 mg, 1.00 mmol) in CH_2Cl_2 (0.5 mL) was treated with **2f** (304 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:5) of the crude product yielded pure **3i** (256 mg, 82%) as a colorless oil; regioisomer **3i′** (13 mg, 4%) was isolated additionally. Data for **3i**: R_f=0.24 (diethyl ether/pentane 1:3); ^{1}H NMR (200 MHz, $CDCl_3$): δ=8.05–8.16 (m, 2H; ArH), 7.27 (m, 8H; ArH), 6.41 (dd, J=11.0, 2.5 Hz, 1H; CHOCOR), 3.39 (dd, J=11.0, 1.5 Hz, 1H; C*H*OH), 2.20 (ddd, J=14.5, 11.0, 1.5 Hz, 1H; C*H*H), 2.05 (brs, 1H; OH), 1.80 (ddd, J=14.5, 11.0, 2.5 Hz, 1H; CH*H*), 0.92 ppm (s, 9H; C(CH_3)$_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=167.9, 144.0, 133.3, 129.8, 129.8, 128.5, 128.4, 127.3, 125.6, 79.15, 69.73, 40.13, 34.68, 26.14 ppm; IR (film): $\tilde{\nu}$=3493, 3063, 3031, 2967, 1697, 1602, 1452, 1368, 1314, 1277, 1117, 1026, 711 cm^{-1}; MS (200 eV, DCI/NH_3): *m*/*z* (%): 954 (10) [3*M*+NH_4]$^+$, 642 (35) [2*M*+NH_4]$^+$, 330 (38) [*M*+NH_4]$^+$, 295 (100); elemental analysis calcd (%) for $C_{20}H_{24}O_3$ (312.41): C 76.89, H 7.74; found: C 77.11, H 7.81. Data for **3i′**: R_f=0.32 (diethyl ether/pentane; 1:3); ^{1}H NMR (200 MHz, $CDCl_3$): δ=8.18–8.07 (m, 2H; ArH), 7.71–7.16 (m, 8H; ArH), 5.25 (dd, J=10.5, 3.0 Hz, 1H; C*H*OH, 4.57 (dd, J=9.5, 3.5 Hz, 1H; C*H*OCOPh), 2.10–1.82 (m, 2H; CH_2), 2.11 (brs, 1H; OH), 1.03 ppm (s, 9H; *t*Bu); ^{13}C NMR (50 MHz, $CDCl_3$): δ=166.5, 141.1, 133.2, 130.0, 129.7, 128.6, 128.4, 127.9, 126.1, 75.10, 74.24, 39.84, 34.56, 25.74 ppm; IR (film): $\tilde{\nu}$=3508, 3090, 3064, 2961, 2870, 1721, 1394, 1275, 1115 cm^{-1}.

1,3-Diol monoester 3j/3j′: Following general procedure 2, a solution of ketone aldol **1c** (158 mg, 1.00 mmol) in CH_2Cl_2 (0.5 mL) was treated with **2d** (369 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:5) of the crude product yielded **3j/3j′** as a colorless oil (258 mg 86%, 20:1 mixture of regioisomers). Data for **3j**: R_f=0.52 (diethyl ether/pentane 1:3); ^{1}H NMR (200 MHz, $CDCl_3$): δ=5.23 (m, 1H; CHOCOR), 3.08 (dd, J=11.0, 2.0 Hz, 1H; C*H*OH), 2.54 (brs, 1H; OH), 2.23 (m, 1H; CHCOOR), 1.78–1.20 (m, 11H; CH_2, CH), 0.98–0.90 (m, 12H; CH_3), 0.89 ppm (s, 9H; C(CH_3)$_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=177.5, 74.76, 72.86, 49.48, 45.52, 34.43, 33.58, 26.96, 25.12, 25.09, 22.04, 22.09, 11.94, 11.93, 11.86, 11.69 ppm; IR (film): $\tilde{\nu}$=3519, 2964, 2876, 1710, 1462, 1386, 1363, 1271, 1235, 1191, 1148, 1070, 1011, 942, 821 cm^{-1}; MS (200 eV, DCI/NH_3): *m*/*z* (%): 618 (1) [2*M*+NH_4]$^+$, 318 (100) [*M*+NH_4]$^+$, 301 (12) [*M*+H]$^+$; elemental analysis calcd (%) for $C_{18}H_{36}O_3$ (300.48): C 71.95, H 12.08; found: C 71.74, H 11.79.

1,3-Diol monoester 3k/3k′: Following general procedure 2, a solution of ketone aldol **1c** (158 mg, 1.00 mmol) in CH_2Cl_2 (0.5 mL) was treated with **2e** (361 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/

pentane 1:5) of the crude product yielded **3k**/**3k′** as a colorless oil (243 mg, 75%, 20:1 mixture of regioisomers). Data for **3k**: R_f=0.42 (diethyl ether/pentane 1:3); ^{1}H NMR (200 MHz, $CDCl_3$): δ=4.94 (ddd, J=10.5, 5.5, 2.5 Hz, 1H; CHOCOR), 2.99 (dd, J=10.5, 2.0 Hz, 1H; C*H*OH), 2.84 (brs, 1H; OH), 2.28 (m, 1H; CHCOOR), 0.94–2.00 (m, 23H; CH_2, CH), 0.88 ppm (s, 9H; $C(CH_3)_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=177.3, 75.16, 74.63, 43.59, 42.15, 34.39, 33.92, 29.41, 29.32, 29.21, 28.12, 26.39, 26.13, 26.06, 25.97, 25.74, 25.48, 25.46 ppm; IR (film): $\tilde{\nu}$=3517, 2931, 2855, 1710, 1451, 1364, 1313, 1249, 1176, 1134, 1073, 1011, 974, 941, 894, 827 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 666 (15) $[2M+NH_4]^+$, 359 (13) $[M+NH_3NH_4]^+$, 342 (100) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_{20}H_{36}O_3$ (324.50): C 74.03, H 11.18; found: C 74.04, H 10.98.

1,3-Diol monoester 3l/3l′: Following general procedure 2, a solution of ketone aldol **1c** (158 mg, 1.00 mmol) in CH_2Cl_2 (0.5 mL) was treated with **2b** (418 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:5) of the crude product yielded **3l**/**3l′** as a colorless oil (289 mg, 88%, 15:1 mixture of regioisomers). Data for **3l**: R_f=0.53 (diethyl ether/pentane 1:3); ^{1}H NMR (200 MHz, $CDCl_3$): δ=5.10 (m, 1H; CHOCOR), 3.07 (dd, J=10.5, 2.5 Hz, 1H; C*H*OH), 2.63 (brs, 1H; OH), 2.34 (t, J=7.0 Hz, 2H; CHCOOR), 1.76–1.18 (m, 20H; CH_2), 0.97–0.81 ppm (m, 15H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=175.1, 74.63, 72.09, 37.05, 35.15, 34.63, 34.33, 31.73, 31.48, 29.06, 28.86, 25.89, 25.54, 25.17, 22.57, 22.53, 14.06, 14.03 ppm; IR (film): $\tilde{\nu}$=3519, 2924, 2360, 1714, 1465, 1364, 1174, 1101, 1010 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 674 (100) $[2M+NH_4]^+$, 346 (93) $[M+NH_4]^+$, 329 (9) $[M+H]^+$; elemental analysis calcd (%) for $C_{20}H_{40}O_3$ (328.53): C 73.12, H 12.27; found: C 72.78, H 11.98.

1,3-Diol monoester 3m/3m′: Following general procedure 2, a solution of ketone aldol **1c** (158 mg, 1.00 mmol) in CH_2Cl_2 (0.5 mL) was treated with **2g** (224 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:4) of the crude product yielded pure **3m** (156 mg, 65%) as a colorless oil; **3m′** (12 mg, 5%) was isolated additionally. Data for **3m**: R_f=0.42 (diethyl ether/pentane 1:2); ^{1}H NMR (200 MHz, $CDCl_3$): δ=4.43 (ddd, J=10.0, 9.0, 2.5 Hz, 1H; CHOCOR), 3.08 (dd, J=2.0, 10.5 Hz, 1H; C*H*OH), 2.62 (brs, 1H; OH), 1.89–1.57 (m, 3H; CH_2, CHCOOR), 1.26–0.83 (m, 5H; 4× cyclopropyl-C*H*H, cyclopropyl-CH), 0.91 (s, 9H; $C(CH_3)_3$), 0.64–0.23 ppm (m, 4H; 4×cyclopropyl-C*H*H); ^{13}C NMR (50 MHz, $CDCl_3$): δ=176.0, 76.71, 74.58, 37.17, 34.35, 25.90, 15.74, 13.10, 8.73, 8.54, 3.68, 2.96 ppm; IR (film): $\tilde{\nu}$=3487, 3081, 2958, 2870, 1703, 1471, 1335, 1205, 821, 744 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 498 (1) $[2M+NH_4]^+$, 258 (100) $[M+NH_4]^+$, 241 (5) $[M+H]^+$; HRMS (ESI): calcd for $C_{28}H_{48}NaO_6$: 503.3343; found: 503.3339 $[2M+Na]^+$. Data for **3m′**: R_f=0.25 (diethyl ether/pentane; 1:2); ^{1}H NMR (200 MHz, $CDCl_3$): δ=4.81 (m, 1H; CHOCOR), 2.90 (brs, 1H; OH), 2.67 (ddd, J=8.0, 5.5, 3.0 Hz, 1H; C*H*OH), 1.80–1.56 (m, 3H; CHCH_2CH, CHCOOR), 1.03–0.77 (m, 5H; cyclopropyl-CH, cyclopropyl-CH_2), 0.92 (s, 9H; *t*Bu), 0.67–0.09 ppm (m, 4H; cyclopropyl-CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ=176.0, 76.67, 74.54, 37.13, 34.31, 25.86, 15.70, 13.06, 8.69, 8.50, 3.64, 2.92 ppm; MS (200 eV, DCI/NH_3): m/z (%): 498 (1) $[2M+NH_4]^+$, 258 (65) $[M+NH_4]^+$, 223 (100).

1,3-Diol monoester 3n/3n′: Following general procedure 2 a solution of ketone aldol **1d** (178 mg, 1.00 mmol) in CH_2Cl_2 (0.5 mL) was treated with **2b** (418 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:6) of the crude product yielded pure **3n** (250 mg, 72%) as a colorless oil; **3n′** (25 mg, 7%) was isolated additionally. Data for **3n**: R_f=0.58 (diethyl ether/pentane 1:2); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.40–7.25 (m, 5H; ArH), 5.19 (m, 1H; CHOCOR), 4.59 (dd, J=8.8, 4.5 Hz, 1H; C*H*OH), 3.36 (brs, 1H; OH), 2.36 (t, J=7.5 Hz, 2H; CH_2COOR), 1.88 (m, 2H; CH_2), 1.82–1.14 (m, 18H; CH_2), 0.99–0.78 ppm (m, 6H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=175.1, 143.8, 128.3, 127.3, 125.5, 71.53, 69.82, 44.90, 34.79, 34.53, 31.65, 31.42, 28.97, 28.82, 25.32, 25.07, 22.48, 22.45, 14.00 ppm; IR (film): $\tilde{\nu}$=3455, 3063, 3030, 2930, 2859, 1732, 1455, 1379, 1174, 1060, 758, 700 cm^{-1}; UV (CH_3CN): λ_{max} (lg ε)=201.0 (3.993), 204.0 nm (3.948); MS (200 eV, DCI/NH_3): m/z (%): 714 (48) $[2M+NH_4]^+$, 366 (69) $[M+NH_4]^+$, 331 (100) $[M-OH]^+$; elemental analysis calcd (%) for $C_{22}H_{36}O_3$ (348.52): C 75.82, H 10.41; found: C 75.48, H 10.14. Data for **3n′**: R_f=0.37 (diethyl ether/pentane; 1:2); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.40–7.31 (m, 5H; ArH), 6.05 (dd, J=10.5, 3.0 Hz, 1H; CHOCOR), 3.58 (m, 1H; C*H*OH), 2.65 (brs, 1H; OH), 2.38 (t, J=8.0 Hz, 2H; CH_2COOR), 1.98 (ddd, J=14.0, 10.5, 3.0 Hz, 1H; CHC*H*HCH), 1.77 (ddd, J=14.0, 10.5, 3.0 Hz, 1H; CHCH*H*CH), 1.70–1.19 (m, 18H; $(CH_2)_5$, $(CH_2)_4$), 0.95–0.80 ppm (m, 6H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=174.1, 140.7, 128.5, 127.8, 126.2, 72.98, 67.54, 45.17, 37.17, 34.53, 31.79, 31.41, 29.27, 28.77, 25.67, 24.97, 22.59, 22.46, 14.05, 13.98 ppm.

1,3-Diol monoester 3o/3o′: Following general procedure 2, a solution of ketone aldol **1d** (178 mg, 1.00 mmol) in CH_2Cl_2 (0.5 mL) was treated with **2a** (274 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:5) of the crude product yielded pure **3o** (185 mg, 70%) as a colorless oil; **3o′** (13 mg, 5%) was isolated additionally. Data for **3o**: R_f=0.42 (diethyl ether/pentane 1:2); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.40–7.25 (m, 5H; ArH), 5.05 (dt, J=8.0, 5.5 Hz, 1H; CHOCOR), 4.54 (dd, J=7.5, 5.5 Hz, 1H; C*H*OH), 3.30 (brs, 1H; OH), 2.65 (sept, 1H; J=7.0 Hz, C*H*$(CH_3)_2$), 1.98–1.75 (m, 3H; CH_2, C*H*$(CH_3)_2$), 1.23 (d, J=7.0 Hz, 6H; CH(C*H*$_3)_2$), 0.94 (d, J=7.0 Hz, 3H; CH(C*H*$_3)_2$), 0.93 ppm (d, J=7.0 Hz, 3H; CH(C*H*$_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=178.5, 144.0, 128.4, 127.3, 125.5, 75.36, 69.82, 42.14, 34.39, 32.16, 19.23, 19.18, 18.72, 17.50 ppm; IR (film): $\tilde{\nu}$=3489, 3063, 3029, 2968, 2877, 1731, 1470, 1389, 1269, 1201, 1162, 1052, 758, 701 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 810 (1) $[3M+NH_4]^+$, 546 (20) $[2M+NH_4]^+$, 282 (50) $[M+NH_4]^+$, 247 (100) $[M-OH]^+$. elemental analysis calcd (%) for $C_{16}H_{24}O_3$ (264.36): C 72.69, H 9.15; found: C 72.68, H 8.92. Data for **3o′**: R_f=0.25 (diethyl ether/pentane; 1:2); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.39–7.30 (m, 5H; ArH), 6.04 (dd, J=11.0, 3.5 Hz, 1H; CHOCOR), 3.60 (m, 1H; C*H*OH), 2.62 (sept, J=7.0 Hz, 1H; C*H*$(CH_3)_2$), 2.60 (brs, 1H; OH), 1.84 (m, 1H; C*H*$(CH_3)_2$), 1.66–1.46 (m, 2H; CH_2), 1.21 (d, J=7.0 Hz, 3H; CH(C*H*$_3)_2$), 1.19 (d, J=7.0 Hz, 3H; CH(C*H*$_3)_2$), 0.93 ppm (d, J=7.0 Hz, 6H; CH-(C*H*$_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=178.6, 141.0, 128.5, 127.7, 126.0, 72.94, 72.16, 42.04, 34.18, 33.56, 19.08, 18.88, 18.56, 17.55 ppm.

1,3-Diol monoester 3p/3p′: Following general procedure 2, a solution of ketone aldol **1e** (208 mg, 1.00 mmol) in CH_2Cl_2 (0.5 mL) was treated with **2a** (274 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:3) of the crude product yielded pure **3p** (245 mg, 83%) as a white solid; **3p′** (20 mg, 7%) was isolated additionally. Data for **3p**: R_f=0.47 (diethyl ether/pentane 1:1); m.p.=78°C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.46 (dd, J=8.0, 2.0 Hz, 1H; ArH), 7.25 (dt, J=2.0, 8.0 Hz, 1H; ArH), 6.99 (dt, J=2.0, 8.0 Hz, 1H; ArH), 6.86 (dd, J=8.0, 2.0 Hz, 1H; ArH), 5.06 (ddd, J=9.0, 5.0, 3.0 Hz, 1H; CHOCOR), 4.86 (dd, J=9.5, 3.0 Hz, 1H; C*H*OH), 3.82 (s, 3H; OCH_3), 2.85 (brs, 1H; OH), 2.63 (sept, J=7.0 Hz, 1H; C*H*$(CH_3)_2$), 2.00–1.70 (m, 3H; C*H*$(CH_3)_2$, CH_2), 1.23 (d, J=7.0 Hz, 3H; CH(C*H*$_3)_2$), 1.24 (d, J=7.0 Hz, 3H; CH(C*H*$_3)_2$), 0.93 (d, J=7.0 Hz, 3H; CH(C*H*$_3)_2$), 0.92 ppm (d, J=7.0 Hz, 3H; CH-(C*H*$_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=178.2, 155.7, 132.3, 128.1, 126.2, 120.8, 110.2, 75.48, 65.09, 55.22, 40.04, 34.47, 32.07, 19.24, 19.09, 18.66, 17.68 ppm; IR (KBr): $\tilde{\nu}$=3497, 3065, 3047, 2974, 2838, 1702, 1600, 1490, 1461, 1392, 1251, 1168, 1056, 956, 834, 759, 520 cm^{-1}; UV (CH_3CN): λ_{max} (lg ε)=202.0 (3.941), 217.0 (3.875), 271.0 nm (3.287); MS (70 eV, EI): m/z (%): 294 (2) $[M]^+$, 206 (36) $[M-OH^+]$, 163 (100) $[M-C_3H_7]^+$, 137 (100), 135 (32) $[M-COCH(CH_3)_2]^+$, 107 (25) $[C_6H_4OCH_3]^+$, 77 (13) $[C_6H_5]^+$, 43 (39) $[C_3H_7]^+$; elemental analysis calcd (%) for $C_{17}H_{26}O_3$ (294.39): C 69.36, H 8.90; found: C 69.20, H 8.66. Data for **3p′**: R_f=0.33 (diethyl ether/pentane; 1:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.37 (d, J=8.0 Hz, 1H; ArH), 7.26 (t, J=8.0 Hz, 1H; ArH), 6.97 (t, J=8.0 Hz, 1H; 5′-H), 6.87 (d, J=8.0 Hz, 1H; ArH), 6.46 (dd, J=10.0, 3.0 Hz, 1H; CHOCOR), 3.88 (s, 3H; OMe), 3.34 (ddd, J=10.0, 6.0, 2.5 Hz, 1H; C*H*OH), 2.63 (m, 1H; C*H*$(CH_3)_2$), 2.50 (brs, 1H; OH), 1.93 (ddd, J=14.0, 10.0, 2.5 Hz, 1H; CHC*H*HCH), 1.80 (ddd, J=14.0, 10.0, 3.0 Hz, 1H; CHCH*H*CH), 1.68 (m, 1H; C*H*$(CH_3)_2$), 1.21 (d, J=7.0 Hz, 3H; CH(C*H*$_3)_2$), 1.19 (d, J=7.0 Hz, 3H; CH(C*H*$_3)_2$), 0.93 (d, J=7.0 Hz, 3H; CH(C*H*$_3)_2$), 0.90 ppm (d, J=7.0 Hz, 3H; CH(C*H*$_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=177.1, 155.8, 129.3, 128.6, 126.0, 120.5, 110.5, 72.34, 67.74, 55.36, 40.25, 34.13, 33.44, 19.01, 18.91, 18.60, 17.81 ppm.

1,3-Diol monoester 3q/3q′: Following general procedure 2, a solution of ketone aldol **1e** (208 mg, 1.00 mmol) in CH_2Cl_2 (0.5 mL) was treated with **2b** (418 μL, 3.00 mmol). Flash chromatography (silica gel, diethyl ether/pentane 1:7) of the crude product yielded pure **3q** (286 mg, 82%)

as a colorless oil; **3q′**(24 mg, 7%) was isolated additionally. Data for **3q**: R_f=0.53 (diethyl ether/pentane 1:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ= 7.45 (dd, J=8.0, 1.5 Hz, 1H; ArH), 7.24 (dt, J=1.5, 8.0 Hz, 1H; ArH), 6.98 (dt, J=1.5, 8.0 Hz, 1H; ArH), 6.86 (dd, J=8.0, 1.5 Hz, 1H; ArH), 5.18 (m, 1H; CHOCOR), 4.90 (dd, J=9.0, 3.0 Hz, 1H; C*H*OH), 3.83 (s, 3H; OCH_3), 2.94 (ddd, J=3.0, 9.0, 14.0 Hz, 1H; CHCH*H*CH), 2.85 (ddd, J=3.0, 9.0, 14.0 Hz, 1H; CHC*H*HCH), 2.55 (brs, 1H; OH), 2.39 (t, J= 7.5 Hz, 2H; CH_2COOR), 1.75–1.16 (m, 18H; CH_2), 0.80–0.96 ppm (m, 6H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=174.8, 155.9, 132.1, 128.1, 126.4, 120.8, 110.2, 71.78, 65.57, 55.24, 42.65, 34.78, 34.70, 31.74, 31.51, 29.09, 28.88, 25.34, 25.18, 22.56, 22.50, 14.06 ppm; IR (film): $\tilde{\nu}$=3506, 3069, 3035, 2930, 2858, 1731, 1602, 1589, 1492, 1464, 1378, 1240, 1049, 754 cm^{-1}; UV (CH_3CN): λ_{max} (lg ε)=217.0 (3.886), 272.0 nm (3.277); MS (70 eV, EI): m/z (%): 378 (13) $[M]^+$, 360 (20) $[M-H_2O]^+$, 248 (100) $[M-C_3H_7]^+$, 137 (100), 135 (32) $[M-COCH(CH_3)_2]^+$, 107 (25) $[C_6H_4OCH_3]^+$, 77 (13) $[C_6H_5]^+$, 43 (39) $[C_3H_7]^+$; elemental analysis calcd (%) for $C_{23}H_{38}O_4$ (378.55): C 72.98, H 10.12; found: C 72.75, H 9.92. Data for **3q′**: R_f=0.36 (diethyl ether/pentane; 1:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.36 (d, J=8.0 Hz, 1H; ArH), 7.26 (t, J=8.0 Hz, 1H; ArH), 6.96 (t, J=8.0 Hz, 1H; ArH), 6.87 (d, J=8.0 Hz, 1H; ArH), 6.43 (dd, J= 10.0, 3.0 Hz, 1H; CHOCOR), 3.83 (s, 3H; OMe), 3.57 (m, 1H; C*H*OH), 2.90 (brs, 1H; OH), 2.38 (t, J=8.0 Hz, 2H; CH_2COOR), 1.92 (ddd, J= 14.0, 10.5, 3.0 Hz, 1H; CHC*H*HCH), 1.81 (ddd, J=14.0, 10.0, 3.5 Hz, 1H; CHCH*H*CH), 1.17–1.16 (m, 18H; $(CH_2)_5$, $(CH_2)_4$), 0.98–0.77 ppm (m, 6H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=174.1, 155.8, 129.1, 128.7, 126.2, 120.5, 110.5, 67.71, 67.71, 55.40, 43.42, 37.01, 34.55, 31.80, 31.42, 29.28, 28.79, 25.74, 24.99, 22.57, 22.46, 14.06, 13.98 ppm.

1,3-Diol monoester 17: A solution of **1a** (124 μL, 1.00 mmol) and **2f** (203 μL, 2.00 mmol) in CH_2Cl_2 (4 mL) was cooled to −20°C before Zr(O*t*Bu)$_4$ (39 μL, 0.10 mmol) was added. The resulting solution was stirred for 24 h at −20°C, then **2a** (182 μL, 2.00 mmol) and Zr(O*t*Bu)$_4$ (39 μL, 0.10 mmol) were added successively. Stirring was continued for 30 min before addition of 0.5 M aqueous HCl solution (4 mL). The mixture was allowed to reach room temperature. The layers were separated and the aqueous layer was extracted with diethyl ether (3×15 mL). The combined organic layers were dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. Purification of the crude product by flash chromatography (silica gel, diethyl ether/pentane 1:5) yielded compound **17** as a colorless oil (113 mg, 48%). R_f=0.33 (diethyl ether/ pentane 2:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.27–7.40 (m, 5H; ArH), 6.02 (dd, J=10.5, 3.0 Hz, 1H; CHOCOR), 3.78 (m, 1H; C*H*OH), 2.76 (brs, 1H; OH), 2.63 (sept, J=7.5 Hz, 1H; C*H*$(CH_3)_2$), 2.07–1.71 (m, 2H; CH_2), 1.22 (d, J=7.5 Hz, 6H; CH($CH_3)_2$), 1.18 ppm (d, J=7.5 Hz, 1H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=177.3, 140.6, 128.5, 127.8, 126.0, 72.85, 63.65, 46.79, 34.25, 23.06, 18.97, 18.86 ppm; IR (film): $\tilde{\nu}$=3450, 3032, 2931, 2877, 1730, 1458, 1340, 1036, 957, 756 cm^{-1}; UV (CH_3CN): λ_{max} (lg ε)=201.0 (3.834), 206 nm (3.819); HRMS (ESI): calcd for $C_{14}H_{20}NaO_3$: 259.1305; found: 259.1307 $[M+Na]^+$.

Synthesis of 1,3-*anti*-diols 9 through hydrolysis of 1,3-*anti*-diol monoesters 3/3′ (general procedure 3): KOH (224 mg, 4.00 mmol) was added to a stirred solution of diol monoesters **3/3′** (1.00 mmol) in methanol (5 mL) at room temperature and stirring was continued for 24 h. The solution was concentrated under reduced pressure, and the crude product was filtered through a plug of silica gel with diethyl ether to obtain *anti*-diols **9** in almost quantitative yields and as single stereoisomers. The assignment of product configuration was accomplished through conversion of a small sample of the respective diols to the corresponding 1,3-*anti*-diol acetonides **10** (dimethoxypropane, cat. PPTS, RT, 24 h), the configuration of which can be reliably deduced from the ^{13}C NMR data according to the method of Rychnovsky.[25]

Diol 9a: R_f=0.31 (diethyl ether); ^{1}H NMR (200 MHz, $CDCl_3$): δ=4.16 (m, 1H; C*H*OH), 3.68 (ddd, J=3.0, 6.0, 9.0 Hz, 1H; C*H*OH), 2.41 (brs, 2H; OH), 180–1.55 (m, 2H; CHC*H*HCH, C*H*$(CH_3)_2$), 1.55 (ddd, J=14.5, 7.5, 3.0 Hz, 1H; CHCH*H*CH), 1.26 (d, J=6.0 Hz, 3H; CH_3), 0.96 (d, J= 6.5 Hz, 3H; CH($CH_3)_2$), 0.91 ppm (d, J=6.5 Hz, 3H; CH($CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=73.64, 65.37, 41.15, 33.74, 23.41, 18.64, 18.03 ppm; IR (film): $\tilde{\nu}$=3361, 2964, 2935, 1465, 1376, 1147, 1120, 1068, 985 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 282 (9) $[2M+NH_4]^+$, 265 (3) $[2M+H]^+$, 167 (1) $[M+NH_3+NH_4]^+$, 150 (100), $[M+NH_4]^+$, 133 (3) $[M+H]^+$; HRMS (ESI): calcd for $C_7H_{16}NaO_2$: 155.1043; found: 155.1042 $[M+Na]^+$. A small portion of diol **9a** was converted to the corresponding acetonide **10a**: ^{13}C NMR (50 MHz, [D_6]benzene): δ=100.1, 71.56, 62.96, 38.31, 33.31, 25.25, 24.77, 22.04, 18.71, 17.84 ppm.

Diol 9b: R_f=0.36 (diethyl ether); ^{1}H NMR (200 MHz, $CDCl_3$): δ=4.18 (sext, J=6.0 Hz, 1H; C*H*OH), 3.90–4.00 (m, 1H; C*H*OH), 2.30 (brs, 2H; OH), 1.65–1.58 (m, 2H; CHCH_2CH), 1.25 (d, J=6.0 Hz, 3H; CH_3), 1.57–1.20 (m, 10H; $(CH_2)_5$), 0.94–0.84 ppm (m, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=69.11, 65.19, 44.17, 37.43, 31.87, 29.39, 25.83, 23.44, 22.65, 14.10 ppm; IR (film): $\tilde{\nu}$=3384 , 3351, 2958, 2927, 2858, 1460, 1411, 1375, 1120, 1095, 1045 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 366 (1) $[2M+NH_4]^+$, 192 (100) $[M+NH_4]^+$, 175 (3) $[M+H]^+$; HRMS (ESI): calcd for $C_{10}H_{22}NaO_2$: 197.1512; found: 197.1513 $[M+Na]^+$. A small portion of diol **9b** was converted to the corresponding acetonide **10b**: ^{13}C NMR (50 MHz, [D_6]benzene): δ=100.0, 66.56, 62.76, 40.72, 36.53, 32.25, 29.70, 25.81, 25.29, 25.16, 23.02, 22.05, 14.03 ppm.

Diol 9c: R_f=0.35 (diethyl ether); m.p. 45°C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=4.26–3.95 (m, 2H; C*H*OH), 2.90 (brs, 2H; OH), 1.72 (m, 1H; C*H*$(CH_3)_2$), 1.62–1.54 (m, 2H; CH_2), 1.49 (ddd, J=14.0, 9.0, 6.0 Hz, 1H; CHC*H*HCH), 1.23 (ddd, J=14.0, 9.0, 5.0 Hz, 1H; CHCH*H*CH), 1.24 (d, J=6.5 Hz. 3H; CH_3), 0.92 ppm (d, J=6.5 Hz, 6H; CH($CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=67.17, 65.31, 46.40, 44.42, 24.53, 23.45, 23.21, 22.19 ppm; IR (KBr): $\tilde{\nu}$=3356, 2958, 2870, 1468, 1369, 1133, 1047, 954 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 164 (100) $[M+NH_4]^+$, 147 (5) $[M+H]^+$; HRMS (ESI): calcd for $C_8H_{18}NaO_2$: 169.1199; found: 169.1199 $[M+Na]^+$. A small portion of diol **9c** was converted to the corresponding acetonide **10c**: ^{13}C NMR (50 MHz, [D_8]toluene): δ=101.0, 65.64, 63.76, 46.68, 42.21, 26.20, 26.10, 25.69, 24.59, 23.23, 23.04 ppm.

Diol 9d: R_f=0.38 (diethyl ether); ^{1}H NMR (200 MHz, $CDCl_3$): δ=4.16 (m, 1H; C*H*OH), 3.96 (ddd, J=9.5, 5.0, 2.5 Hz, 1H; C*H*OH), 2.60 (brs, 2H; OH), 1.75–1.18 (m, 6H; C*H*$(CH_2CH_3)_2$, CHC*H*HCH), 1.68 (ddd, J= 14.5, 9.5, 3.5 Hz, 1H; CHCH*H*CH), 1.25 (d, J=6.5 Hz, 3H; CH_3), 0.91 ppm (t, J=7.0 Hz, 6H; CHCH($CH_2CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=69.89, 65.53, 46.69, 40.89, 23.34, 21.68, 21.31, 11.53, 11.51 ppm; IR (film): $\tilde{\nu}$=3390, 3357, 2962, 2931, 2873, 1460, 1411, 1377, 1120, 1078, 1028 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 178 (100) $[M+NH_4]^+$, 161 (5) $[M+H]^+$; HRMS (ESI): calcd for $C_9H_{20}NaO_2$: 183.1356; found: 183.1354 $[M+Na]^+$. A small portion of diol **9d** was converted to the corresponding acetonide **10d**: ^{13}C NMR (50 MHz, [D_8]toluene): δ=101.1, 68.81, 64.03, 46.97, 39.63, 26.12, 25.71, 23.03, 22.36, 22.16, 12.51, 12.10 ppm.

Diol 9e: R_f=0.26 (diethyl ether/pentane 10:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ=4.16 (m, 1H; C*H*OH), 3.68 (ddd, J=9.0, 6.0, 3.0 Hz, 1H; C*H*OH), 2.32 (brs, 2H; OH), 1.96–0.86 (m, 13H; cyclohexyl-CH_2, cyclohexyl-CH, CHCH_2CH), 1.24 ppm (d, J=6.5 Hz, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=73.20, 65.47, 43.54, 41.03, 28.99, 28.44, 26.46, 26.19, 26.08, 23.44 ppm; IR (film): $\tilde{\nu}$=3375, 3350, 2927, 2852, 1448, 1411, 1311, 1118, 1064, 977 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 205 (20) $[M+NH_3+NH_4]^+$, 190 (100) $[M+NH_4]^+$. 188 (96); HRMS (ESI): calcd for $C_{10}H_{20}NaO_2$: 195.1356; found: 195.1356 $[M+Na]^+$. A small portion of diol **9e** was converted to the corresponding acetonide **10e**: ^{13}C NMR (50 MHz, [D_6]benzene): δ=100.1, 70.57, 62.95, 43.05, 38.43, 29.24, 28.32, 27.05, 26.45, 26.29, 25.13, 24.75, 22.05 ppm.

Diol 9f: R_f=0.50 (diethyl ether); m.p. 75°C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=3.65 (dt, J=5.5, 7.0 Hz, 2H; C*H*OH), 2.00 (brs, 2H; OH), 1.70 (octet, J=7.0 Hz, 2H; C*H*$(CH_3)_2$), 1.60 (dd, J=7.0, 5.5 Hz, 2H; CH_2), 0.96 (d, J=7.0 Hz, 6H; CH($CH_3)_2$), 0.91 ppm (d, J=7.0 Hz, 6H; CH($CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=74.18, 36.50, 33.72, 18.69, 18.09 ppm; IR (KBr): $\tilde{\nu}$=3348, 2961, 2873, 1473, 1329, 1103, 1046, 1005, 898 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 178 (100) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_9H_{20}O_2$ (160.26): C 67.45, H 12.58; found: C 67.12, H 12.53. A small portion of diol **9f** was converted to the corresponding acetonide **10f**: ^{13}C NMR (50 MHz, $CDCl_3$): δ=100.1, 71.97, 34.46, 33.06, 24.34, 18.90, 17.66 ppm.

Diol 9g: R_f=0.54 (diethyl ether); m.p. 51°C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=3.93 (m, 1H; C*H*OH), 3.68 (ddd, J=9.0, 6.0, 3.0 Hz, 1H; C*H*OH), 2.30 (brs, 2H; OH), 1.67 (sept., J=7.0 Hz, 1H; C*H*$(CH_3)_2$),

1.73–1.20 (m, 12H; $(CH_2)_5$, $CHCH_2CH$), 0.95–0.84 (m, 3H; CH_2CH_3), 0.95 (d, J=7.0 Hz, 3H; $CH(CH_3)_2$), 0.90 ppm (d, J=7.0 Hz, 3H; $CH(CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=73.92, 69.57, 39.32, 37.42, 33.79, 31.84, 29.36, 25.87, 22.63, 18.63, 18.03, 14.10 ppm; IR (KBr): $\tilde{\nu}$=3322, 2956, 2920, 1468, 1329, 1069, 998, 674 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 220 (100) $[M+NH_4]^+$, 203 (2) $[M+H]^+$; HRMS (ESI): calcd for $C_{12}H_{26}NaO_2$: 225.1825; found: 225.1825 $[M+Na]^+$. A small portion of diol **9g** was converted to the corresponding acetonide **10g**: ^{13}C NMR (50 MHz, $CDCl_3$): δ=100.0, 71.79, 66.87, 36.78, 36.07, 33.02, 31.87, 29.27, 25.43, 24.67, 24.41, 22.64, 18.86, 17.62, 14.10 ppm.

Diol 9h: R_f=0.51 (diethyl ether); m.p. 95 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=3.60 (ddd, J=8.0, 6.5, 3.0 Hz, 1H; C*H*OH), 3.59 (dd, J=10.0, 2.5 Hz, 1H; C*H*OH), 2.10 (brs, 2H; OH), 1.74 (octet, J=6.5 Hz, 1H; $CH(CH_3)_2$), 1.61 (ddd, J=14.0, 8.0, 2.5 Hz, 1H; CHC*H*HCH), 1.50 (ddd, J=14.0, 10.0, 3.0 Hz, 1H; CHCH*H*CH), 0.98 (d, J=6.5 Hz, 3H; $CH(CH_3)_2$), 0.92 (s, 9H; *t*Bu), 0.91 ppm (d, J=6.5 Hz, 3H; $CH(CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=76.04, 74.45, 34.73, 34.43, 33.48, 25.63, 18.90, 18.27 ppm; IR (KBr): $\tilde{\nu}$=3346, 2958, 1470, 1401, 1055, 1007, 819 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 192 (100) $[M+NH_4]^+$, 176 (35); elemental analysis calcd (%) for $C_{10}H_{22}O_2$ (174.28): C 68.92, H 12.72; found: C 68.64, H 12.45. A small portion of diol **9h** was converted to the corresponding acetonide **10h**: ^{13}C NMR (50 MHz, [D_6]benzene): δ=100.2, 74.01, 72.17, 33.55, 33.43, 31.79, 25.50, 24.55, 24.34, 18.77, 18.02 ppm.

Diol 9i:[26] R_f=0.04 (diethyl ether/pentane 1:4); m.p. 99 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.45–7.20 (m, 5H; ArH), 5.08 (dd, J=7.5, 4.0 Hz, 1H; C*H*OH), 3.51 (dd, J=10.0, 2.5 Hz, 1H; C*H*OH), 2.80 (brs, 1H; OH), 1.93 (ddd, J=14.0, 7.5, 2.5 Hz, 1H; C*H*H), 1.85 (ddd, J=14.0, 10.0, 4.0 Hz, 1H; CH*H*), 1.62 (brs, 1H; OH), 0.95 ppm (s, 9H; *t*Bu); ^{13}C NMR (50 MHz, $CDCl_3$): δ=144.7, 128.4, 127.2, 125.5, 76.22, 71.89, 39.28, 34.66, 25.49 ppm; IR (KBr): $\tilde{\nu}$=3443, 3063, 3030, 2955, 1476, 1398, 1075, 1051, 760, 699, 541 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 226 (90) $[M+NH_4]^+$, 208 (100), $[M-H_2O+NH_4]^+$, 156 (30), 117 (20). A small portion of diol **9i** was converted to the corresponding acetonide **10i**: ^{13}C NMR (50 MHz, [D_6]benzene): δ=143.0, 128.4, 127.3, 126.0, 100.7, 73.71, 69.17, 35.67, 33.49, 25.23, 25.01, 24.00 ppm.

Diol 9j: R_f=0.28 (diethyl ether/pentane 1:1); m.p. 91 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=3.91 (m, 1H; C*H*OH), 3.58 (dd, J=10.0, 2.5 Hz, 1H; C*H*OH), 2.22 (brs, 2H; OH), 1.62 (ddd, J=14.5, 8.5, 2.5 Hz, 1H; CHC*H*HCH), 1.65–1.20 (m, 6H; CHCH*H*CH, $CH(CH_2CH_3)_2$), 1.00–0.85 (m, 6H; $CH(CH_2CH_3)_2$), 0.92 ppm (s, 9H; *t*Bu); ^{13}C NMR (50 MHz, $CDCl_3$): δ=76.20, 70.46, 46.39, 34.80, 34.56, 25.69, 21.77, 21.21, 11.44, 11.35 ppm; IR (KBr): $\tilde{\nu}$=3417, 2957, 2872, 1467, 1062, 1008, 831 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 220 (88) $[M+NH_4]^+$, 193 (36), 178 (100); elemental analysis calcd (%) for $C_{12}H_{26}O_2$ (202.34): C 71.23, H 12.95; found: C 71.11, H 12.85. A small portion of diol **9j** was converted to the corresponding acetonide **10j**: ^{13}C NMR (50 MHz, [D_6]benzene): δ=100.2, 74.08, 68.40, 46.01, 33.55, 31.89, 25.52, 24.60, 24.38, 21.31, 21.15, 11.48, 11.08 ppm.

Diol 9k: R_f=0.55 (diethyl ether); m.p. 135 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=3.61 (dt, J=3.0, 7.5 Hz, 1H; C*H*OH), 3.58 (dd, J=10.5, 2.5 Hz, 1H; C*H*OH), 2.10 (bs, 2H; OH), 1.98–0.93 (m, 13H; cyclohexyl-CH_2, cyclohexyl-CH, $CHCH_2CH$), 0.90 ppm (s, 9H; *t*Bu); ^{13}C NMR (50 MHz, $CDCl_3$): δ=76.16, 73.90, 43.19, 34.76, 34.20, 29.20, 28.74, 26.45, 26.16, 26.06, 25.61 ppm; IR (KBr): $\tilde{\nu}$=3342, 2933, 2850, 1480, 1362, 1074, 996, 931 cm^{-1}; MS (200 eV, DCI/NH_3): m/z (%): 446 (1) $[2M+NH_4]^+$, 232 (100) $[M+NH_4]^+$, 215 (5) $[M+H]^+$; elemental analysis calcd (%) for $C_{13}H_{26}O_2$ (214.35): C 72.85, H 12.23; found: C 73.07, H 11.91. A small portion of diol **9k** was converted to the corresponding acetonide **10k**: ^{13}C NMR (50 MHz, [D_6]benzene): δ=100.2, 74.03, 71.22, 43.15, 33.57, 31.87, 29.31, 28.46, 27.05, 26.51, 26.32, 25.51, 24.57, 24.32 ppm.

Diol 9l: R_f=0.56 (diethyl ether); m.p. 77 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=3.92 (m, 1H; C*H*OH), 3.60 (dd, J=8.0, 4.5 Hz, 1H; C*H*OH), 2.12 (brs, 2H; OH), 1.20–1.68 (m, 12H; $(CH_2)_5$, $CHCH_2CH$), 0.93–0.88 (m, 3H; CH_3), 0.91 ppm (s, 9H; *t*Bu); ^{13}C NMR (50 MHz, $CDCl_3$): δ=75.99, 69.79, 37.15, 36.98, 34.64, 31.80, 29.32, 25.96, 25.58, 22.59, 14.06; IR (KBr): $\tilde{\nu}$=3345, 2953, 2868, 1467, 1361, 1322, 1250, 1115, 1070, 1011, 672 ppm; MS (200 eV, DCI/NH_3): m/z (%):234 (100) $[M+NH_4]^+$, 216 (5) $[M-H_2O+NH_4]^+$; elemental analysis calcd (%) for $C_{13}H_{28}O_2$ (216.36): C 72.17, H 13.04; found: C 72.47, H 12.88. A small portion of diol **9l** was converted to the corresponding acetonide **10l**: ^{13}C NMR (50 MHz, [D_6]benzene): δ=100.2, 73.16, 67.18, 36.61, 34.35, 33.51, 32.25, 29.74, 25.94, 25.48, 24.58, 24.41, 23.03, 14.31 ppm.

Diol 9m: R_f=0.54 (diethyl ether); m.p. 104 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=3.68 (dd, J=9.5, 3.5 Hz, 1H; C*H*OH), 3.15 (ddd, J=9.5, 6.5, 4.0 Hz, 1H; C*H*OH), 2.17 (brs, 2H; OH), 1.73 (ddd, J=15.0, 6.5, 3.5 Hz, 1H; CHC*H*HCH), 1.67 (ddd, J=15.0, 9.5, 4.0 Hz, 1H; CHCH*H*CH), 1.03 (m, 1H; cyclopropyl-CH), 0.92 (s, 9H; *t*Bu), 0.61–0.48 (m, 2H; cyclopropyl-CH_2), 0.28–0.16 ppm (m, 2H; cyclopropyl-CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ=76.04, 74.79, 36.96, 34.65, 25.66, 17.30, 3.43, 2.34 ppm; IR (KBr): $\tilde{\nu}$=3327, 2952, 2867, 1473, 1365, 1325, 1080, 976, 918 cm^{-1}; HRMS (ESI): calcd for $C_{10}H_{20}NaO_2$: 195.1356; found: 195.1357 $[M+Na]^+$. A small portion of diol **9m** was converted to the corresponding acetonide **10m**: ^{13}C NMR (50 MHz, [D_6]benzene): δ=100.1, 73.82, 71.50, 33.74, 33.53, 25.44, 24.97, 24.35, 16.31, 3.41, 2.00 ppm.

Diol 9n: R_f=0.45 (diethyl ether); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.39–7.20 (m, 5H; ArH), 5.03 (dd, J=5.5, 2.0 Hz, 1H; C*H*OH), 3.84 (m, 1H; C*H*OH), 3.20 (brs, 2H; OH), 1.90 (ddd, J=10.0, 5.0, 2.0 Hz, 1H; CHC*H*HCH), 1.80 (ddd, J=10.0, 5.5, 2.5 Hz, 1H; CHCH*H*CH), 1.65–1.14 (m, 10H; $(CH_2)_5$), 0.93–0.83 ppm (m, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ=144.5, 128.3, 127.2, 125.5, 71.55, 69.23, 44.48, 37.35, 31.75, 29.24, 25.57, 22.55, 14.04 ppm; IR (film): $\tilde{\nu}$=3362, 3063, 3030, 2929, 2857, 1709, 1454, 1057, 756, 700 cm^{-1}; UV (CH_3CN): λ_{max} (lg ε)=197.0 (3.744), 205.0 nm (3.788); MS (200 eV, DCI/NH_3): m/z (%): 726 (20) $[3M+NH_4]^+$, 490 (100) $[2M+NH_4]^+$, 271 (9) $[M+NH_3+NH_4]^+$, 254 (75) $[M+NH_4]^+$, 236 (3) $[M-H_2O+NH_4]^+$; HRMS (ESI): calcd for $C_{15}H_{24}NaO_2$: 259.1669; found: 259.1669 $[M+Na]^+$. A small portion of diol **9n** was converted to the corresponding acetonide **10n**: ^{13}C NMR (50 MHz, [D_6]benzene): δ=142.7, 128.4, 127.3, 126.0, 100.7, 68.59, 66.86, 40.32, 35.99, 31.79, 29.20, 25.29, 25.09, 24.68, 22.58, 14.07 ppm.

Diol 9o: R_f=0.41 (diethyl ether); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.48–7.20 (m, 5H; ArH), 5.07 (t, J=7.0 Hz, 1H; C*H*OH), 3.62 (q, J=7.0 Hz, 1H; C*H*OH), 2.30 (brs, 2H; OH), 1.88 (t, J=7.0 Hz, 2H; CH_2), 1.70 (octet, J=7.0 Hz, 1H; $CH(CH_3)_2$), 0.92 (d, J=7.0 Hz, 3H; $CH(CH_3)_2$), 0.88 ppm (d, J=7.0 Hz, 3H; $CH(CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=144.7, 128.4, 127.2, 125.5, 73.80, 71.73, 41.61, 33.73, 18.53, 17.71 ppm; IR (film): $\tilde{\nu}$=3435, 3060, 3033, 2953, 2889, 1454, 1401, 1343, 1171, 1073, 1034, 701, 756 cm^{-1}; UV (CH_3CN): λ_{max} (lg ε)=207.0 (3.712), 210.0 (3.715), 257.0 nm (2.275); MS (70 eV, EI): m/z (%): 194 (15) $[M]^+$, 176 (23) $[M-H_2O]^+$, 151 (2) $[M-C_3H_7]^+$, 133 (60), 107 (100) $[C_7H_7O]^+$, 105 (100) $[PhCO]^+$, 43 (10) $[C_3H_7]^+$; HRMS (ESI): calcd for $C_{12}H_{18}NaO_2$: 217.1199; found: 217.1199 $[M+Na]^+$. A small portion of diol **9o** was converted to the corresponding acetonide **10o**: ^{13}C NMR (50 MHz, [D_6]benzene): δ=143.8, 128.5, 127.5, 127.2, 100.7, 71.79, 68.87, 38.96, 33.31, 25.15, 24.53, 18.67, 17.76 ppm.

Diol 9p: R_f=0.68 (diethyl ether); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.45 (dd, J=8.0, 2.0 Hz, 1H; ArH), 7.27 (dt, J=2.0, 8.0 Hz, 1H; ArH), 6.98 (dt, J=2.0, 8.0 Hz, 1H; ArH), 6.87 (dd, J=8.0, 1.5 Hz, 1H; ArH), 5.28 (dd, J=8.0, 4.0 Hz, 1H; C*H*OH), 3.84 (s, 3H; OMe), 3.59 (ddd, J=7.0, 6.0, 3.0 Hz, 1H; C*H*OH), 2.62 (brs, 2H; OH), 1.98 (ddd, J=14.0, 8.0, 3.0, 1H; C*H*H), 1.86 (ddd, J=14.0, 6.0, 4.0, 1H; CH*H*), 1.72 (octet, J=7.0 Hz, 1H; $CH(CH_3)_2$), 0.93 (d, J=7.0 Hz, 3H; $CH(CH_3)_2$), 0.90 ppm (d, J=7.0 Hz, 3H; $CH(CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ=155.9, 132.4, 128.1, 126.5, 120.7, 110.2, 74.22, 67.94, 55.18, 39.47, 33.55, 18.55, 17.88 ppm; IR (film): $\tilde{\nu}$=3379, 3357, 2960, 2837, 1597, 1488, 1392, 754 cm^{-1}; UV (CH_3CN): λ_{max} (lg ε)=199.0 (0.7373), 202.0 (3.892), 217.0 (3.769), 270.0 nm (3.171); MS (70 eV, EI): m/z (%): 224 (13) $[M]^+$, 206 (10) $[M-H_2O]^+$, 137 (100), 107 (20) $[MeOC_6H_4]^+$, 77 (10) $[C_6H_5]^+$, 43 (5) $[C_3H_7]^+$; HRMS (ESI): calcd for $C_{13}H_{20}NaO_3$: 247.1305; found: 247.1305 $[M+Na]^+$. A small portion of diol **9p** was converted to the corresponding acetonide **10p**: ^{13}C NMR (50 MHz, $CDCl_3$): δ=155.8, 131.7, 127.8, 126.2, 120.7, 110.1, 100.6, 71.89, 63.31, 55.26, 37.24, 32.97, 24.91, 24.55, 18.81, 17.58 ppm.

Diol 9q: R_f=0.71 (diethyl ether); ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.44 (dd, J=8.0, 2.0 Hz, 1H; ArH), 7.26 (dt, J=2.0, 8.0 Hz, 1H; ArH), 7.00 (dt, J=2.0, 8.0 Hz, 1H; ArH), 6.88 (dd, J=8.0, 1.5 Hz, 1H; ArH), 5.29

(dd, $J=8.0$, 4.0 Hz, 1H; C*H*OH), 3.85 (m, 1H; C*H*OH), 3.84 (s, 3H; OMe), 2.68 (br s, 2H; OH), 2.00 (ddd, $J=14.5$, 8.0, 3.0 Hz, 1H; CHC*H*HCH), 1.85 (ddd, $J=14.5$, 8.0, 4.0 Hz, 1H; CHCH*H*CH), 1.67–1.10 (m, 10H; $(CH_2)_5$), 0.94–0.80 ppm (m, 3H; CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta=155.8$, 132.3, 127.9, 126.4, 120.6, 110.1, 69.40, 67.37, 55.07, 42.15, 37.18, 31.75, 29.24, 25.54, 22.51, 13.99 ppm; IR (film): $\tilde{\nu}=3364$, 3073, 2929, 2857, 1602, 1464, 1240, 1050, 754 cm^{-1}; UV (CH_3CN): λ_{max} (lg ε) = 198.0 (0.7510), 219.0 (3.671), 270.0 nm (3.082); MS (200 eV, DCI/NH_3): *m*/*z* (%): 532 (10) $[2M-H_2O+NH_4]^+$, 284 (11) $[M+NH_4]^+$, 266 (100) $[M-H_2O+NH_4]^+$; HRMS (ESI): calcd for $C_{16}H_{26}NaO_3$: 289.1774; found: 289.1775 $[M+Na]^+$. A small portion of diol **9q** was converted to the corresponding acetonide **10q**: ^{13}C NMR (50 MHz, $CDCl_3$): $\delta=155.8$, 131.6, 127.8, 126.2, 120.7, 110.1, 100.5, 66.90, 63.13, 55.24, 39.43, 35.92, 31.81, 29.23, 25.32, 24.94, 24.94, 22.58, 14.05 ppm.

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