Facially Controlled *C*-Methylation of Oxolanyl and Cyclopentyl Acetate Enolates: Application to the Total Synthesis of (+)-Nephromopsinic Acid

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Keywords: Alkylation / Configuration determination / Enolates / Natural product synthesis / Paraconic acids / Stereoelectronic effects

The stereoselectivity of the *C*-methylation of oxolanyl and cyclopentyl acetate enolates **5a**–**22a** was investigated. The configuration of the *C*-methyl diastereomers was elucidated by a combination of crystal structure analysis, NMR spectroscopy and chemical correlations. Generally, the methylation proceeded *re**-selectively, although with very different degrees of selectivity. The most important stereodirecting effect was a steric one exerted by the 5-phenethyl substituent, and this steric effect was strongly increased by the stereodirecting effect of a 3-OR group. Contrary to previous literature evidence, the endocyclic oxolanyl oxygen does not exert an effect. These findings were applied in a highly stereoselective synthesis of (+)-nephromopsinic acid (**94**).

Introduction

Alkylations of ester enolates in which the enolate carbon is adjacent to a suitably substituted cyclopentane ring proceed with high stereoselectivity [Scheme 1; eq. (1) and (2)].[1] On the other hand, the oxolanyl-substituted acetate in Scheme 1 [eq. (3)] exhibits only a moderate selectivity of 67:33.[2] If, however, there is an ether function in the *cis*-3-position, as in esters **1** (with various R groups) and **3**, the *C*-methyl derivatives **2** and **4** are formed with extremely high (>99%) stereocontrol [Scheme 1; eqs. (4) and (5)].[3]

As proposed by Frater,[4] the facial selectivity found in eqs. (1) and (2) can be rationalized by an $A^{1,3}$-strain-controlled transition-state conformation,[5] which is attacked by the electrophile from the less-hindered (*re**) face[6] (Figure 1). The stereochemical course in eq. (3), however, was explained by McGarvey and Williams[2] as being due to a stereoelectronic effect of the oxygen lone pair *anti* to the ring bond, which donates electrons into the π*-orbital of the enolate and activates the *re**-face towards electrophilic attack (Figure 2, structure **I**). In light of this assumption, the enhanced selectivity exhibited by esters **1** [Scheme 1; eq. (4)] and **3** [Scheme 1; eq. (5)] may be attributed to the combined effects of the endocyclic oxygen and the lone

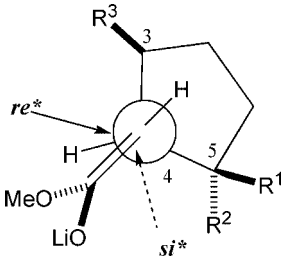

Figure 1. Transition state of the enolate alkylation

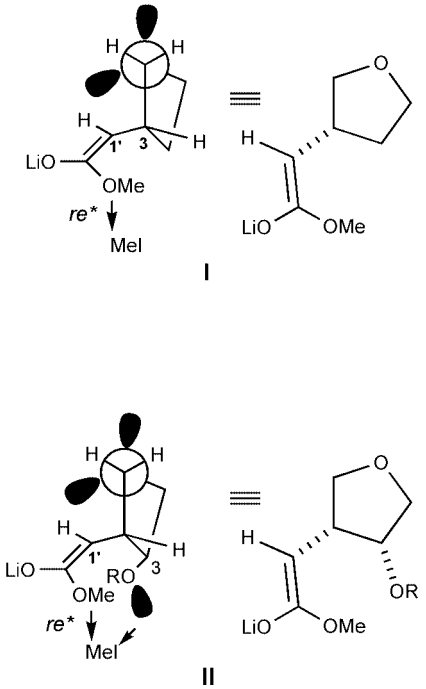

Figure 2. Facial stereoelectronic effects in the enolate alkylation

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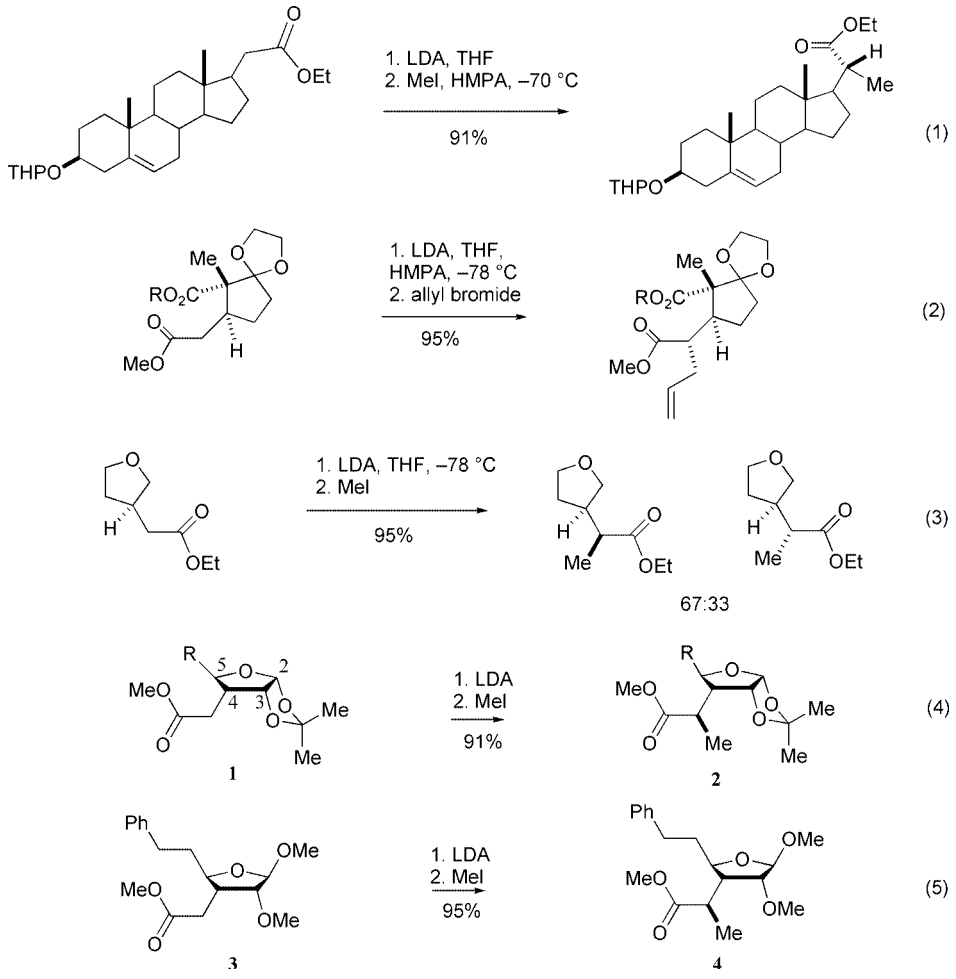
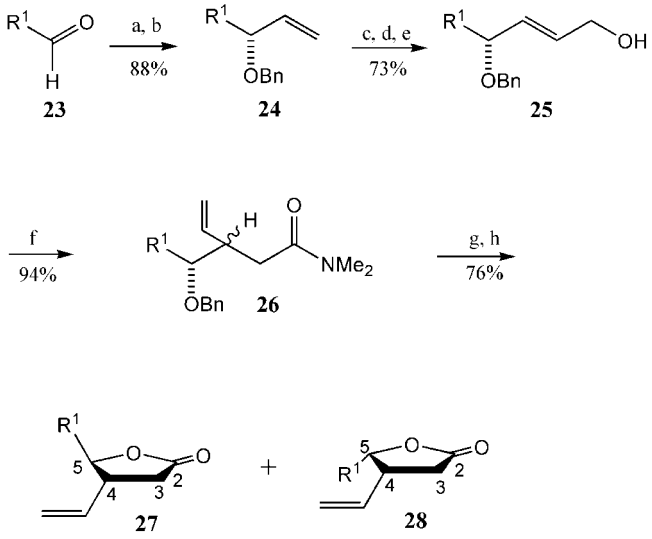


Scheme 1. *C*-Methylation of oxolanyl and cyclopentyl acetate enolates



Scheme 2. $R^1 = CH_2CH_2Ph$; reagents and conditions: a) vinylmagnesium bromide, THF, room temp.; b) NaH, DMF, BnCl; c) O_3, –78 °C, MeOH, then Me_2S; d) $(EtO)_2POCH_2CO_2Me$, NaH, THF; e) DIBALH, toluene; f) $MeC(OMe)_2NMe_2$, 120 °C, toluene; g) Na, NH_3(l), THF; h) NaOH, MeOH

pairs at O-3, which donate electrons into the σ*-orbital of the electrophile and direct it to the *re**-face of the enolate (Figure 2, structure **II**).

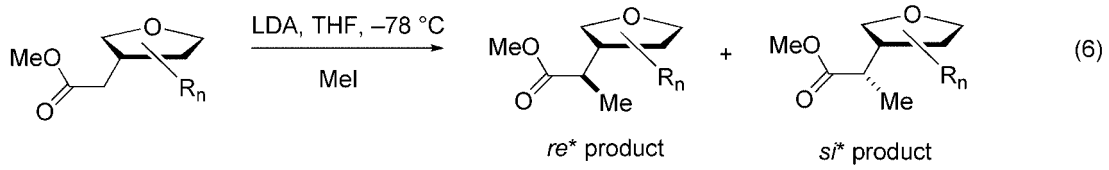
To validate these assumptions we synthesized the model compounds **5a**–**22a** (see reaction conditions a, b in Scheme 2), which are partially or completely devoid of these oxygen functions, and investigated the facial selectivity in the *C*-methylation of the corresponding enolates.

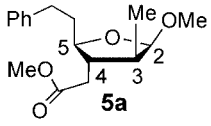
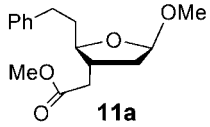
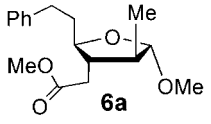
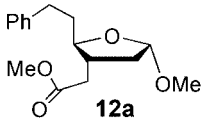
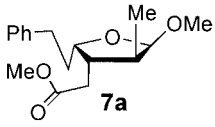
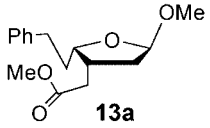
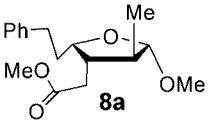
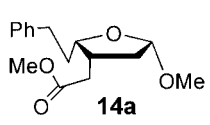
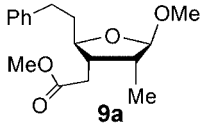
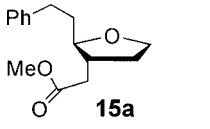
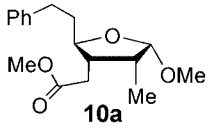
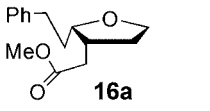
Results and Discussion

The methyl 2-[5-(2′-phenethyl)oxolan-4-yl]acetates **5a**–**16a** were prepared in racemic form, and *C*-methylated via the ester enolates to give diastereomeric mixtures of **5b**,**c**–**16b**,**c** [eq. (6) in Table 1]. The details of the synthesis and the configurational assignments are given below. Table 1 shows that the general preference for the *re**-facial attack is maintained, although the selectivity in most cases is significantly lower than for esters **1** and **3**.

In particular, the 3-methyl derivatives **5a**–**10a** give diastereomeric ratios of only 62:38 to 82:18 depending on the relative configurations at C-2, C-3, and C-5. Remarkably,

Table 1. Diastereomeric ratios and combined yields for the *C*-methylation of esters **5**–**16a**

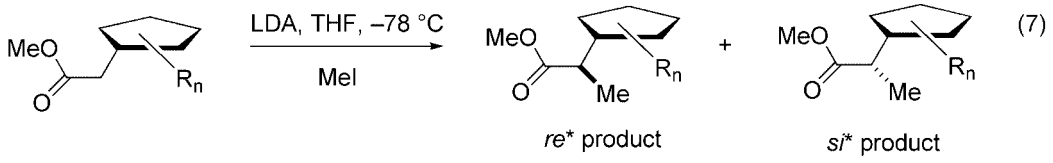


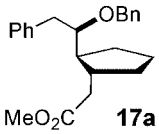
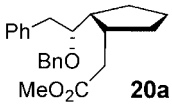
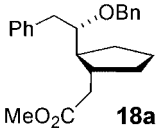
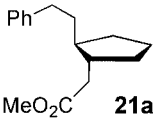
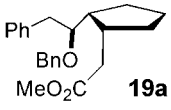
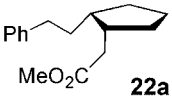
Entry	Substrate	Yield	Products (*re**:*si**)	Entry	Substrate	Yield	Products (*re**:*si**)
1	 **5a**	92%	**5b:5c** 70:30	7	 **11a**	79%	**11b:11c** 86:14
2	 **6a**	89%	**6b:6c** 82:18	8	 **12a**	73%	**12b:12c** 96:4
3	 **7a**	81%	**7b:7c** 63:37	9	 **13a**	79%	**13b:13c** 86:14
4	 **8a**	95%	**8b:8c** 62:38	10	 **14a**	73%	**14b:14c** 96:4
5	 **9a**	95%	**9b:9c** 80:20	11	 **15a**	94%	**15b:15c** 89:11
6	 **10a**	98%	**10b:10c** 80:20	12	 **16a**	96%	**16b:16c** 92:8

the relative configurations at C-5 and C-3 are of minor importance. For compounds **11**–**14**, the anomeric center at C-2 acts very much like the 3-OR group in **1** and **3**, as a 2-OMe in the position *cis* to the C-4 appendage enhances the *re**-selectivity relative to the corresponding *trans*-1-OMe derivatives. The presence of the 3-Me group in systems **5**–**10** neutralizes this effect. The still existing *re**-preference in all systems can only be due to the stereoelectronic effect of the endocyclic oxygen and the steric shielding of the 5-phenethyl residue, both of which should induce *re**-facial selectivity despite a counteracting steric effect from the 3-methyl substituents. In fact, the absence of the 3-methyl group in model compounds **11a**–**14a** results in a pronounced increase of the *re**-facial selectivity, which is also observed for the 2,3-unsubstituted systems **15a** and **16a**.

It remained to clarify the influence of the endocyclic oxygen. Thus, the cyclopentyl analogs **17**–**22a** were prepared in racemic form and methylated as before [eq. (7) in Table 2]. Surprisingly, the *re**-facial selectivities are about the same as for the oxolanyl derivatives. Now the only stereodirecting effect is a steric one exerted by the 5-phenethyl substituent. Indeed, if the bulkiness of this residue is enhanced by introducing a 1′-*O*-benzyl function (as in **17**–**20**), the *re**-selectivity is higher in most cases than in the unbranched analogs **21** and **22**. Unlike the 3-OR functions in compounds **1** and **3**, the *O*-benzyl ether functions in **17**–**20** are not properly located to exert an attractive effect on the incoming alkyl halide that would direct them towards the *si**-face of the enolate. In conclusion, the observed *re**-facial selectivity can be interpreted in terms of a steric effect exerted by a phenethyl appendage in the 5-position. This selectivity may be enhanced by a stereoelectronic effect from the 3-OR substituents on the ring. The presence of an endocyclic oxygen is of no importance.

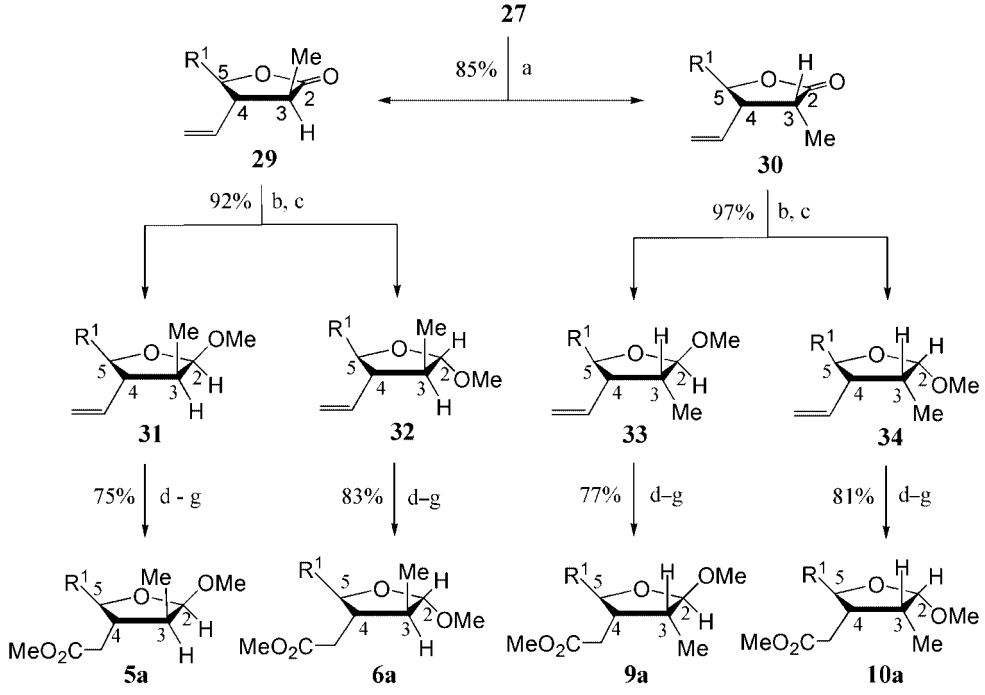
Table 2. Diastereomeric ratios and combined yields for the *C*-methylation of esters **17**–**22a**



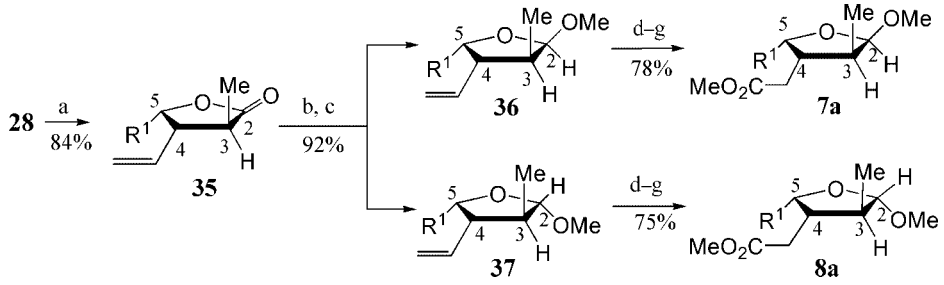
Entry	Substrate	Yield	Products (*re**:*si**)	Entry	Substrate	Yield	Products (*re**:*si**)
1	 **17a**	95%	**17b:17c** 80:20	4	 **20a**	95%	**20b:20c** 91:9
2	 **18a**	98%	**18b:18c** 93:7	5	 **21a**	93%	**21b:22c** 89:11
3	 **19a**	96%	**19b:19c** 90:10	6	 **22a**	95%	**22b:22c** 8 :16

Synthesis and Configurational Assignments of Compounds 5–22(a–c)

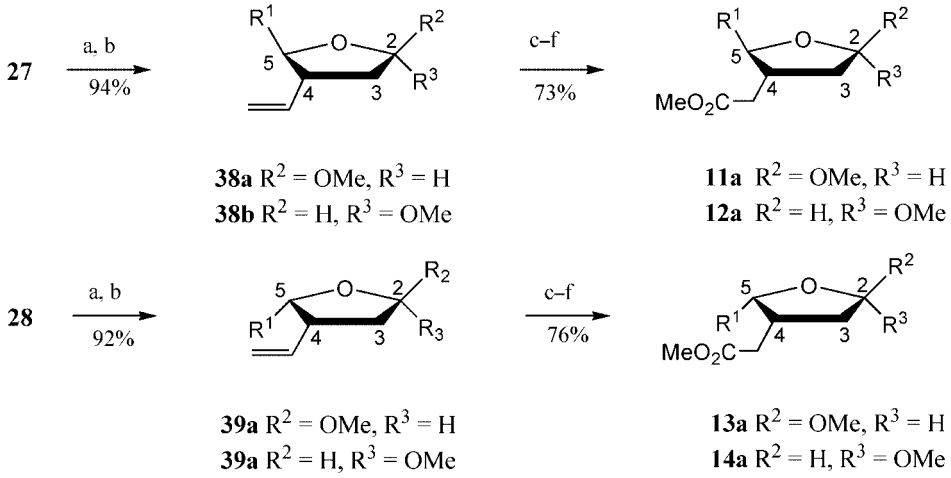
The synthesis (Scheme 2) started with aldehyde **23**, which was first converted into the allylic alcohol **25** and then subjected to a Claisen–Eschenmoser rearrangement to form a diastereomeric mixture of amides **26**. Without separation, this mixture was transformed into the lactones **27** and **28**, which are easily separable by chromatography. The relative configurations were safely assigned by ^{1}H NMR spec-



Scheme 3. R^1 = CH_2CH_2Ph; reagents and conditions: a) LDA, THF, –78 °C, MeI; b) DIBALH, –70 °C, toluene; c) MeOH, *p*TsOH; d) 9-BBN, THF, then H_2O_2, NaOH; e) DMSO, DCC, pyridine, TFA, toluene; f) $KMnO_4$, *t*BuOH, pH 7 buffer; g) CH_2N_2, diethyl ether



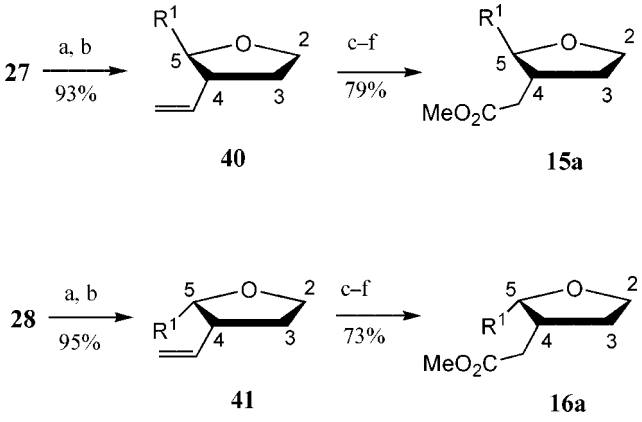
Scheme 4. R^1 = CH_2CH_2Ph; reagents and conditions: a) LDA, THF, –78 °C, MeI; b) DIBALH, –70 °C, toluene; c) MeOH, *p*TsOH; d) 9-BBN, THF, then H_2O_2, NaOH; e) DMSO, DCC, pyridine, TFA, toluene; f) $KMnO_4$, *t*BuOH, pH 7 buffer; g) CH_2N_2, diethyl ether



Scheme 5. R^1 = CH_2CH_2Ph; reagents and conditions: a) DIBALH; b) MeOH, *p*TsOH; c) 9-BBN, H_2O_2; d) DMSO, DCC; e) $KMnO_4$, *t*BuOH, pH 7 buffer; f) CH_2N_2

troscopy. Thus, the signals of both 4- and 5-H in the *trans*-compound **27** are shifted upfield by about 0.3 ppm compared to **28**. Additional evidence came from NOE experiments. On monomethylation with LDA/MeI (Scheme 3) **27** forms the diastereomers **29** and **30**, which were separated and structurally assigned by NOE difference spectroscopy. Both **29** and **30** were converted into mixtures of the anomers **31**/**32** and **33**/**34**, respectively. After chromatographic separation the relative configurations of the anomers could be assigned by ^1H NMR spectroscopy; for instance, the 2-OMe group induces an anisotropic effect on the 1′-CH_2 group of the 5-*cis*-phenethyl side-chain in **31** and **33**, which appears in the form of two one-proton multiplets at δ = 1.65 and 1.85 ppm. In **32** and **34**, the 1′-CH_2 group appears as one, two-proton multiplet at δ = 1.70 ppm.

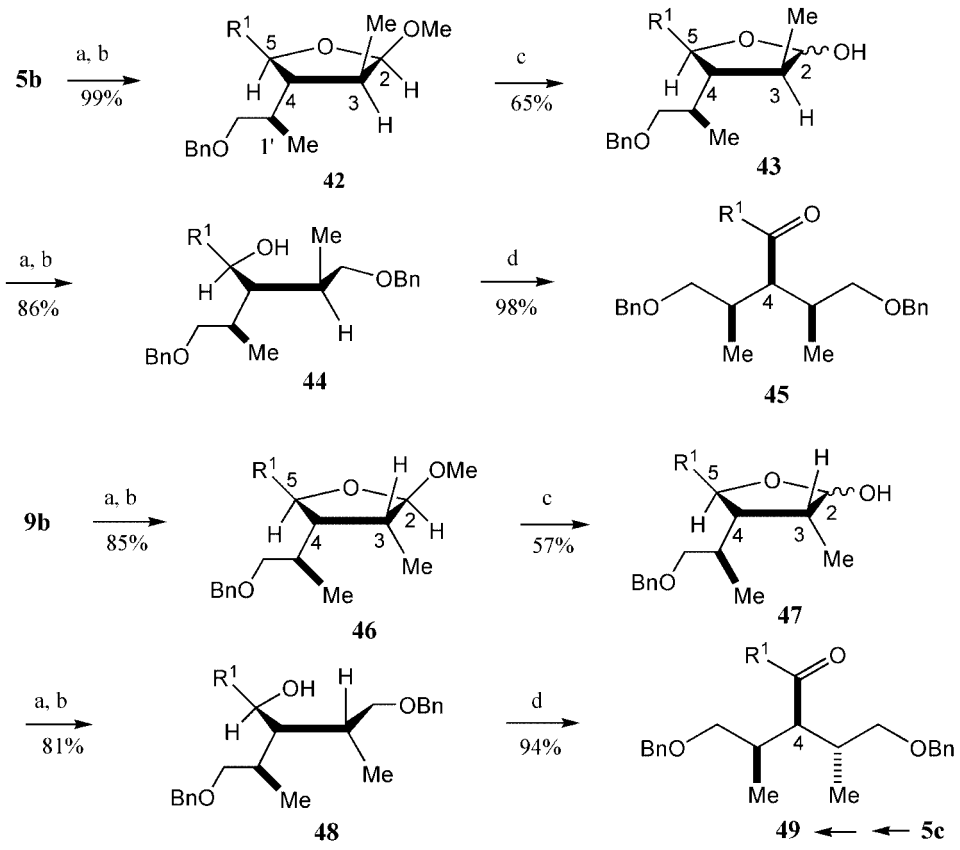
The diastereomers **31**–**34** were transformed into the methyl acetates **5a**, **6a**, **9a**, and **10a** by a hydroboration/oxidation sequence (Scheme 3). By an analogous procedure, methyl esters **7a** and **8a** were prepared from **28** (Scheme 4), **11a**/**12a** from **27** and **13a**/**14a** from **28** (Scheme 5), and **15a** from **27** and **16a** from **28** (Scheme 6). Compounds **7a**/**8a** and **11a**/**12a** can be distinguished by the above-mentioned anisotropy criterion of the 1′′-CH_2 group in the ^1H NMR spectra. Additionally, **11a** has previously been synthesized



Scheme 6. R^1 = CH_2CH_2Ph; reagents and conditions: a) LAH; b) *p*TsCl, pyridine, DMAP; c) 9-BBN, H_2O_2; d) DMSO, DCC; e) $KMnO_4$, *t*BuOH, pH 7 buffer; f) CH_2N_2

in an optically active form from D-glucose following a stereochemically unambiguous route.[3]

For the configurational assignment of **5b** and **9b** the pseudosymmetrical relationship between C-3 and C-1′ was utilized (Scheme 7). Thus, **5b** and **9b** were converted into the benzyl ethers **42** and **46**, respectively. The ketal was hy-



Scheme 7. $R^1 = CH_2CH_2Ph$; reagents and conditions: a) LAH, THF, Δ; b) NaH, DMF, BnCl, Δ; c) *p*TsOH, acetonitrile, water; d) Swern oxidation

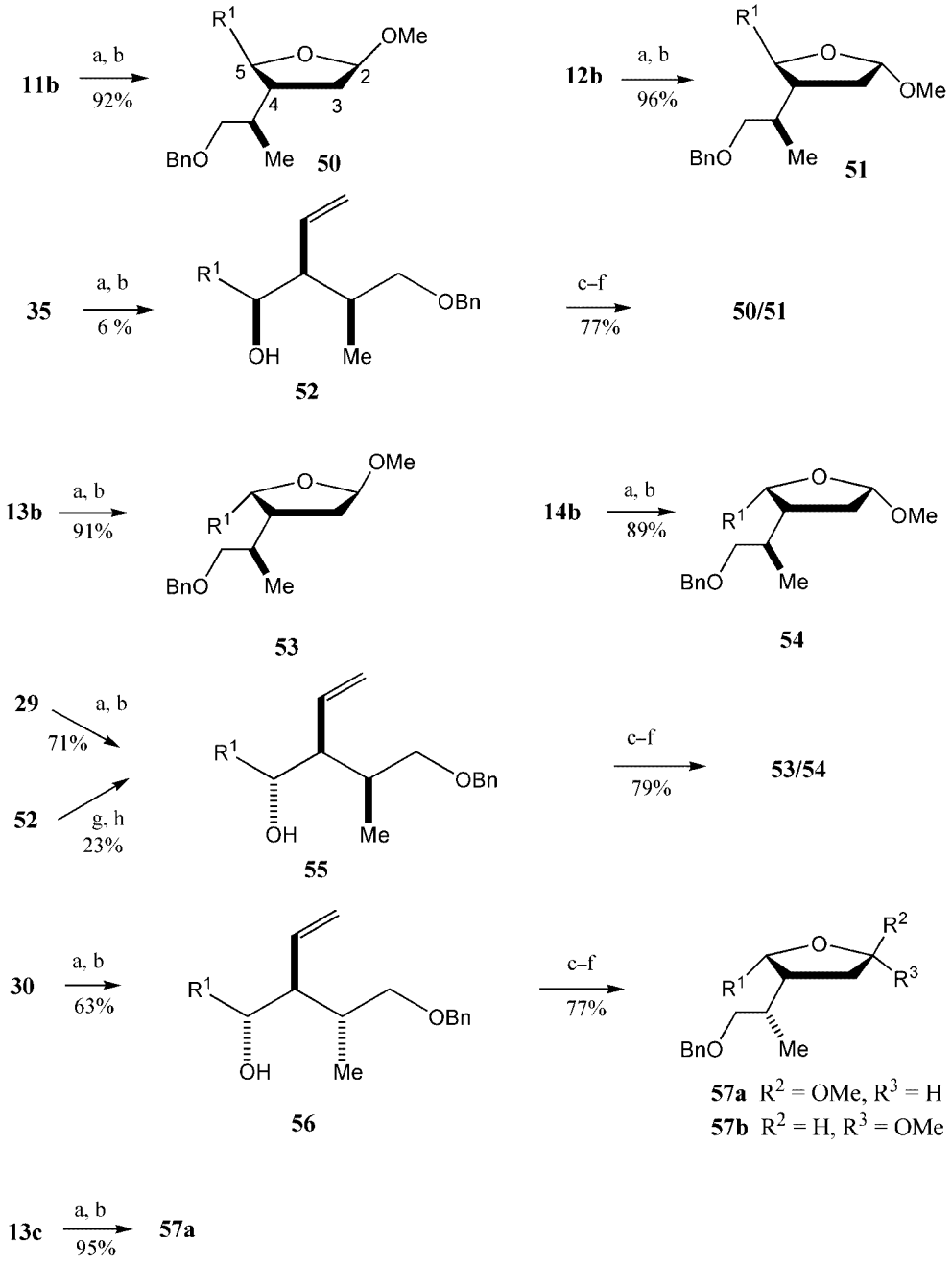
drolyzed to an anomeric mixture of the hemi-ketals **43** and **47**, which were reduced to the diols and selectively monobenzylated at the primary position to give the dibenzyl ethers **44** and **48**. After Swern oxidation the ketones **45** and **49** were generated. Compound **45** contains a pseudoasymmetric center at C-4, and, as a *meso* compound, shows only one ^{1}H NMR signal for the two methyl groups. In contrast, **49** contains a chirotopic nonstereogenic center at C-4, and thus the two methyl groups appear as two individual signals in the ^{1}H NMR spectrum (see Supporting Information for spectra). Following an analogous sequence, **49** was prepared from **5c**. The configurations of **6b**,**c**, **7b**,**c**, **8b**,**c**, **9c**, and **10b**,**c** were assigned in a similar manner.

Esters **11b** and **12b** were converted into the benzyl ethers **50** and **51**; identical products were obtained after chromatographic separation from **35** via intermediate **52** along the obvious route outlined in Scheme 8. Similarly, **13b** and **14b** were converted into **53** and **54**, and these compounds were correlated, via **55**, with **29**. Additionally, **52** was transformed into **55** by a Mitsunobu inversion. Compounds **30** and **13c** were correlated via relay compounds **56** and **57**. To assign the configurations of **15b**, **16b**, and **16c**, intermediates **52**, **55**, and **56** were transformed into **58**, **59**, and **60**, respectively, which were obtained in diastereomerically identical form from **15b**, **16b**, and **16c** (Scheme 9).

The synthesis of the racemic cyclopentyl derivatives **21a** and **22a** (Scheme 10) began with aldehyde **61**, which was converted via **62** into enoate **63**. Free-radical cyclization[7] was used to close the cyclopentane ring and the diastereomeric esters **21a** and **22a** were formed in good yield. After separation of the diastereomers an inspection of the ^{1}H NMR spectra made clear that the signals had too much overlap to allow a safe assignment of the configurations (see Supporting Information for spectra). The same observation was made after methylation of **21a** and **22a** to **21b**,**c** and **22b**,**c**, respectively, and after transformation into the benzyl ethers **64a**,**b** and **65a**,**b**, respectively. To obtain better suited ^{1}H NMR spectra we decided to prepare the oxygenated derivatives **17**–**20a** and to correlate them later with **21** and **22** (vide infra; Scheme 11).

Thus, the *trans*-fused lactones **70** and **72** were formed by debenzylation of **17a** and **17b**, respectively, upon activation with TMSCl, whereas the formation of the *cis*-lactones **75** and **77** from **19a** and **20a** proceeded spontaneously.

Compounds **71a**,**b** were generated from **70**, **73a**,**b** from **72**, **76a**,**b** from **75**, and **78a**,**b** from **77**, all by monomethylation. The diastereomeric pairs were separated and structurally assigned by extensive NOE difference spectroscopy. Additionally, **78a** was crystallized and subjected to a single-crystal structural analysis (Figure 3).[8] In the crystal struc-



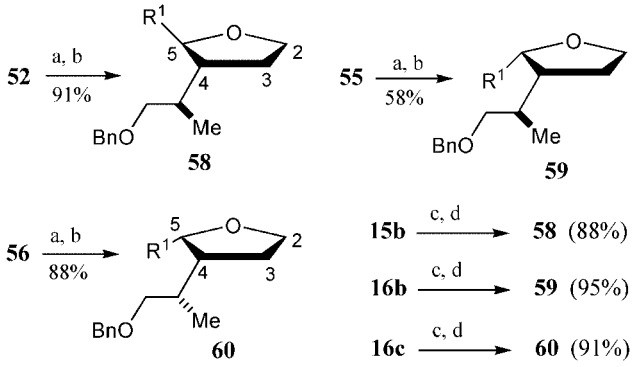
Scheme 8. $R^1 = CH_2CH_2Ph$; reagents and conditions: a) LAH; b) NaH, DMF, BnCl; c) DHP, PPTS; d) 9-BBN, H_2O_2; e) DCC, DMSO; f) MeOH, PPTS; g) DEAD, PPh_3, $PhCO_2H$, THF; h) NaOH, MeOH

ture the lactone ring adopts an approximate $B_{1,4}$-boat conformation with the benzyl appendage in the equatorial and the methyl group in the axial position. The *trans*-lactone enolates react virtually unselectively with methyl iodide (Scheme 12), whereas the *cis*-lactones show moderate selectivity (Scheme 13). The monomethylated lactones **71a**,**b**, **73a**,**b**, **76a**,**b**, and **78a**,**b** were obtained in identical form upon hydrogenation/lactonization of **17b**,**c**–**20b**,**c**, thus proving the configurations of these compounds given in Schemes 11–13.

Additionally, **71a**,**b** were converted into **74a**,**b**, **76a** into **80a**, and **78a** into **80b**. Compounds **74a**,**b** were monodeoxygenated to **64a**,**b** and **80a**,**b** to **65a**. These compounds were shown to be identical with the corresponding products obtained from **21a**,**b** and **22a** (Schemes 10, 12, and 13).

Application to the Synthesis of Nephromopsinic Acid

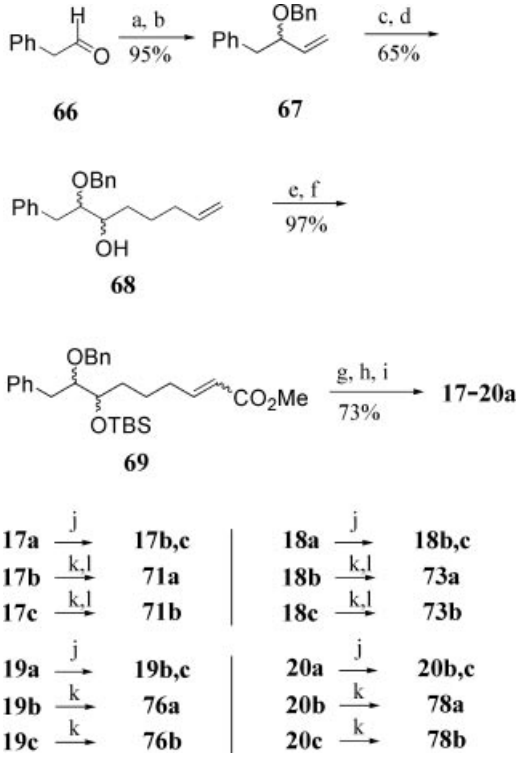
In effect, the *C*-methylation of ester enolates such as **1** and **3** provides a highly stereoselective access to compounds



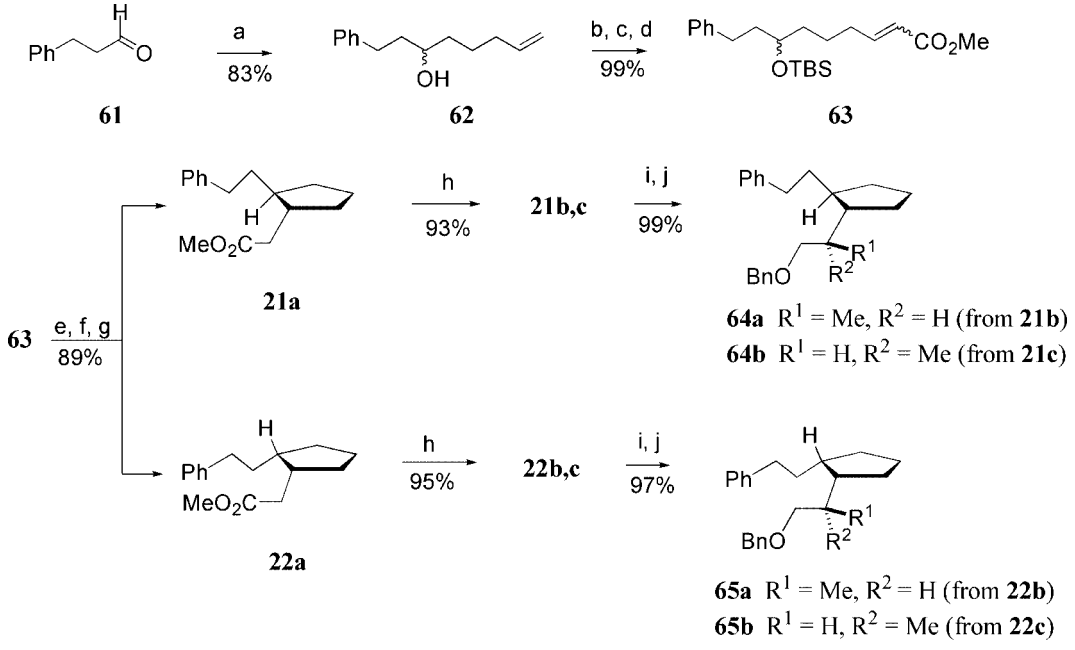
Scheme 9. R^1 = CH_2CH_2Ph; reagents and conditions: a) 9-BBN, H_2O_2; b) *p*TsCl, pyridine; c) $LiAlH_4$, THF; d) NaH, DMF, BnCl

with the general functionalization pattern **81** (Scheme 14). Whilst looking for natural products fitting into this general pattern we came across the paraconic acids **82**, i.e. γ-butyrolactones having a carboxylic acid in the 3-position.[9] Paraconic acids occur naturally in lichens and show antineoplastic and antibiotic properties. A number of stereoselective syntheses have been developed for a variety of paraconic acids in racemic and optically active form.[10]

In earlier work we have described the preparation of roccellaric acid[11] and (–)-nephromopsinic acid.[12] In the current context, we realized that (+)-nephromopsinic acid (**94**), the unnatural enantiomer, stereochemically matched our *C*-methylation protocol. Thus, the known[3] methyl ester **83** was converted into **84** by selective degradation of the exocyclic acetonide moiety (Scheme 15). As expected, **84** was-



Scheme 11. Reagents and conditions: a) vinylmagnesium bromide, THF; b) NaH, DMF, BnCl; c) O_3, MeOH, –78 °C, then PPh_3; d) (4-pentenyl)magnesium bromide, THF; e) TBSCl, imidazole, DMF; f) $Ph_3P{=}CHCO_2Me$, MeOH; g) 80% HOAc, THF; h) PhOCSCl, pyridine, DMAP, CH_2Cl_2; i) nBu_3SnH, AIBN, toluene, reflux; j) LDA, THF, –78 °C, MeI; k) H_2/Pd, MeOH, 1 bar, 22 °C; l) TMSCl, diethyl ether, lactonization; for yields see Supporting Information



Scheme 10. Reagents and conditions: a) (4-pentenyl)magnesium bromide, THF; b) TBSCl, imidazole, DMF; c) O_3, MeOH, –78 °C, then PPh_3; d) $Ph_3P{=}CHCO_2Me$, MeOH; e) 80% HOAc, THF; f) PhOCSCl, pyridine, DMAP, CH_2Cl_2; g) nBu_3SnH, AIBN, toluene, reflux; h) LDA, THF, –78 °C, MeI; i) $LiAlH_4$, THF; j) NaH, DMF, BnCl

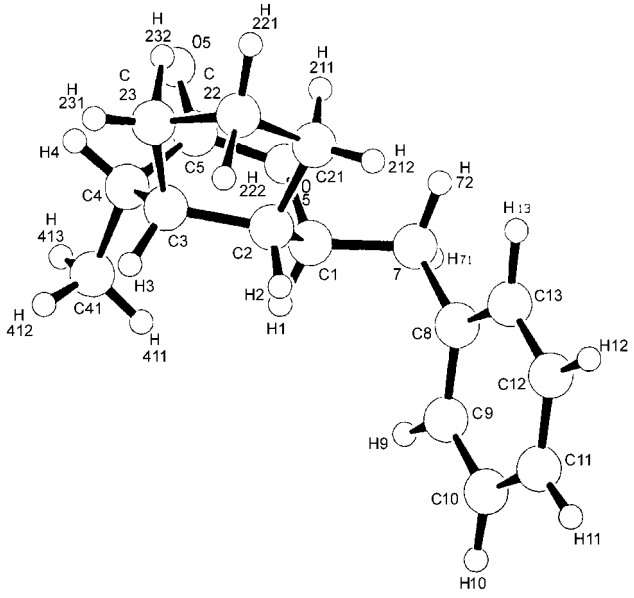
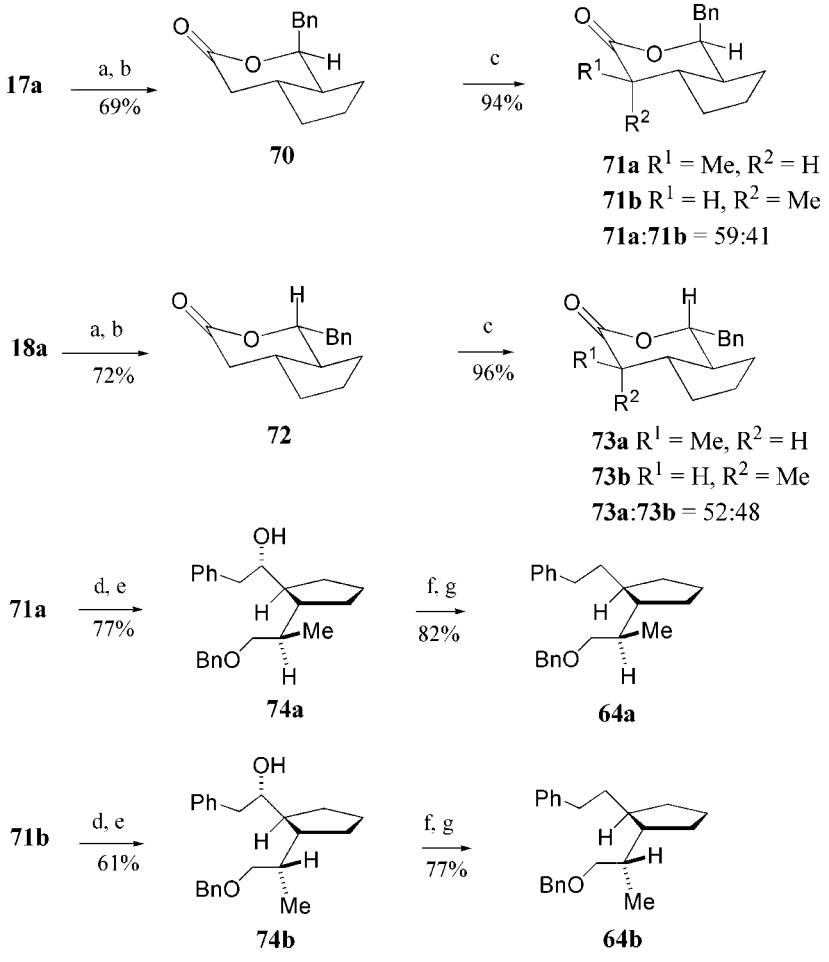
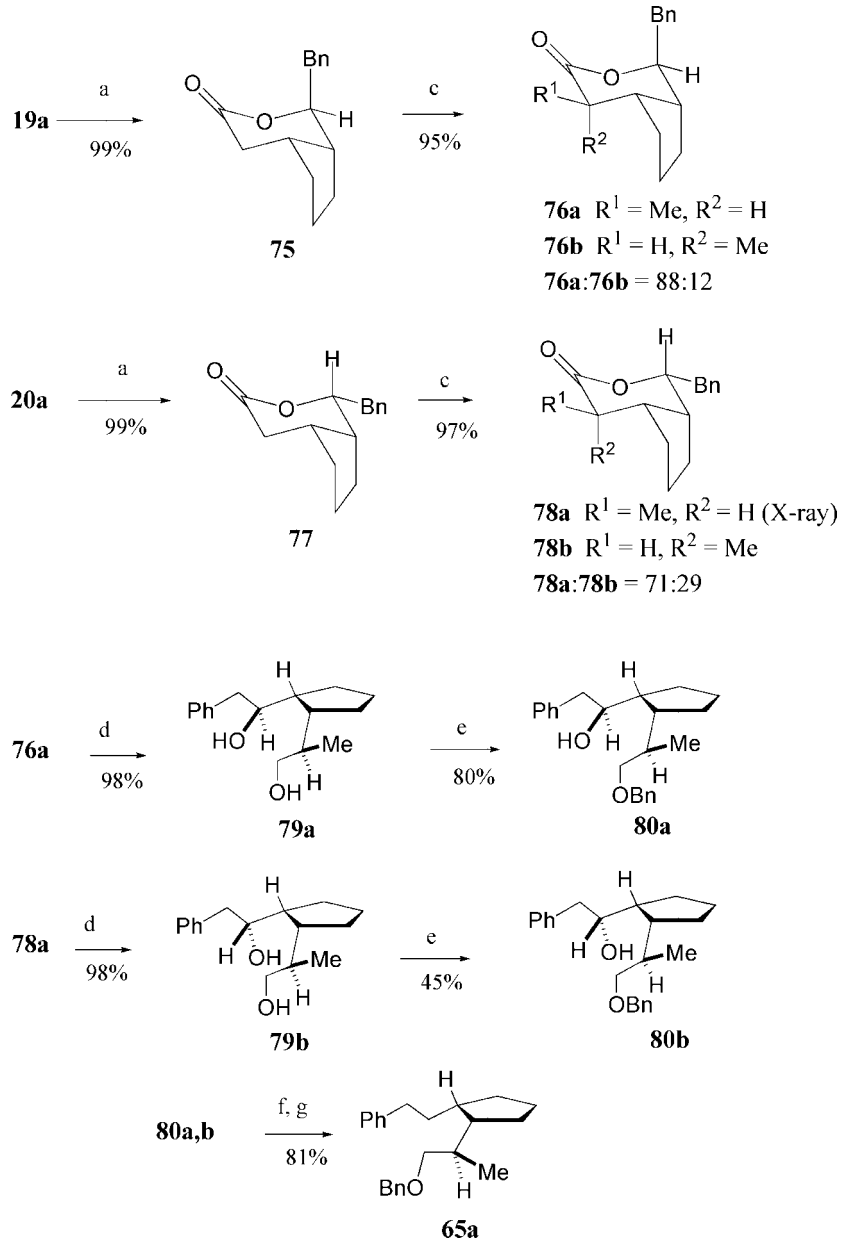


Figure 3. Crystal structure of lactone **78a** (enantiomer shown)

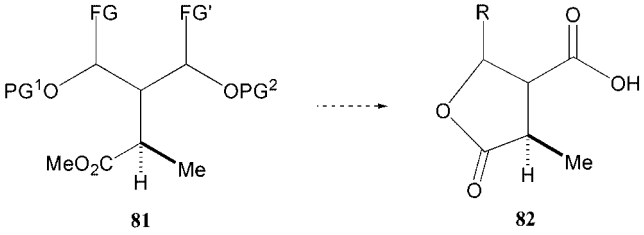
methylated with greater than 98% stereoselectivity to give diastereomer **85**, which, on the basis of our previous results, was tentatively assigned to have a (1′*R*)-configuration. Next, the furanose template had to be disconnected without affecting the newly created stereogenic center. Hence, **85** was transformed into the benzyl ether **86** and the ketal was cleaved with acetic anhydride in the presence of BF_3 as catalyst to give diacetate **88** stereoselectively. This result may be interpreted by formation of a dioxolanylium intermediate **87**, which is attacked by an acetate anion from the less-hindered face. Basic hydrolysis of the acetate groups led to a dihydroxyaldehyde, which immediately cyclized to hydroxy lactol **89**. Glycol cleavage followed by reduction gave diol **90**. After protection-reprotection alcohol **91** was formed, which furnished hydroxy lactol **92** on Pfitzner–Moffat oxidation followed by acidic workup to remove the THP group. Oxidation to lactone **93**, TBS removal, and oxidation with PDC yielded (+)-nephromopsinic acid (**94**), which was identical in all respects, except the sign of the optical rotation, with the enantiomer obtained previously.[9,12]



Scheme 12. Reagents and conditions: a) H_2, Pd/C, MeOH, 1 bar, 22 °C; b) TMSCl, diethyl ether; c) LDA, THF, –78 °C, MeI; d) $LiAlH_4$, THF; e) NaH, DMF, BnCl; f) PhOCSCl, pyridine, DMAP; g) nBu$_3$SnH, AIBN, toluene, reflux



Scheme 13. Reagents and conditions: a) H_2, Pd/C, MeOH, 1 bar, 22 °C; b) TMSCl, diethyl ether; c) LDA, THF, –78 °C, MeI; d) $LiAlH_4$, THF; e) NaH, DMF, BnCl; f) PhOCSCl, pyridine, DMAP; g) nBu$_3$SnH, AIBN, toluene, reflux



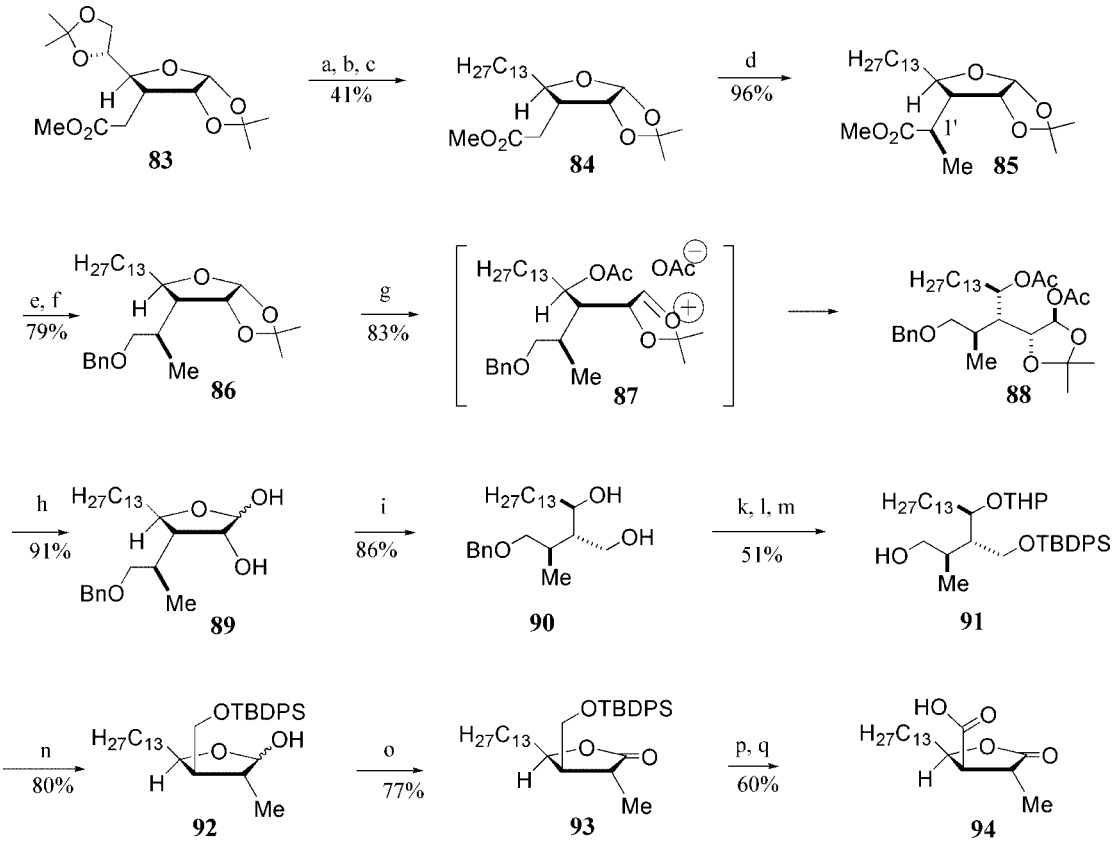
Scheme 14.

Conclusions

We have shown that ester enolates containing a five-membered oxolanyl or cyclopentyl ring adjacent to the enolate carbon atom can be methylated with a stereoselectivity of up to 99% depending on the substituents on the ring. The stereoelectronic effect of an endocyclic oxygen postulated by McGarvey and Williams could not be confirmed for our systems. Our results were applied to a stereocontrolled synthesis of (+)-nephromopsinic acid.

Experimental Section

General Methods: ^{1}H and ^{13}C spectra were recorded on Bruker AC 250 or Bruker AM 270 (^{1}H at 250 or 270 MHz, ^{13}C at 62.5 or 67.5 MHz) spectrometers, with $CDCl_3$ as internal standard. IR spectra were recorded on a Perkin–Elmer 580B or 125 spectrometer. Mass spectra were recorded on Finigan MAT 112 S (EI, CI)



Scheme 15. Reagents and conditions: a) 50% HOAc, 2 d, 22 °C, 89%; b) $Pb(OAc)_4$, CH_2Cl_2, 22 °C, then added to $C_{11}H_{23}C{=}PPh_3$ in THF, 14 h, 22 °C, 51%; c) Pd/C (10), MeOH/EtOAc (10:1), 2 bar H_2, 22 °C, 90%; d) LDA, THF, –50 °C, MeI, 3 h, 96%; e) $LiAlH_4$, Et_2O, 1 h, 22 °C, 98%; f) BnCl, NaH, DMF, 22 °C, 12 h, 81%; g) Ac_2O, BF_3-etherate, CH_2Cl_2, 5 h, 22 °C, 8%; h) NaOMe in MeOH, 3 h, 22 °C, 91%; i) H_5IO_6, THF, 1 h, 22 °C, then $LiAlH_4$, Et_2O, 1 h, 22 °C, 86%; k) TBDPSCl, DMF, imidazole, 5 h, 22 °C, 85%; l) dihydropyran, *p*TsOH, Et_2O, 14 h, 22 °C, 72%; m) Na, NH_3, –50 °C, Et_2O, Na, 83%; n) DMSO, DCC, pyridine, TFA, toluene, 3 h, 22 °C, then *p*TsOH, THF/H_2O, 1 h, 22 °C, 80%; o) PCC, CH_2Cl_2, 14 h, 22 °C, 77%; p) TBAF, THF, 5 h, 22 °C, 74%; q) PDC, DMF, 15 h, 22 °C, 81%

or Finigan MAT 711 (high resolution) spectrometers. Elemental analyses were performed with a Perkin–Elmer 240 or 2400 CHN Elemental Analyzer. Melting points are uncorrected and were obtained with a Buechi SMP 20. All solvents were dried according to standard procedures, and DMF was dried over 4-Å molecular sieves. Flash chromatography was performed with silica gel 60 (0.040–0.063 mm, 230–400 mesh) purchased from Merck. Reactions were monitored by TLC on DC Alufolien Kieselgel 60 F_{254} (from Merck) and visualized by spraying with 60% sulfuric acid and appropriate heating. HPLC analyses and separations were performed with equipment from Knauer and Waters-Millipore.

Methylation of Methyl Esters 5a–22a: A lithium diisopropylamide solution was prepared as follows. At 0 °C, 1 molar equivalent of *n*BuLi (1.6 M in hexane) was added dropwise to 1.01 molar equivalents of anhydrous diisopropylamine in anhydrous THF (1.6–2.3 mL/mmol). The solution was stirred for 15 min at 0 °C and 30 min at room temperature. At –78 °C, a solution of the ester in anhydrous THF (4.5–5.5 mL/mmol) was added dropwise to the LDA solution in THF. After stirring for 3 h, methyl iodide (1 mL per gram of ester) was added. The reaction mixture was stirred for an additional 30 min at –78 °C, the cooling bath was removed, and the reaction mixture was allowed to reach room temperature. Water was added (1 mL per 2 mL of THF), the layers were separated, and the aqueous phase was extracted with hexane (3 × 2 mL per 1 mL of water). The combined organic phases were dried with magnesium sulfate and concentrated on a rotary evaporator. The diastereomeric mixtures were separated by HPLC (vide infra for **5b/c**).

(2*RS*,3*SR*,4*RS*,5*RS*)-2-Methoxy-4-[(1*RS*)-1-(methoxycarbonyl)-ethyl]-3-methyl-5-phenethyloxolane (5b) and (2*RS*,3*SR*,4*RS*,5*RS*)-2-Methoxy-4-[(1*SR*)-1-(methoxycarbonyl)ethyl]-3-methyl-5-phenethyl-oxolane (5c): Analytical HPLC: hexane/ethyl acetate = 90:10, 2 mL min^{-1}, 100 bar, Nucleosil 50-5, 4 × 250 mm, UV = 254 nm. t_R (**5b**) = 3.02 min, t_R (**5c**) = 3.39 min. Mechanical integration: **5b/5c** = 70:30 [1.98 g were separated by HPLC (hexane/ethyl acetate = 90:10, 80 mL min^{-1}, 40 bar, Nucleosil 50-7, 32 × 250 mm, UV = 254 nm)].

5b: Yield: 1.329 g (66%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.08 (d, *J* = 7.5 Hz, 3 H), 1.16 (d, *J* = 7 Hz, 3 H), 1.62 (ddd, *J* = 8.5, 7.5, 4.5 Hz, 1 H), 1.69–1.94 (m, 2 H), 2.06 (m_c, 1 H), 2.55 [dq, *J* (d) = 8.5, *J* (q) = 7 Hz, 1 H], 2.66 (ddd, *J* = 13.5, 9.5, 7.5 Hz, 1 H), 2.85 (ddd, *J* = 13.5, 9.5, 5 Hz, 1 H), 3.32 (s, 3 H), 3.58 (s, 3 H), 3.79 [dt, *J* (t) = 8, *J* (d) = 3.5 Hz, 1 H), 4.61 (s, 1 H), 7.14–7.34 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.16 (1′-p), 19.56 (p), 32.42 (s), 37.14 (s), 41.74 (t), 43.55 (t), 51.17 (p), 53.99 (t), 54.10 (p), 80.54 (t), 110.13 (t), 125.58 (t), 128.14 (t), 128.34 (t), 141.88 (q), 175.86 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (vw), 3090 (w), 3070 (m), 3030 (m), 2960 (s), 2940 (s), 2920 (s), 2890 (s), 2840 (m), 1945 (vw), 1875 (vw), 1805 (vw), 1735 (vs), 1605 (m), 1585 (w), 1500 (m), 1460 (s), 1435 (s), 1380 (m), 1370 (m), 1350 (m), 1300 (m), 1260 (s), 1200 (s), 1170 (s), 1145 (m), 1125 (s), 1100 (s), 1070 (s), 1030 (s), 1010 (s), 960 (s), 930 (m), 885 (m), 855 (m), 835 (w), 825 (w), 770 (w),

750 (m), 700 (s) cm^{-1}. $C_{18}H_{26}O_4$ (306.41): calcd. C 70.56, H 8.55; found C 69.65, H 8.58. MS (EI, 80 eV, 40 °C): *m/z* (%) = 306 (0.27) [M^+], 274 (22.29), 234 (8.17), 187 (70.29), 169 (19.34), 109 (20.35), 104 (32.47), 91 (100), 85 (78.77), 55 (27.84), 41 (30.1). HRMS calcd. for $C_{18}H_{26}O_4$ [M^+] 306.18311; found 306.18284.

5c: Yield: 0.572 g (28%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.07 (d, *J* = 7.5 Hz, 6 H), 1.62 (ddd, *J* = 9.5, 7, 3.5 Hz, 1 H), 1.76–2.04 (m, 3 H), 2.59 [dq, *J* (d) = 9.5, *J* (q) = 7.5 Hz, 1 H), 2.70 (ddd, *J* = 13.5, 9.5, 7.5 Hz, 1 H), 2.84 (ddd, *J* = 13.5, 9.5, 5 Hz, 1 H), 3.31 (s, 3 H), 3.65 (s, 3 H), 3.80 (ddd, *J* = 8.5, 7.5, 3.5 Hz, 1 H), 4.60 (s, 1 H), 7.14–7.34 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.69 (1′-p), 19.29 (p), 32.52 (s), 38.07 (s), 42.82 (t), 45.22 (t), 51.36 (p), 53.52 (t), 54.13 (p), 79.97 (t), 110.15 (t), 125.70 (t), 128.24 (t), 128.38 (t), 141.84 (q), 176.01 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (m), 2960 (s), 2940 (s), 2920 (s), 2880 (s), 2840 (m), 1950 (w), 1875 (w), 1805 (w), 1735 (vs), 1605 (m), 1585 (w), 1500 (m), 1455 (s), 1435 (s), 1380 (s), 1370 (m), 1360 (m), 1300 (m), 1285 (m), 1260 (s), 1235 (m), 1210 (s), 1195 (s), 1165 (s), 1125 (s), 1100 (s), 1085 (s), 1070 (s), 1050 (m), 1030 (s), 1010 (s), 985 (m), 965 (s), 945 (s), 930 (m), 890 (m), 850 (w), 835 (w), 825 (w), 815 (vw), 775 (w), 750 (m), 700 (s), 670 (w) cm^{-1}. $C_{18}H_{26}O_4$ (306.41): calcd. C 70.56, H 8.55; found C 70.78, H 8.92.

6b/c: Mixture, not separable by HPLC. ^1H NMR ($CDCl_3$): δ = 0.98 (d, *J* = 6.5 Hz, 3 H, major isomer), 1.00 (d, *J* = 6.5 Hz, 3 H, minor isomer), 1.09 (d, *J* = 7.5 Hz, 3 H, 1′-Me/major isomer), 1.14 (d, *J* = 7.5 Hz, 3 H, 1′-Me/minor isomer), 1.72–2.12 (m, 8 H), 2.45–2.60 (m, 2 H), 2.61–2.76 (m, 2 H), 2.84–2.98 (m, 2 H), 3.38 (s, 6 H), 3.63 (s, 3 H, minor isomer), 3.65 (s, 3 H, major isomer), 3.88 (m_c, 2 H), 4.74 (d, *J* = 4.5 Hz, 2 H), 7.14–7.34 (m, 10 H) ppm. According to the ^1H NMR analysis the ratio was 82:18. ^{13}C NMR ($CDCl_3$): δ = 11.98 (p), 12.41 (p), 13.54 (1′-p), 13.65 (1′-p), 32.73 (s), 39.62 (t), 39.75 (s), 40.31 (t), 41.40 (t), 42.60 (t), 50.97 (t), 51.12 (p), 54.16 (p), 80.95 (t), 81.80 (t), 106.15 (t), 106.33 (t), 125.46 (t), 128.08 (t), 128.16 (t), 141.96 (q), 175.14 (q), 175.39 (q) ppm. $C_{18}H_{26}O_4$ (306.41): calcd. C 70.56, H 8.55; found C 71.15, H 8.46. MS (EI, 80 eV, 40 °C): *m/z* (%) = 306 (0.37) [M^+], 274 (19.88), 234 (18.17), 217 (22.74), 187 (36.24), 169 (32.09), 109 (36.6), 104 (37.27), 91 (100), 85 (63.55), 72 (25.02), 55 (29.53), 41 (31.62). HRMS calcd. for $C_{18}H_{26}O_4$ [M^+] 306.18311; found 306.18302.

7b: Yield: 0.71 g (51%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.05 (d, *J* = 7 Hz, 3 H), 1.20 (d, *J* = 7.5 Hz, 3 H, 1′-Me), 1.56–1.83 (m, 2 H), 2.11–2.36 (m, 2 H), 2.51–2.70 (m, 2 H), 2.88 (ddd, *J* = 15, 10, 5 Hz, 1 H), 3.37 (s, 3 H), 3.62 (s, 3 H), 4.16 (ddd, *J* = 10, 7, 3 Hz, 1 H), 4.80 (d, *J* = 5 Hz, 1 H), 7.14–7.34 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.87 (p), 15.04 (1′-p), 32.27 (s), 32.89 (s), 38.74 (t), 40.23 (t), 48.35 (t), 51.20 (p), 54.42 (p), 77.65 (t), 104.79 (t), 125.52 (t), 128.06 (t), 128.17 (t), 141.75 (q), 176.13 (q) ppm. IR (KBr): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (s), 2980 (s), 2960 (s), 2940 (s), 2900 (s), 2840 (s), 1950 (w), 1870 (w), 1805 (w), 1735 (vs), 1605 (m), 1585 (w), 1550 (w), 1540 (w), 1495 (s), 1455 (s), 1435 (s), 1390 (s), 1365 (s), 1350 (s), 1330 (s), 1305 (m), 1255 (s), 1240 (s), 1195 (vs), 1170 (s), 1155 (s), 1110 (s), 1080 (vs), 1030 (vs), 960 (s), 930 (s), 915 (s), 880 (m), 855 (m), 830 (m), 810 (m), 770 (m), 750 (m), 725 (m), 700 (s), 670 (w), 650 (w), 580 (m), 545 (m), 525 (w), 505 (m) cm^{-1}. $C_{18}H_{26}O_4$ (306.41): calcd. C 70.56, H 8.55: calcd. C 70.95, H 8.56.

7c: Yield 0.42 g (30%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 0.91 (d, *J* = 6 Hz, 3 H), 1.15 (d, *J* = 7 Hz, 3 H, 1′-Me), 1.71 (m_c, 2 H), 2.12–2.29 (m, 2 H), 2.50 (quint, *J* = 7 Hz, 1 H), 2.63 [dt, *J* (d) = 14, *J* (t) = 8 Hz, 1 H], 2.92 [dt, *J* (d) = 14, *J* (t) = 7 Hz, 1 H], 3.36 (s, 3 H), 3.64 (s, 3 H), 4.15 (m_c, 1 H), 4.79 (d, *J* = 4.5 Hz, 1 H), 7.14–7.34 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 12.20 (p), 16.48 (1′-p), 32.57 (s), 32.73 (s), 38.44 (t), 39.80 (t), 48.95 (t), 51.13 (p), 54.68 (p), 78.38 (t), 105.51 (t), 125.60 (t), 128.14 (t), 128.31 (t), 141.93 (q), 175.61 (q) ppm. IR (KBr): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3060 (m), 3030 (s), 2980 (s), 2950 (s), 2910 (s), 2830 (m), 1940 (w), 1870 (w), 1800 (w), 1735 (vs), 1600 (m), 1580 (w), 1535 (w), 1495 (s), 1450 (s), 1430 (s), 1380 (s), 1360 (s), 1330 (s), 1275 (s), 1260 (s), 1190 (s), 1155 (s), 1120 (s), 1100 (s), 1080 (vs), 1060 (s), 1025 (vs), 990 (s), 955 (s), 935 (m), 915 (s), 880 (m), 860 (m), 840 (m), 825 (m), 780 (m), 750 (s), 725 (m), 700 (s), 675 (w), 660 (m), 620 (w), 585 (m), 550 (m), 500 (m), 475 (w) cm^{-1}. $C_{18}H_{26}O_4$ (306.41): calcd. C 70.56, H 8.55; found C 70.97, H 8.36.

8b: Yield: 0.68 g (59%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.19 (d, *J* = 7 Hz, 3 H), 1.24 (d, *J* = 7.5 Hz, 3 H, 1′-Me), 1.47–1.62 (m, 1 H), 1.80–1.96 (m, 1 H), 2.06 [dquint, *J* (quint) = 7, *J* (d) = 3 Hz, 1 H], 2.19 [dt, *J* (d) = 10, *J* (t) = 7 Hz, 1 H], 2.52–2.67 (m, 2 H), 2.93 (ddd, *J* = 14, 10, 5 Hz, 1 H), 3.44 (s, 3 H), 3.60 (s, 3 H), 4.16 (ddd, *J* = 12, 7, 2.5 Hz, 1 H), 4.60 (d, *J* = 3 Hz, 1 H), 7.12–7.32 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.97 (1′-p), 18.90 (p), 32.61 (s), 33.17 (s), 39.48 (t), 43.09 (t), 50.94 (t), 51.21 (p), 55.39 (p), 80.85 (t), 112.66 (t), 125.43 (t), 128.03 (t), 128.20 (t), 141.98 (q), 176.08 (q) ppm. IR (KBr): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (s), 2960 (s), 2940 (s), 2880 (s), 2840 (m), 1950 (w), 1870 (w), 1800 (w), 1735 (vs), 1605 (m), 1585 (w), 1540 (w), 1495 (s), 1455 (s), 1435 (s), 1385 (s), 1370 (s), 1360 (m), 1330 (s), 1255 (s), 1195 (s), 1170 (s), 1140 (s), 1100 (vs), 1080 (s), 1025 (s), 1015 (s), 965 (s), 920 (s), 885 (m), 855 (m), 835 (m), 805 (m), 770 (m), 750 (m), 700 (s), 680 (m), 655 (w), 640 (w), 625 (w), 580 (m), 565 (m), 535 (w), 500 (m), 485 (m) cm^{-1}. $C_{18}H_{26}O_4$ (306.41): calcd. C 70.56, H 8.55; found C 70.70, H 8.63.

8c: Yield: 0.42 g (36%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 0.97 (d, *J* = 7 Hz, 3 H), 1.10 (d, *J* = 7 Hz, 3 H, 1′-Me), 1.52–1.66 (m, 1 H), 1.84–2.13 (m, 3 H), 2.45 [dq, *J* (d) = 9.5, *J* (q) = 7 Hz, 1 H], 2.62 (ddd, *J* = 14, 10, 7.5 Hz, 1 H), 2.98 (ddd, *J* = 14, 10, 5 Hz, 1 H), 3.48 (s, 3 H), 3.66 (s, 3 H), 4.10 (ddd, *J* = 12, 6, 2.5 Hz, 1 H), 4.60 (d, *J* = 4 Hz, 1 H), 7.14–7.34 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.43 (2 × p), 32.30 (s), 32.41 (s), 39.16 (t), 42.89 (t), 51.14 (p), 52.25 (t), 55.88 (p), 80.28 (t), 113.46 (t), 125.56 (t), 128.15 (t), 128.31 (t), 142.00 (q), 175.54 (q) ppm. IR (KBr): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (s), 2980 (s), 2960 (s), 2950 (s), 2920 (s), 2880 (s), 2840 (s), 1945 (w), 1870 (w), 1800 (w), 1735 (vs), 1600 (m), 1580 (w), 1550 (w), 1540 (w), 1495 (s), 1450 (s), 1430 (s), 1375 (s), 1360 (s), 1330 (m), 1320 (m), 1270 (s), 1260 (s), 1240 (s), 1220 (m), 1195 (s), 1165 (s), 1155 (s), 1100 (s), 1080 (s), 1060 (s), 1030 (s), 1010 (s), 985 (s), 965 (s), 940 (m), 915 (m), 895 (m), 880 (m), 855 (m), 830 (w), 800 (w), 790 (w), 750 (m), 700 (s), 650 (w), 640 (w), 625 (w), 585 (m), 575 (w), 555 (w), 510 (m), 470 (w) cm^{-1}. $C_{18}H_{26}O_4$ (306.41): calcd. C 70.56, H 8.55; found C 70.88, H 8.64.

9b: Yield: 1.182 g (76%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 0.93 (d, *J* = 7 Hz, 3 H), 1.18 (d, *J* = 6.5 Hz, 3 H, 1′-Me), 1.61 (m_c, 2 H), 2.26–2.49 (m, 3 H), 2.66 [dt, *J* (d) = 14, *J* (t) = 8 Hz, 1 H], 2.89 [dt, *J* (d) = 14, *J* (t) = 7 Hz, 1 H], 3.37 (s, 3 H), 3.57 (s, 3 H), 3.96 (m_c, 1 H), 4.62 (s, 1 H), 7.12–7.34 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.35 (p), 16.35 (1′-p), 32.52 (s), 38.44 (s), 38.29 (t), 41.62 (t), 48.04 (t), 51.03 (p), 53.78 (p), 80.24 (t), 109.23 (t), 125.43 (t), 128.06 (t), 128.18 (t), 142.09 (q), 175.75 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (vw), 3090 (w), 3070 (m), 3030 (m), 2980 (s), 2950 (s), 2920 (s), 2840 (m), 1945 (vw), 1875 (vw), 1805 (vw), 1735 (vs), 1605 (m), 1585 (w), 1560 (w), 1540 (w), 1500 (m), 1455 (s), 1435 (m), 1385 (m), 1375 (m), 1365 (m), 1350 (m), 1310 (m), 1260 (s), 1235 (m), 1195 (s), 1170 (s), 1120 (m), 1110 (s), 1090 (s), 1080 (s), 1055 (s), 1030 (s), 1005 (s), 970 (m), 955 (s), 940 (s), 930 (s), 895

(w), 875 (m), 855 (m), 840 (w), 820 (vw), 770 (w), 750 (m), 700 (s), 670 (w), 660 vw cm^{-1}. $C_{18}H_{26}O_4$ (306.41): calcd. C 70.56, H 8.55; found C 70.51, H 8.66.

9c: Yield: 0.294 g (19%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 0.91 (d, J = 7.5 Hz, 3 H), 1.13 (d, J = 7 Hz, 3 H, 1′-Me), 1.76–2.06 (m, 2 H), 2.26–2.60 (m, 3 H), 2.64 (ddd, J = 13.5, 10, 7.5 Hz, 1 H), 2.98 (dd, J = 13.5, 9 Hz, 1 H), 3.38 (s, 3 H), 3.68 (s, 3 H), 3.84 (ddd, J = 10, 7.5, 2.5 Hz, 1 H), 4.60 (s, 1 H), 7.14–7.36 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 12.50 (p), 17.15 (1′-p), 33.11 (s), 40.55 (s), 39.08 (t), 42.62 (t), 47.33 (t), 51.54 (p), 54.16 (p), 81.08 (t), 110.56 (t), 125.68 (t), 128.28 (t), 128.37 (t), 142.09 (q), 175.90 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (vw), 3090 (w), 3070 (m), 3030 (m), 2960 (s), 2920 (s), 2870 (m), 2840 (m), 1950 (vw), 1875 (vw), 1800 (vw), 1735 (vs), 1605 (m), 1585 (w), 1500 (m), 1460 (s), 1435 (m), 1385 (m), 1375 (m), 1355 (m), 1330 (m), 1320 (m), 1305 (m), 1260 (s), 1230 (m), 1215 (m), 1200 (s), 1160 (s), 1145 (s), 1105 (s), 1090 (vs), 1065 (s), 1050 (m), 1030 (s), 1010 (m), 985 (m), 960 (s), 940 (s), 930 (s), 910 (m), 895 (w), 880 (m), 855 (m), 845 (w), 820 (w), 750 (m), 700 (s), 670 (w) cm^{-1}. $C_{18}H_{26}O_4$ (306.41): calcd. C 70.56, H 8.55; found C 71.41, H 8.66. MS (EI, 80 eV, 50 °C): m/z (%) = 306 (0.12) [M^+], 274 (35.93), 187 (79.56), 169 (31.55), 109 (40.01), 104 (33.53), 91 (100), 85 (56.31), 55 (25.88), 41 (28.43). HRMS calcd. for $C_{18}H_{26}O_4$ [M^+] 306.18311; found 306.18332.

10b/c: Not separable by HPLC. ^1H NMR ($CDCl_3$): δ = 0.90 (d, J = 7 Hz, 3 H, major isomer), 1.02 (d, J = 7.5 Hz, 3 H, minor isomer), 1.08 (d, J = 7 Hz, 3 H, 1′-Me/major isomer), 1.19 (d, J = 7 Hz, 3 H, 1′-Me/minor isomer), 1.64–1.98 (m, 4 H), 2.03 (m_c, 1 H, minor isomer), 2.16–2.46 (m, 3 H), 2.58–2.90 (m, 6 H), 3.33 (s, 3 H, major isomer), 3.38 (s, 3 H, minor isomer), 3.56 (s, 3 H, minor isomer), 3.66 (s, 3 H, major isomer), 3.89 (m_c, 1 H, major isomer), 3.96 (m_c, 1 H, minor isomer), 4.76 (d, J = 4.5 Hz, 1 H, major isomer), 4.85 (d, J = 4.5 Hz, 1 H, minor isomer), 7.12–7.32 (m, 10 H) ppm. According to the ^1H NMR analysis the ratio was 80:20. ^{13}C NMR ($CDCl_3$): δ = 8.64 (p), 8.72 (p), 16.66 (1′-p), 17.32 (1′-p), 31.85 (s), 37.60 (s), 38.30 (s), 39.27 (t), 39.64 (t), 39.89 (t), 40.48 (t), 46.08 (t), 48.48 (t), 50.87 (p), 51.12 (p), 54.10 (p), 54.82 (p), 79.32 (t), 79.38 (t), 105.92 (t), 106.39 (t), 125.37 (t), 125.47 (t), 128.02 (t), 128.18 (t), 141.70 (q), 141.93 (q), 175.94 (q), 177.11 (q) ppm. $C_{18}H_{26}O_4$ (306.41): calcd. C 70.56, H 8.55; found C 70.51, H 8.63.

11b: Yield: 0.436 g (68%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.12 (d, J = 6.5 Hz, 3 H), 1.64–1.86 (m, 3 H), 2.08 (dd, J = 12.5, 7 Hz, 1 H), 2.28–2.44 (m, 2 H), 2.68 [dt, J (d) = 14, J (t) = 8 Hz, 1 H], 2.86 [dt, J (d) = 14, J (t) = 7 Hz, 1 H], 3.34 (s, 3 H), 3.56 (s, 3 H), 3.81 (q, J = 6.5 Hz, 1 H), 4.95 (d, J = 5 Hz, 1 H), 7.11–7.30 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.94 (p), 32.55 (s), 37.22 (s), 38.75 (s), 42.30 (t), 45.12 (t), 51.16 (p), 54.10 (p), 82.35 (t), 104.29 (t), 125.47 (t), 128.08 (t), 128.22 (t), 141.92 (q), 175.42 (q) ppm. IR (KBr): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (s), 2980 (s), 2950 (s), 2920 (s), 2860 (m), 2830 (m), 1945 (w), 1875 (w), 1800 (w), 1735 (vs), 1600 (m), 1580 (w), 1545 (w), 1495 (m), 1455 (s), 1435 (s), 1375 (m), 1360 (s), 1345 (m), 1320 (m), 1260 (s), 1225 (s), 1195 (s), 1160 (s), 1100 (s), 1070 (s), 1050 (s), 1025 (s), 980 (s), 960 (s), 950 (s), 930 (m), 910 (m), 890 (m), 860 (m), 850 (m), 810 (m), 780 (m), 750 (m), 725 (m), 700 (s), 680 (m), 650 (w), 595 (w), 580 (w), 555 (w), 540 (w), 520 (w), 510 (w), 505 (w), 490 (w), 470 (w) cm^{-1}. $C_{17}H_{24}O_4$ (292.38): calcd. C 69.84, H 8.27; found C 69.64, H 8.35.

11c: Yield: 0.72 g (11%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.12 (d, J = 7 Hz, 3 H), 1.74–1.96 (m, 3 H), 2.08 (dd, J = 12.5, 7.5 Hz, 1 H), 2.32 (m_c, 1 H), 2.45 (quint, J = 7 Hz, 1 H), 2.71 [dt, J (d) = 14, J (t) = 8 Hz, 1 H], 2.92 [dt, J (d) = 14, J (t) = 7 Hz, 1 H], 3.38 (s, 3 H), 3.64 (s, 3 H), 3.83 (q, J = 6.5 Hz, 1 H), 4.96 (d, J = 5 Hz, 1 H), 7.14–7.32 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.92 (p), 32.92 (s), 37.54 (s), 39.60 (s), 42.36 (t), 45.54 (t), 51.48 (p), 54.44 (p), 82.11 (t), 104.83 (t), 125.73 (t), 128.32 (t), 128.40 (t), 142.04 (q), 175.48 (q) ppm. IR (KBr): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (m), 2980 (s), 2950 (s), 2920 (s), 2860 (m), 2830 (m), 1945 (w), 1870 (w), 1805 (w), 1735 (vs), 1620 (w), 1600 (m), 1580 (w), 1545 (w), 1495 (s), 1450 (s), 1435 (s), 1380 (s), 1360 (s), 1320 (m), 1260 (s), 1195 (s), 1165 (s), 1100 (s), 1055 (s), 1030 (s), 985 (s), 960 (s), 910 (m), 895 (m), 855 (s), 835 (m), 810 (m), 785 (m), 750 (s), 725 (m), 700 (s), 675 (m), 650 (m), 620 (w), 595 (m), 580 (m), 555 (m), 520 (m), 500 (m) cm^{-1}. $C_{17}H_{24}O_4$ (292.38): calcd. C 69.84, H 8.27; found C 69.73, H 8.40.

12b: Yield: 0.308 g (68%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.14 (d, J = 6.5 Hz, 3 H), 1.64–1.88 (m, 3 H), 2.00–2.12 (m, 1 H), 2.20 (ddd, J = 13, 10.5, 5.5 Hz, 1 H), 2.54 [dq, J (d) = 8, J (q) = 6.5 Hz, 1 H), 2.65 (ddd, J = 13.5, 10, 7.5 Hz, 1 H), 2.81 (ddd, J = 13.5, 9.5, 5.5 Hz, 1 H), 3.34 (s, 3 H), 3.58 (s, 3 H), 3.76 (ddd, J = 8.5, 6.5, 3.5 Hz, 1 H), 4.99 (dd, J = 5.5, 1.5 Hz, 1 H), 7.12–7.28 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.38 (p), 32.17 (s), 35.94 (s), 36.45 (s), 41.90 (t), 45.57 (t), 51.30 (p), 54.39 (p), 80.20 (t), 104.12 (t), 125.63 (t), 128.20 (t), 128.36 (t), 142.00 (q), 176.11 (q) ppm. IR (KBr): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (m), 2980 (s), 2950 (s), 2930 (s), 2910 (s), 2870 (m), 2840 (m), 1945 (w), 1875 (w), 1800 (w), 1735 (vs), 1600 (m), 1580 (w), 1545 (w), 1535 (w), 1525 (w), 1495 (m), 1455 (s), 1435 (s), 1365 (m), 1355 (m), 1345 (s), 1315 (m), 1260 (s), 1240 (s), 1210 (s), 1195 (s), 1165 (s), 1125 (s), 1105 (s), 1075 (s), 1050 (s), 1030 (s), 990 (s), 975 (s), 930 (m), 910 (m), 885 (m), 840 (m), 810 (w), 800 (w), 785 (m), 775 (m), 750 (m), 725 (m), 700 (s), 680 (m), 660 (w), 650 (w), 645 (w), 625 (w), 615 (w), 585 (m), 575 (m), 565 (m), 540 (w), 525 (m), 510 (w), 490 (w), 480 (w), 465 (w) cm^{-1}. $C_{17}H_{24}O_4$ (292.38): calcd. C 69.84, H 8.27; found C 69.51, H 8.18.

12c: Yield: 0.021 g (5%) of a clear, pale-yellow oil. ^1H NMR ($CDCl_3$): δ = 1.11 (d, J = 7.5 Hz, 3 H), 1.66 (ddd, J = 13.5, 5, 1 Hz, 1 H), 1.73–2.08 (m, 3 H), 2.22 (ddd, J = 13.5, 10, 5.5 Hz, 1 H), 2.61 [dq, J (d) = 9, J (q) = 7.5 Hz, 1 H], 2.69 (ddd, J = 14, 10, 7.5 Hz, 1 H), 2.85 (ddd, J = 14, 10, 5.5 Hz, 1 H), 3.33 (s, 3 H), 3.65 (s, 3 H), 3.80 (ddd, J = 8.5, 7, 3 Hz, 1 H), 5.00 (dd, J = 5.5, 1 Hz, 1 H), 7.16–7.34 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.16 (p), 32.32 (s), 37.37 (s), 37.43 (s), 42.84 (t), 45.43 (t), 51.47 (p), 54.37 (p), 79.52 (t), 104.30 (t), 125.76 (t), 128.30 (t), 128.43 (t), 141.94 (q), 176.08 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (m), 2980 (s), 2950 (s), 2930 (s), 2870 (m), 2830 (m), 1945 (w), 1875 (w), 1800 (w), 1735 (vs), 1600 (m), 1580 (w), 1545 (w), 1535 (w), 1495 (m), 1450 (s), 1430 (s), 1375 (s), 1365 (s), 1350 (s), 1320 (m), 1260 (s), 1230 (s), 1210 (s), 1195 (s), 1165 (s), 1100 (s), 1055 (s), 1030 (s), 990 (s), 965 (s), 910 (m), 890 (m), 840 (m), 810 (w), 790 (m), 750 (m), 725 (m), 700 (s), 675 (m) cm^{-1}. $C_{17}H_{24}O_4$ (292.38): calcd. C 69.84, H 8.27;. found C 69.37, H 8.16.

13b: Yield: 0.228 g (87%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.16 (d, J = 7 Hz, 3 H), 1.53–1.68 (m, 2 H), 1.76 (ddd, J = 13.5, 10, 5.5 Hz, 1 H), 1.96 (ddd, J = 13.5, 7.5, 2 Hz, 1 H), 2.42 [dq, J (d) = 9, J (q) = 7 Hz, 1 H], 2.55–2.93 (m, 3 H), 3.35 (s, 3 H), 3.59 (s, 3 H), 4.16 [dt, J (t) = 8, J (d) = 5.5 Hz, 1 H], 4.98 (d, J = 4.5 Hz, 1 H), 7.12–7.32 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.22 (p), 32.50 (s), 32.58 (s), 35.69 (s), 39.13 (t), 41.96 (t), 51.44 (p), 54.38 (p), 78.78 (t), 103.40 (t), 125.64 (t), 128.17 (t), 128.31 (t), 141.91 (q), 176.02 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (m), 2990 (s), 2950 (s), 2920 (s), 2870 (m), 2840 (m), 1945 (w), 1870 (w), 1805 (w), 1735 (vs), 1620 (w), 1605 (m), 1580 (w), 1525 (w), 1495 (m), 1455 (s), 1435 (s), 1375 (m), 1365 (m),

1345 (m), 1335 (m), 1285 (m), 1265 (s), 1250 (s), 1220 (m), 1195 (s), 1170 (s), 1155 (s), 1100 (s), 1075 (s), 1055 (s), 1030 (s), 1000 (s), 985 (m), 965 (m),950 (m), 910 (m), 885 (m), 870 (m), 850 (m), 815 (w), 805 (w), 775 (m), 750 (m), 725 (m), 700 (s) cm^{-1}. $C_{17}H_{24}O_4$ (292.38): calcd. C 69.84, H 8.27; found C 69.71, H 8.24.

13c: Yield: 0.015 g (6%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.14 (d, J = 6 Hz, 3 H), 1.60–1.80 (m, 2 H), 1.83 (ddd, J = 13.5, 6.5, 1.5 Hz, 1 H), 2.00 (ddd, J = 13.5, 8, 5.5 Hz, 1 H), 2.39–2.72 (m, 3 H), 2.91 (ddd, J = 14, 9.5, 5.5 Hz, 1 H), 3.36 (s, 3 H), 3.65 (s, 3 H), 4.13 (ddd, J = 9.5, 6, 4.5 Hz, 1 H), 4.96 (dd, J = 5.5, 1.5 Hz, 1 H), 7.16–7.40 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.81 (p), 32.09 (s), 32.63 (s), 35.89 (s), 38.87 (t), 43.79 (t), 51.57 (p), 54.68 (p), 78.67 (t), 103.91 (t), 125.84 (t), 128.36 (t), 128.47 (t), 142.04 (q), 175.88 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (m), 2980 (s), 2950 (s), 2920 (s), 2870 (m), 2840 (m), 1945 (w), 1870 (w), 1805 (w), 1735 (vs), 1605 (m), 1580 (w), 1495 (m), 1455 (s), 1440 (s), 1380 (s), 1355 (s), 1305 (m), 1280 (m), 1260 (m), 1240 (m), 1220 (s), 1200 (s), 1170 (s), 1110 (s), 1085 (m), 1065 (s), 1045 (s), 1030 (s), 1005 (m), 990 (m), 970 (s), 950 (m), 915 (m), 890 (m), 870 (m), 855 (m), 840 (m), 810 (w), 790 (m), 750 (m), 700 (s), 660 (w) cm^{-1}. MS (EI, 80 eV, 40 °C): *m/z* (%) = 292 (0.71) [M^+], 260 (19.92), 173 (17.74), 155 (21.81), 104 (16.93), 91 (62.6), 71 (100), 41 (23.14). HRMS calcd. for $C_{17}H_{24}O_4$ 292.16746 [M^+]; found 292.16705.

14b: Yield: 0.211 g (80%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.19 (d, J = 6.5 Hz, 3 H), 1.48–1.66 (m, 2 H), 1.83 (m_c, 1 H), 2.28–2.54 (m, 3 H), 2.60 (ddd, J = 13.5, 9.5, 7 Hz, 1 H), 2.93 (ddd, J = 13.5, 10, 4.5 Hz, 1 H), 3.46 (s, 3 H), 3.58 (s, 3 H), 4.05 (ddd, J = 12, 6, 2.5 Hz, 1 H), 5.04 (t, J = 5 Hz, 1 H), 7.12–7.32 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 17.32 (p), 32.40 (s), 32.57 (s), 36.09 (s), 39.71 (t), 44.86 (t), 51.41 (p), 55.63 (p), 79.62 (t), 105.33 (t), 125.54 (t), 128.15 (t), 128.37 (t), 142.20 (q), 175.85 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (m), 2980 (s), 2950 (s), 2920 (s), 2870 (m), 2830 (m), 1945 (w), 1870 (w), 1800 (w), 1735 (vs), 1620 (w), 1605 (m), 1585 (w), 1530 (w), 1495 (m), 1450 (s), 1435 (s), 1375 (s), 1350 (m), 1330 (m), 1315 (m), 1295 (m), 1255 (s), 1230 (m), 1215 (s), 1195 (s), 1160 (s), 1105 (s), 1080 (s), 1025 (vs), 985 (m), 965 (s), 950 (s), 910 (m), 885 (m), 855 (m), 805 (w), 795 (w), 750 (m), 725 (m), 700 (s), 680 (m), 665 (w) cm^{-1}. $C_{17}H_{24}O_4$ (292.38): calcd. C 69.84, H 8.27; found C 69.49, H 8.30.

14c: Yield: 0.016 g (6%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.11 (d, J = 6 Hz, 3 H), 1.48–1.71 (m, 2 H), 1.89 (m_c, 1 H), 2.21–2.50 (m, 3 H), 2.63 (ddd, J = 13.5, 10, 7.5 Hz, 1 H), 2.98 (ddd, J = 13.5, 10, 4.5 Hz, 1 H), 3.49 (s, 3 H), 3.66 (s, 3 H), 4.04 (ddd, J = 12, 6, 2.5 Hz, 1 H), 5.05 (dd, J = 6, 5 Hz, 1 H), 7.16–7.36 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.53 (p), 32.02 (s), 32.41 (s), 36.39 (s), 39.78 (t), 45.55 (t), 51.57 (p), 55.94 (p), 78.99 (t), 106.11 (t), 125.79 (t), 128.38 (t), 128.51 (t), 142.25 (q), 175.99 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (m), 2980 (s), 2950 (s), 2920 (s), 2860 (m), 2830 (m), 1945 (w), 1870 (w), 1805 (w), 1735 (vs), 1605 (m), 1580 (w), 1495 (m), 1450 (s), 1435 (s), 1380 (s), 1365 (s), 1345 (s), 1330 (m), 1285 (m), 1255 (s), 1240 (m), 1195 (s), 1155 (vs), 1125 (s), 1095 (vs), 1075 (s), 1055 (s), 1045 (s), 1025 (s), 995 (s), 985 (s), 955 (m), 905 (m), 890 (m), 865 (s), 850 (s), 795 (m), 750 (m), 725 (m), 700 (s), 675 (m), 665 (w) cm^{-1}. MS (EI, 80 eV, 40 °C): *m/z* (%) = 260 (32.66), 173 (31.07),155 (47.05), 112 (68.84), 104 (38.26), 91 (100), 71 (99.82), 41 (47.21). HRMS calcd. for $C_{16}H_{20}O_3$ [$M - CH_3O^+$] 260.14125; found 260.14184.

15b: Yield: 0.436 (83%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.15 (d, J = 7.5 Hz, 3 H), 1.60–1.80 (m, 3 H), 1.97–2.16 (m, 2 H), 2.40 [dq, J (q) = 7.5, J (d) = 7 Hz, 1 H], 2.63 [dt, J (d) = 13.5, J (t) = 8 Hz, 1 H], 2.75–2.86 (m, 1 H), 3.58 (s, 3 H), 3.61 (m_c, 1 H), 3.73–3.86 (m, 2 H), 7.10–7.30 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.98 (p), 29.89 (s), 32.34 (s), 36.61 (s), 41.93 (t), 46.93 (t), 51.26 (p), 66.35 (s), 81.42 (t), 125.52 (t), 128.13 (t), 128.27 (t), 142.04 (q), 175.83 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3060 (m), 3030 (m), 2970 (s), 2940 (s), 2880 (m), 2860 (s), 1945 (w), 1870 (w), 1800 (w), 1730 (vs), 1600 (m), 1580 (w), 1540 (w), 1495 (m), 1450 (s), 1430 (s), 1375 (m), 1360 (m), 1345 (m), 1260 (s), 1190 (s), 1160 (s), 1140 (m), 1080 (s), 1060 (s), 1040 (s), 1030 (s), 985 (m), 965 (m), 950 (m), 930 (m), 910 (m), 890 (m), 870 (w), 850 (m), 835 (w), 805 (w), 750 (m), 720 (m), 700 (s), 680 (w) cm^{-1}. $C_{16}H_{22}O_3$ (262.35): calcd. C 73.25, H 8.45; found C 73.02, H 8.39.

15c: Yield 0.056 g (11%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.14 (d, J = 7 Hz, 3 H), 1.55–1.86 (m, 3 H), 1.98–2.12 (m, 2 H), 2.48 (quint, J = 7 Hz, 1 H), 2.66 (ddd, J = 13.5, 10, 7.5 Hz, 1 H), 2.84 (ddd, J = 13.5, 8.5, 6 Hz, 1 H), 3.60–3.69 (m, 1 H), 3.64 (s, 3 H), 3.72–3.88 (m, 2 H), 7.14–7.34 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.95 (p), 30.65 (s), 32.58 (s), 37.35 (s), 42.20 (t), 47.24 (t), 51.42 (p), 66.56 (s), 80.97 (t), 125.71 (t), 128.29 (t), 128.38 (t), 142.06 (q), 175.84 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3060 (m), 3030 (m), 2970 (s), 2940 (s), 2880 (m), 2860 (m), 1945 (w), 1870 (w), 1800 (w), 1730 (vs), 1600 (m), 1580 (w), 1495 (m), 1450 (s), 1430 (m), 1375 (m), 1360 (m), 1345 (m), 1260 (s), 1235 (m), 1190 (s), 1160 (s), 1105 (m), 1080 (s), 1060 (m), 1040 (m), 1030 (m), 985 (m), 960 (w), 950 (w), 910 (m), 885 (m), 850 (m), 835 (m), 805 (w), 785 (w), 750 (m), 720 (m), 700 (s), 665 (w) cm^{-1}. $C_{16}H_{22}O_3$ (262.35): calcd. C 73.25, H 8.45; found C 72.90, H 8.60.

16b: Yield: 0.464 g (88%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.19 (d, J = 6.5 Hz, 3 H), 1.50–1.72 (m, 3 H), 1.92–2.04 (m, 1 H), 2.32–2.52 (m, 2 H), 2.59 [dt, J (d) = 14, J (t) = 8 Hz, 1 H], 2.84 [dt, J (d) = 14, J (t) = 7 Hz, 1 H], 3.58 (s, 3 H), 3.74 (q, J = 8 Hz, 1 H), 3.87–4.02 (m, 2 H), 7.10–7.30 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.50 (p), 28.66 (s), 31.42 (s), 32.19 (s), 39.31 (t), 44.55 (t), 51.19 (p), 65.71 (s), 78.71 (t), 125.40 (t), 127.98 (t), 128.16 (t), 141.92 (q), 175.91 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3060 (m), 3030 (m), 2970 (s), 2940 (s), 2880 (s), 1945 (w), 1870 (w), 1800 (w), 1730 (vs), 1600 (m), 1580 (w), 1540 (w), 1490 (m), 1450 (s), 1430 (s), 1375 (m), 1350 (m), 1330 (m), 1260 (s), 1210 (s), 1190 (s), 1165 (s), 1100 (m), 1080 (s), 1060 (s), 1040 (s), 990 (m), 960 (m), 940 (m), 910 (m), 880 (m), 850 (m), 835 (w), 800 (w), 785 (w), 750 (m), 725 (m), 700 (s), 675 (w) cm^{-1}. $C_{16}H_{22}O_3$ (262.35): calcd. C 73.25, H 8.45;: calcd. C 72.92; H 8.28.

16c: Yield: 0.040 g (8%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.14 (d, J = 6 Hz, 3 H), 1.48–1.82 (m, 3 H), 1.86–2.00 (m, 1 H), 2.27–2.48 (m, 2 H), 2.62 (ddd, J = 13.5, 9.5, 7.5 Hz, 1 H), 2.88 (ddd, J = 13.5, 9.5, 5 Hz, 1 H), 3.67 (s, 3 H), 3.80 (q, J = 8.5 Hz, 1 H), 3.88–4.04 (m, 2 H), 7.14–7.34 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.60 (p), 29.08 (s), 30.87 (s), 32.25 (s), 39.66 (t), 45.95 (t), 51.54 (p), 66.10 (s), 78.34 (t), 125.78 (t), 128.35 (t), 128.45 (t), 142.18 (q), 176.20 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3060 (m), 3030 (m), 2970 (s), 2940 (s), 2880 (s), 1945 (w), 1870 (w), 1800 (w), 1735 (vs), 1600 (m), 1580 (w), 1540 (w), 1495 (m), 1450 (s), 1430 (m), 1380 (m), 1360 (m), 1340 (m), 1285 (m), 1260 (s), 1240 (m), 1195 (s), 1170 (s), 1160 (m), 1120 (m), 1105 (m), 1080 (s), 1060 (s), 1050 (s), 1030 (m), 1000 (m), 990 (m), 950 (m), 910 (m), 885 (m), 850 (m), 835 (w), 805 (w), 750 (m), 725 (m), 700 (s), 680 (w) cm^{-1}. $C_{16}H_{22}O_3$ (262.35): calcd. C 73.25, H 8.45; found C 72.96, H 8.24.

17b: Yield: 0.439 g (84%) of a clear, colorless oil. ^1H NMR ($CDCl_3$): δ = 1.07 (d, J = 7.5 Hz, 3 H), 1.30–1.87 (m, 6 H), 1.94–2.10 (m, 1 H), 2.25 (m_c, 1 H), 2.65 (m_c, 1 H), 2.71 (dd, J = 14, 8 Hz, 1 H), 2.92 (dd, J = 14, 3 Hz, 1 H), 3.49 (ddd, J = 8, 6.5, 3 Hz, 1 H), 3.59 (s, 3 H), 4.18 (d, J = 11.5 Hz, 1 H), 4.37 (d, J =

11.5 Hz, 1 H), 7.08–7.34 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 12.79 (p), 25.23 (s), 28.92 (s), 29.05 (s), 38.35 (s), 42.78 (t), 44.13 (t), 45.86 (t), 51.5 (p), 72.11 (s), 84.31 (t), 125.79 (t), 127.11 (t), 127.75 (t), 127.92 (t), 127.97 (t), 138.52 (q), 139.58 (q), 176.57 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3060 (m), 3030 (m), 2950 (s), 2870 (s), 1945 (w), 1875 (w), 1805 (w), 1730 (vs), 1600 (m), 1585 (w), 1540 (w), 1495 (s), 1450 (s), 1430 (s), 1400 (m), 1375 (m), 1350 (m), 1330 (m), 1300 (m), 1255 (m), 1195 (s), 1170 (s), 1160 (s), 1080 (s), 1070 (s), 1030 (m), 1000 (m), 990 (m), 950 (w), 910 (m), 860 (w), 850 (w), 740 (s), 700 (s), 675 (w) cm^{-1}. $C_{24}H_{30}O_3$ (366.50): calcd. C 78.65, H 8.25; found C 77.27, H 7.98.

17c: Yield. 0.033 g (6%) of a clear, colorless oil. ^{1}H NMR ($CDCl_3$): δ = 1.10 (d, J = 7 Hz, 3 H), 1.32–1.88 (m, 6 H, 1.96–2.21 (m, 2 H), 2.53 (quint, J = 7 Hz, 1 H), 2.72 (dd, J = 14, 7.5 Hz, 1 H), 2.91 (dd, J = 14, 3 Hz, 1 H), 3.50 (ddd, J = 7.5, 6.5, 3 Hz, 1 H), 3.60 (s, 3 H), 4.24 (d, J = 11.5 Hz, 1 H), 4.35 (d, = 11.5 Hz, 1 H), 7.10–7.34 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.15 (p), 25.24 (s), 29.18 (s), 30.15 (s), 38.45 (s), 43.60 (t), 44.94 (t), 45.89 (t), 51.10 (p), 72.31 (s), 84.26 (t), 125.96 (t), 127.27 (t), 127.79 (t), 128.11 (t), 128.15 (t), 129.59 (t), 138.78 (q), 139.81 (q), 176.49 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3060 (m), 3030 (s), 2950 (s), 2870 (s), 1945 (w), 1870 (w), 1805 (w), 1730 (vs), 1600 (m), 1585 (w), 1540 (w), 1495 (s), 1450 (s), 1430 (s), 1395 (m), 1380 (s), 1345 (s), 1330 (s), 1305 (m), 1250 (s), 1190 (s), 1160 (s), 1090 (s), 1070 (vs), 1030 (s), 1000 (m), 990 (m), 945 (m), 910 (m), 860 (m), 850 (m), 780 (w), 745 (s), 700 (vs) cm^{-1}. $C_{24}H_{30}O_3$ (366.50): calcd. C 78.65, H 8.25; found C 76.14, H 7.72.

18b/c: Yield: 0.365 g (88%) of a clear, colorless oil.^{1}H NMR ($CDCl_3$): δ = 0.93 (d, J = 7.5 Hz, 3 H, minor isomer), 0.97 (d, J = 7 Hz, 3 H, major isomer), 1.19–1.38 (m, 2 H), 1.42–1.92 (m, 12 H), 2.00 (m_c, 1 H, minor isomer), 2.10–2.34 (m, 3 H), 2.66 (dd, J = 13.5, 8 Hz, 1 H, major isomer), 2.67 (dd, J = 13.5, 8 Hz, 1 H, minor isomer), 2.98 (dd, J = 13.5, 6 Hz, 1 H, major isomer), 3.04 (dd, J = 13.5, 6 Hz, 1 H, minor isomer), 3.44 (s, 3 H, minor isomer), 3.47 (s, 3 H, major isomer), 3.55 (m_c, 1 H, major isomer), 3.64 (m_c, 1 H, minor isomer), 4.40 (d, J = 11 Hz, 1 H, minor isomer), 4.44 (t, J = 11.5 Hz; major isomer, 2 H), 4.50 (d, J = 11 Hz, 1 H, minor isomer), 7.14–7.38 (m, 20 H) ppm.According to the ^{1}H NMR analysis the ratio was 81:19.^{13}C NMR ($CDCl_3$): δ = 13.91 (p), 15.60 (p), 24.37 (s), 24.80 (s), 25.76 (s), 25.95 (s), 29.56 (s), 29.72 (s), 39.40 (s), 39.58 (s), 42.11 (t), 42.59 (t), 43.94 (t), 44.39 (t), 44.95 (t), 45.54 (t), 50.76 (p), 50.97 (p), 71.96 (s), 72.33 (s), 81.21 (t), 81.87 (t), 125.88 (t), 127.15 (t), 127.27 (t), 127.50 (t), 127.66 (t), 127.82 (t), 128.3 (t), 128.08 (t), 128.18 (t), 129.17 (t), 138.72 (q), 138.87 (q), 139.11 (q), 139.17 (q), 176.02 (q), 176.63 (q) ppm.$C_{24}H_{30}O_3$ (366.50): calcd. C 78.65, H 8.25;found C 77.40, H 8.03.

20b: Yield: 0.445 g (86%) of a clear, colorless oil. ^{1}H NMR ($CDCl_3$): δ = 1.13 (d, J = 7.5 Hz, 3 H), 1.32–1.59 (m, 2 H), 1.62–2.09 (m, 6 H), 2.41 [dq, J (d) = 11, J (q) = 7.5 Hz, 1 H), 2.61 (dd, J = 13.5, 9 Hz, 1 H), 3.06 (dd, J = 13.5, 4.5 Hz, 1 H), 3.38 (s, 3 H), 3.76 (ddd, J = 9, 4.5, 1 Hz, 1 H), 4.47 (d, J = 11.5 Hz, 1 H), 4.61 (d, J = 11.5 Hz, 1 H), 7.10–7.40 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 17.70 (p), 24.25 (s), 25.21 (s), 30.13 (s), 38.52 (s), 40.81 (t), 41.65 (t), 46.52 (t), 50.94 (p), 70.45 (s), 80.83 (t), 125.86 (t), 127.09 (t), 127.20 (t), 128.08 (t), 128.22 (t), 129.17 (t), 138.98 (q), 139.11 (q), 177.10 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3060 (m), 3030 (m), 2950 (s), 2870 (s), 1945 (w), 1875 (w), 1805 (w), 1730 (vs), 1600 (m), 1585 (w), 1540 (w), 1495 (s), 1450 (s), 1430 (m), 1395 (m), 1370 (m), 1350 (m), 1330 (m), 1305 (m), 1260 (s), 1225 (m), 1190 (s), 1170 (m), 1150 (s), 1110 (s), 1095 (s), 1070 (s), 1060 (s), 1030 (s), 985 (m), 950 (w), 910 (w), 900 (w), 880 (w), 850 (m), 835 (w), 810 (vw), 750 (m), 735 (s), 700 (vs) cm^{-1}. $C_{24}H_{30}O_3$ (366.50): calcd. C 78.65, H 8.25; found C 78.60, H 8.26.

20c: Yield: 0.043 g (8%) of a clear, colorless oil. ^{1}H NMR ($CDCl_3$): δ = 0.92 (d, J = 7 Hz, 3 H), 1.38–1.89 (m, 6 H), 1.92–2.07 (m, 2 H), 2.42 [dq, J (d) = 11, J (q) = 7 Hz, 1 H], 2.65 (dd, J = 13.5, 8.5 Hz, 1 H), 3.11 (dd, J = 13.5, 5 Hz, 1 H), 3.63 (s, 3 H), 3.72 (ddd, J = 8.5, 5, 2.5 Hz, 1 H), 4.48 (d, J = 11 Hz, 1 H), 4.58 (d, J = 11 Hz, 1 H), 7.12–7.40 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.89 (p), 24.23 (s), 25.15 (s), 30.33 (s), 38.89 (s), 40.33 (t), 41.37 (t), 47.62 (t), 51.15 (p), 71.06 (s), 80.43 (t), 126.17 (t), 127.37 (t), 127.72 (t), 128.34 (t), 128.42 (t), 129.33 (t), 138.77 (q), 139.10 (q), 177.27 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (m), 2950 (s), 2870 (s), 1945 (w), 1875 (w), 1805 (w), 1735 (vs), 1605 (m), 1585 (w), 1545 (w), 1495 (s), 1455 (s), 1435 (m), 1395 (m), 1375 (m), 1355 (m), 1310 (m), 1275 (m), 1260 (m), 1190 (s), 1175 (s), 1160 (s), 1110 (m), 1095 (s), 1070 (s), 1030 (m), 990 (m), 945 (w), 910 (w), 900 (w), 880 (vw), 850 (m), 840 (w), 810 (vw), 790 (vw), 750 (m), 735 (s), 700 (s) cm^{-1}. $C_{24}H_{30}O_3$ (366.50): calcd. C 78.65, H 8.25; found C 77.54, H 8.15.

21b: Yield: 0.262 g (82%) of a clear, colorless oil. ^{1}H NMR ($CDCl_3$): δ = 1.07 (d, J = 7 Hz, 3 H), 1.24–1.92 (m, 10 H), 2.40 (quint, J = 7 Hz, 1 H), 2.51 (ddd, J = 14, 10, 7 Hz, 1 H), 2.67 (ddd, J = 14, 10.5, 5 Hz, 1 H), 3.62 (s, 3 H), 7.12–7.32 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.60 (p), 23.84 (s), 28.74 (s), 31.85 (s), 34.46 (s), 37.01 (s), 42.33 (2 × t), 47.94 (t), 51.01 (p), 125.40 (t), 128.04 (t), 128.09 (t), 142.45 (q), 176.64 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3060 (m), 3030 (s), 2940 (s), 2870 (s), 1940 (w), 1870 (w), 1800 (w), 1735 (vs), 1600 (m), 1580 (w), 1540 (w), 1495 (s), 1450 (s), 1430 (s), 1375 (m), 1355 (m), 1335 (m), 1300 (m), 1260 (m), 1225 (m), 1195 (s), 1165 (s), 1110 (m), 1095 (m), 1080 (m), 1060 (m), 1030 (m), 990 (w), 945 (w), 910 (w), 850 (w), 750 (m), 720 (w), 700 (s) cm^{-1}. $C_{17}H_{24}O_2$ (260.38): calcd. C 78.42, H 9.29; found C 78.92, H 9.25.

21c: Yield: 0.037 g (12%) of a clear, colorless oil. ^{1}H NMR ($CDCl_3$): δ = 1.12 (d, J = 7 Hz, 3 H), 1.22–1.90 (m, 10 H), 2.44 (quint, J = 7 Hz, 1 H), 2.54 (ddd, J = 14, 10, 7 Hz, 1 H), 2.71 (ddd, J = 14, 10.5, 5 Hz, 1 H), 3.61 (s, 3 H), 7.12–7.32 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.81 (p), 24.18 (s), 29.89 (s), 32.30 (s), 34.69 (s), 37.83 (s), 42.08 (t), 43.00 (t), 48.75 (t), 51.12 (p), 125.59 (t), 128.23 (t), 128.31 (t), 142.65 (q), 176.52 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3060 (m), 3030 (s), 2940 (vs), 2870 (s), 1940 (w), 1870 (w), 1800 (w), 1735 (vs), 1600 (m), 1580 (w), 1540 (w), 1495 (s), 1450 (s), 1430 (s), 1380 (m), 1355 (m), 1335 (m), 1255 (s), 1190 (s), 1160 (vs), 1110 (m), 1085 (m), 1060 (m), 1045 (m), 1030 (m), 990 (m), 950 (w), 910 (m), 875 (w), 845 (m), 785 (w), 750 (s), 700 (s) cm^{-1}. $C_{17}H_{24}O_2$ (260.38): calcd. C 78.42, H 9.29; found C 78.92, H 9.02.

22b: Yield: 0.437 g (83%) of a clear, colorless oil. ^{1}H NMR ($CDCl_3$): δ = 1.16 (d, J = 7 Hz, 3 H), 1.14–1.33 (m, 2 H), 1.55–2.10 (m, 8 H), 2.36–2.50 (m, 2 H), 2.71 (ddd, J = 14, 9, 5 Hz, 1 H), 3.60 (s, 3 H), 7.14–7.32 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 17.05 (p), 21.79 (s), 27.42 (s), 29.63 (s), 29.75 (s), 34.12 (s), 40.10 (t), 40.53 (t), 47.02 (t), 50.99 (p), 125.38 (t), 128.00 (t), 128.21 (t), 142.42 (q), 176.90 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3070 (m), 3030 (s), 2950 (s), 2870 (s), 1940 (w), 1870 (w), 1800 (w), 1735 (vs), 1600 (m), 1580 (w), 1540 (w), 1495 (m), 1455 (s), 1435 (m), 1375 (m), 1350 (m), 1340 (m), 1305 (m), 1255 (s), 1225 (m), 1190 (s), 1165 (s), 1100 (m), 1085 (m), 1070 (m), 1055 (m), 1030 (m), 1020 (w), 990 (m), 960 (w), 925 (w), 910 (w), 890 (vw), 855 (m), 800 (vw), 750 (m), 725 (w), 700 (s), 670 (w) cm^{-1}. $C_{17}H_{24}O_2$ (260.38): calcd. C 78.42, H 9.29; found C 78.89, H 9.20.

22c: Yield: 0.068 g (13%) of a clear, colorless oil. ^{1}H NMR ($CDCl_3$): δ = 1.10 (d, J = 7 Hz, 3 H), 1.16–1.38 (m, 2 H), 1.46–

1.76 (m, 6 H), 1.84–2.02 (m, 2 H), 2.36 [dq, *J* (d) = 11, *J* (q) = 7 Hz, 1 H], 2.44 (ddd, *J* = 14, 10, 7.5 Hz, 1 H, 2.75 (ddd, *J* = 14, 10, 5 Hz, 1 H), 3.64 (s, 3 H), 7.12–7.32 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.55 (p), 21.88 (s), 27.84 (s), 28.95 (s), 29.28 (s), 34.16 (s), 39.10 (t), 40.63 (t), 47.66 (t), 51.23 (p), 125.68 (t), 128.27 (t), 128.32 (t), 142.53 (q), 177.37 (q) ppm. IR (NaCl): $\tilde{\nu}$ = 3110 (w), 3090 (m), 3060 (m), 3030 (s), 2940 (vs), 2870 (s), 1940 (w), 1870 (w), 1800 (w), 1735 (vs), 1600 (m), 1580 (w), 1540 (w), 1495 (s), 1450 (s), 1430 (s), 1370 (m), 1345 (m), 1310 (m), 1275 (s), 1255 (s), 1220 (m), 1195 (s), 1165 (vs), 1105 (m), 1080 (m), 1070 (m), 1050 (m), 1030 (m), 990 (m), 945 (w), 910 (w), 890 (w), 855 (m), 805 (w), 750 (s), 725 (m), 700 (s), 645 (w) cm^{-1}. $C_{17}H_{24}O_2$ (260.38): calcd. C 78.42, H 9.29; found C 78.76, H 9.00.

Supporting Information: Experimental procedures and analytical data of all new compounds are described. ^{1}H NMR spectra of compounds **21a**, **22a**, **45**, **49**, **85**, **88**, **93**, and **94** are given (see also the footnote on the first page of this article).

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