Vicinal Dianion of Triethyl Ethanetricarboxylate: Syntheses of (±)-Lichesterinic Acid, (±)-Phaseolinic Acid, (±)-Nephromopsinic Acid, (±)-Rocellaric Acid, and (±)-Dihydroprotolichesterinic Acid

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Dedicated to Professor *Dieter Seebach* on the occasion of his 65th birthday

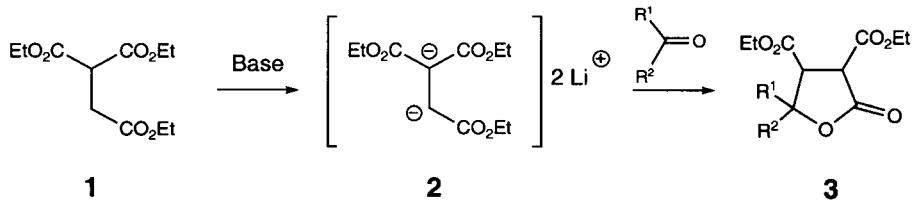
The vicinal dianion **2** derived from triethyl ethanetricarboxylate reacted regioselectively with aldehydes and ketones at C(β) to provide paraconic acid derivatives **5a**–**f** in moderate to high yields as mixtures of diastereoisomers. The paraconic acid derivatives **5e** and **5f** were utilized as the starting materials for the syntheses of (±)-lichesterinic acid (**12**), (±)-phaseolinic acid (**13**), (±)-nephromopsinic acid (**14**), (±)-rocellaric acid (**15**), and (±)-dihydroprotolichesterinic acid (**16**).

1. Introduction. – Dianions of numerous classes of organic compounds have been reported and played important roles in organic synthesis due to their high reactivity and regioselectivity towards electrophiles [1]. The reactions of these dianions have led to the development of new synthetic methods of many classes of organic compounds. Amongst these dianions, the dianions derived from succinic acid derivatives and succinic esters were found to be versatile reagents for the preparation of various types of compounds [2–14].

The vicinal dianions of dialkyl succinates underwent mono- or dialkylation [2] [3] and condensation reactions [4] with appropriate alkylating agents to give good yields of products. We have reported that the vicinal dianion of diethyl succinate could undergo hydroxyalkylation reactions with aliphatic aldehydes and ketones to afford paraconic esters, which could be readily converted into 4-carboxy-2,3-dialkyl-substituted 2-cyclopentenones [3]. Futhermore, paraconic esters have attracted considerable interest because their basic skeletons, trisubstituted γ-butyrolactones, are found in many natural products possessing interesting biological properties.

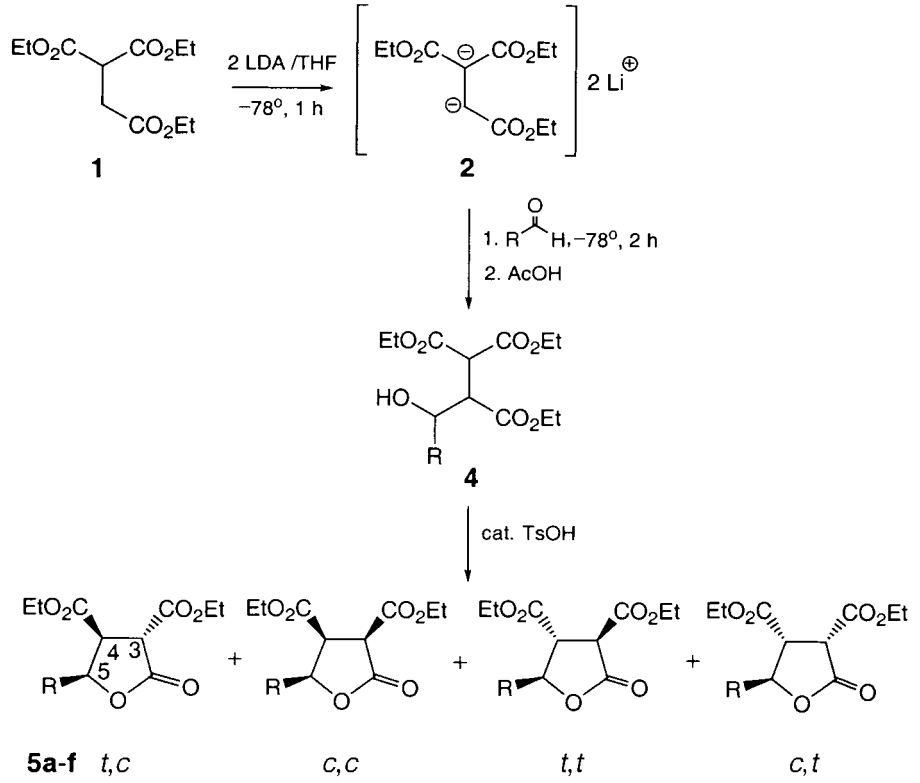
Our previous results, concerning the reactions of diethyl succinate dianion with electrophiles [3], prompted us to study the generation of the vicinal dianion **2** and the regioselectivity towards electrophiles. This dianion has not been previously reported and is expected to be generated by double deprotonation of triethyl ethanetricarboxylate (**1**) upon treatment with appropriate bases as shown in *Scheme 1*. The reaction of the vicinal dianion **2** with carbonyl compounds would provide a new synthetic pathway to functionalized 3,4,5-trisubstituted γ-lactones of type **3**. The lactones of type **3** appear to be useful as synthetic intermediates for the synthesis of several natural α-alkyl-substituted γ-lactones, such as methylenolactocin (**10**) [15], protolichesterinic acid (**11**) [16], lichesterinic acid (**12**) [17], phaseolinic acid (**13**) [18], nephromopsinic acid (**14**) [19], rocellaric acid (**15**) [20], and dihydroprotolichesterinic acid (**16**) [21].

Scheme 1. *Proposed Synthetic Route to γ-Lactone* **3** *by the Reaction of Dianion* **2** *with Carbonyl Compounds*



2. Results and Discussion. – *2.1 Reaction of Dianion* **2** *with Carbonyl Compounds.* Dianion **2** could be easily generated by reacting triester **1** with 2 equiv. of lithium diisopropylamide (LDA) in THF at −78° for 1 h. When dianion **2** was allowed to react with 1.5 equiv. of piperonal (=1,3-benzodioxole-5-carboxaldehyde) at −78° for 2 h, the resulting product mainly consisted of an adduct **4a** (R = 1,3-benzodioxol-5-yl; *Scheme 2*) accompanied by a small amount of the expected γ-lactone **5a** after acidic (1.5M HCl) workup. However, the adduct **4a** could be easily converted into γ-lactone **5a** by treatment of the crude product **4a** with a catalytic amount of *p*-toluenesulfonic acid

Scheme 2. *Generation and Reactions of Dianion* **2** *with Aldehydes*

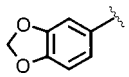
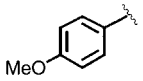


(TsOH) in CH_2Cl_2 at room temperature. More conveniently, complete lactonization could be achieved when the reaction mixture was first quenched with AcOH at $-78°$ and warmed to room temperature, followed by addtion of a catalytic amount of TsOH and stirring at the same temperature overnight. This procedure was used as the standard condition for the reactions of the dianion **2** with other carbonyl compounds (*Scheme 2*).

The γ-lactone **5a** was obtained as a mixture of four diastereoisomers (*t,c, c,c*, *t,t*, and *c,t* isomers, *c* = *cis*, *t* = *trans*) in a ratio of 71:11:16:2 in 78% yield. The relative configurations of these compounds were assigned by their ^{1}H-NMR spectra. Attempted separation of the diastereoisomers of **5a** was performed by prep. TLC to give two bands, a less polar (14% yield) consisting of a 11:89 mixture *c,t*/*t,t*-**5a** and a more polar (64% yield) consisting of a 86:14 mixture of *t,c*/*c,c*-**5a**. The pure diastereoisomer *t,c*-**5a** could be obtained by fractional crystallization from AcOEt/hexane.

Having succeeded in preparing compound **5a**, we next investigated the reaction of dianion **2** with other aldehydes as summarized in *Table 1*. Moderate to high yields of γ-lactones **5a**–**f** could be achieved. The *cis*- and *trans*-configuration at the 4,5-positions of compounds **5a**–**c** and **5e**,**f** could be assigned by their ^{1}H-NMR data (see *Table 2*).

Table 1. *Preparation of γ-Lactones* **5a**–**f**

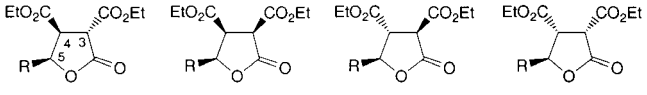
Product	R	Yield[a]) [%]	*t,c*/*c,c*/*t,t*/*c,t*
5a		78	71:11:16:2[b])[c])
5b		81	79:4:14:3[c])
5c	Ph	78	71:6:19:4[d])
5d	^{t}Bu	53	(80:20)[e])
5e	$Me(CH_2)_4$	55	79:6:15:trace[f])
5f	$Me(CH_2)_{12}$	62	86:3:11:trace[f])

[a]) Isolated yield. [b]) Calculated from *Fractions 1* and *2*. [c]) Determined by ^{1}H-NMR (H–C(5)) of the isolated product. [d]) Determined by ^{1}H-NMR (H–C(5)) of the crude product. [e]) The configuration could not be assigned, and the ratio was determined by ^{1}H-NMR (H–C(3)) of the crude product. [f]) Determined by ^{1}H-NMR (H–C(3) and H–C(5)) of the crude product.

The coupling constants J_{cis} and J_{trans} of H–C(5) (OC*H*Ar) of **5a**–**c**,**e**,**f**, which appeared as *d* in the range of δ 4.46–5.97, were 5.2–8.0 and 8.9–9.3 Hz, resp. (see *Table 2*). The configurational assignment of the 3,4-positions of the *t,t* and *c,c* isomers could be accomplished by determining of the coupling constants of H–C(3), which appeared as *d* varying in the range δ 3.67–4.09 ($J_{trans} \approx 7.3–10.8$ and $J_{cis} \approx 7.2–9.5$ Hz). However, the assignments of the *t,c* and *c,t* isomers were ambiguous.

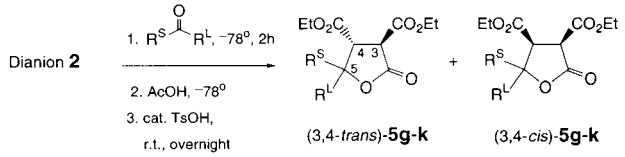
To get more insight into the reaction of dianion **2**, we investigated the reaction of dianion **2** with ketones. As expected, the desired γ-lactones **5g**–**k** were obtained in moderate yields. The results are summarized in *Table 3*. The structures of compounds **5g**–**k** were established by their spectral data.

Table 2. *Significant ^{1}H-NMR Data of γ-Lactones* **5a–c** *and* **5e**,**f**



		H–C(3) (*d*)		H–C(4) (*dd*)		H–C(5) (*d*)	
		δ [ppm]	*J*(3,4) [Hz]	δ [ppm]	*J*(3,4), *J*(4,5) [Hz]	δ [ppm]	*J*(4,5) [Hz]
5a	*t,c*	4.11	7.3	4.07	7.5 (app. *t*)	5.73	7.5
	c,c	–	–	–	–	5.47	5.7
	t,t	3.98	10.7	3.76	10.7, 8.9	5.37	8.9
	c,t	3.92	9.4	3.45	9.4 (app. *t*)	5.79	9.3
5b	*t,c*	4.20	7.6	4.15	7.7 (app. *t*)	5.84	8.0
	c,c	–	–	–	–	5.58	5.7
	t,t	4.06	10.8	–	–	5.47	9.1
	c,t	3.99	9.3	3.53	9.3 (app. *t*)	5.90	9.3
5c	*t,c*	–	–	–	–	5.91	7.0
	c,c	3.95	7.2	–	–	5.65	5.7
	t,t	4.09	10.6	–	–	5.56	8.9
	c,t	4.02	9.3	3.57	9.1 (app. *t*)	5.97	8.9
5e	*t,c*	3.88	8.0	3.81	8.0 (app. *t*)	–	–
	c,c	3.67	7.3	–	–	–	–
	t,t	3.89	10.3	–	10.2, 8.6	–	–
	c,t	–	9.4	–	9.2 (app. *t*)	–	–
5f	*t,c*	3.99	8.0	3.92	7.9 (app. *t*)	–	–
	c,c	3.76	7.3	–	–	4.46	5.2
	t,t	3.98	10.2	3.54	10.2, 8.7	–	–
	c,t	3.84	9.5	3.22	9.4 (app. *t*)	–	–

Table 3. *Preparation of γ-Lactones* **5g–k**



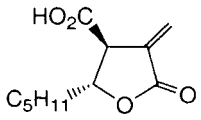
	R^S	R^L	Yield[a]) [%]	3,4-Position *cis*/*trans*[b])
5g	Me	Me	45	0 : 100
5h	$-(CH_2)_5-$		58	0 : 100
5i	Ph	Ph	41	14 : 86
5j	Me	Ph	39	almost *trans*[c])
5k	Me	Et	37	37 : 63[d])

[a]) Isolated yield. [b]) Determined by ^{1}H-NMR (H–C(3)). The *cis/trans* ratio of **5g–k** could be calculated from (*c,t* + *c,c*)/(*t,c* + *t,t*). [c]) **5j** was obtained as a mixture of four diastereoisomers, which contained predominantly only one diastereoisomer. [d]) **5k** was obtained as a mixture of four diastereoisomers whose ratio was determined by ^{1}H-NMR (*Me*CH_2C).

The *cis*- and *trans*-configuration at the 3,4-positions of **5g**–**k** could be assigned by the coupling constants $J(3,4)$ in the ^{1}H-NMR spectra: $J_{cis} = 6.6$ Hz and $J_{trans} = 9.3-11.7$ Hz, resp.

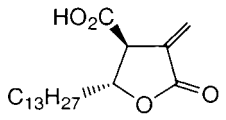
As summarized in *Table 1*, the major isomer obtained from the reaction of dianion **2** with aldehydes was the *t,c* isomer in all cases. The observed high stereoselectivity can be explained by assuming the involvement of the (*E*)-configuration of the dienolate form of dianion **2**, *i.e.*, (*E*)-**2**, as shown in *Scheme 3*. Our assumption was based on the well established fact that esters appear to give (*E*)-enolates [22] upon deprotonation with LDA. The relative stereochemical outcome at C(4) and C(5) of γ-lactone **5** was determined by using the models of the 6-membered transition states **6A** and **6B** of the aldol condensation of dianion (*E*)-**2** with aldehydes at $-78°$. Due to the less important 2,3-steric interaction between the aryl or alkyl and alkoxy groups, the transition state **6A** is more favored than the transition state **6B**. Consequently, the addition preferentially proceeds *via* the alkoxide intermediate *anti*-**7** rather than the *syn*-**7**. These alkoxides are then protonated upon hydrolysis with acid to afford the hydroxy esters **8** and **9,** respectively. Compound **8** is lactonized under thermodynamic-control conditions to give the more stable lactone *t,c*-**5** as the major isomer and the less stable lactone *c,c*-**5** as the minor isomer. Similarly, lactonization of hydroxy ester **9** leads to the formation of *t,t*-**5** and *c,t*-**5** (*Scheme 3*).

2.2. *Syntheses of (±)-Lichesterinic Acid* (**12**), *(±)-Phaseolinic Acid* (**13**), *(±)-Nephromopsinic Acid* (**14**), *(±)-Rocellaric Acid* (**15**), *and (±)-Dihydroprotolichesterinic Acid* (**16**). The synthesis of trisubstituted γ-butyrolactones, in particular the β-carboxy derivatives (paraconic acids), has attracted considerable attention in recent years, because of the wide range of their biological activities. Some of these compounds are methylenolactocin (**10**) [15], protolichesterinic acid (**11**) [16], lichesterinic acid (**12**) [17], phaseolinic acid (**13**) [18], nephromopsinic acid (**14**) [19], rocellaric acid (**15**) [20], and dihydroprotolichesterinic acid (**16**) [21]. Several synthetic approaches towards



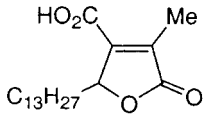
10

Methylenolactocin



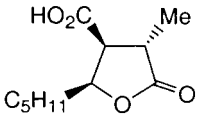
11

Protolichesterinic acid



12

Lichesterinic acid



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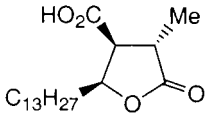
Phaseolinic acid



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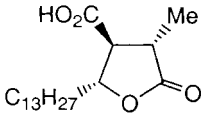
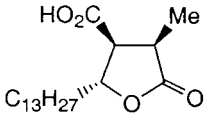
Nephromopsinic acid



15

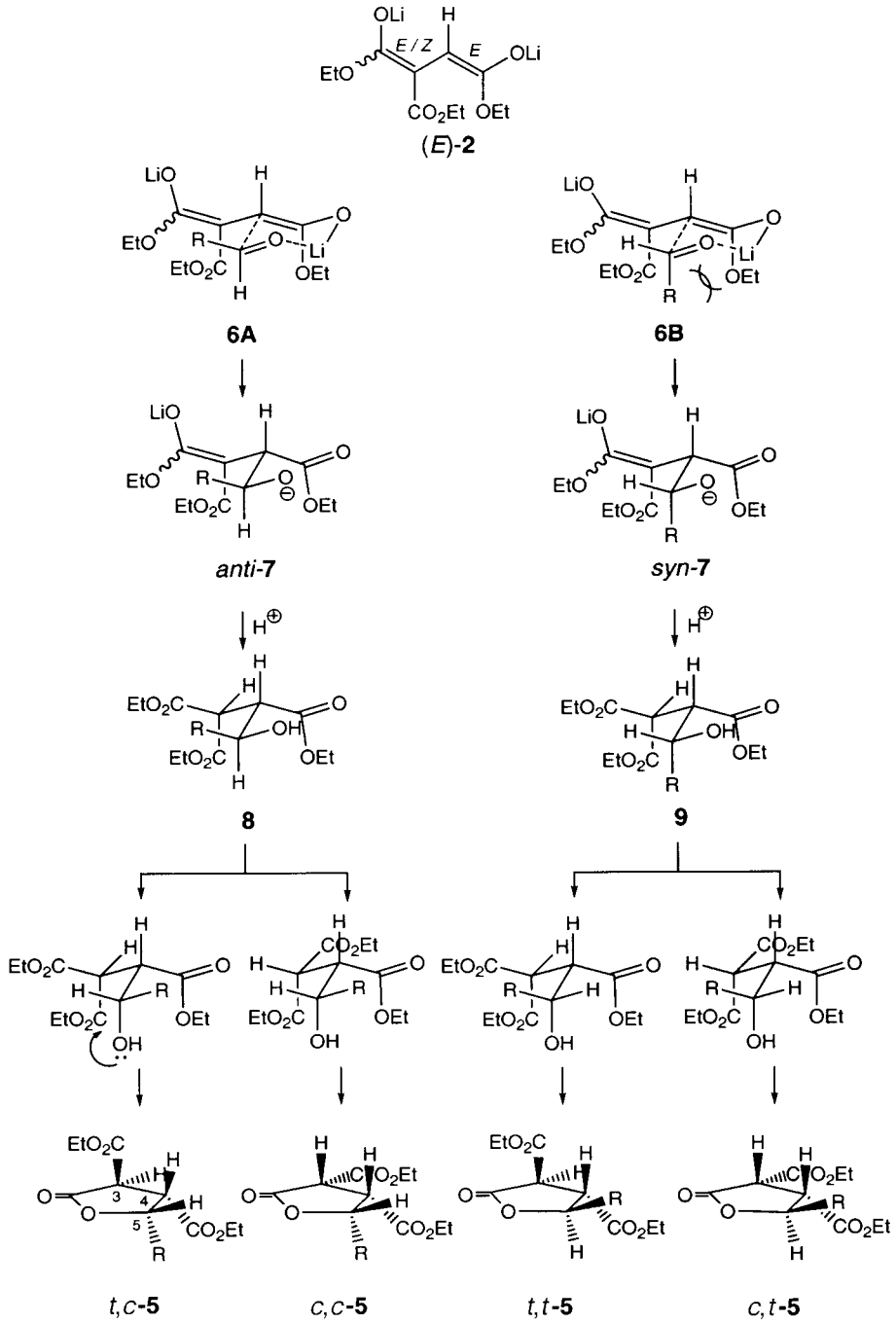
Rocellaric acid



16

Dihydroprotolichesterinic acid

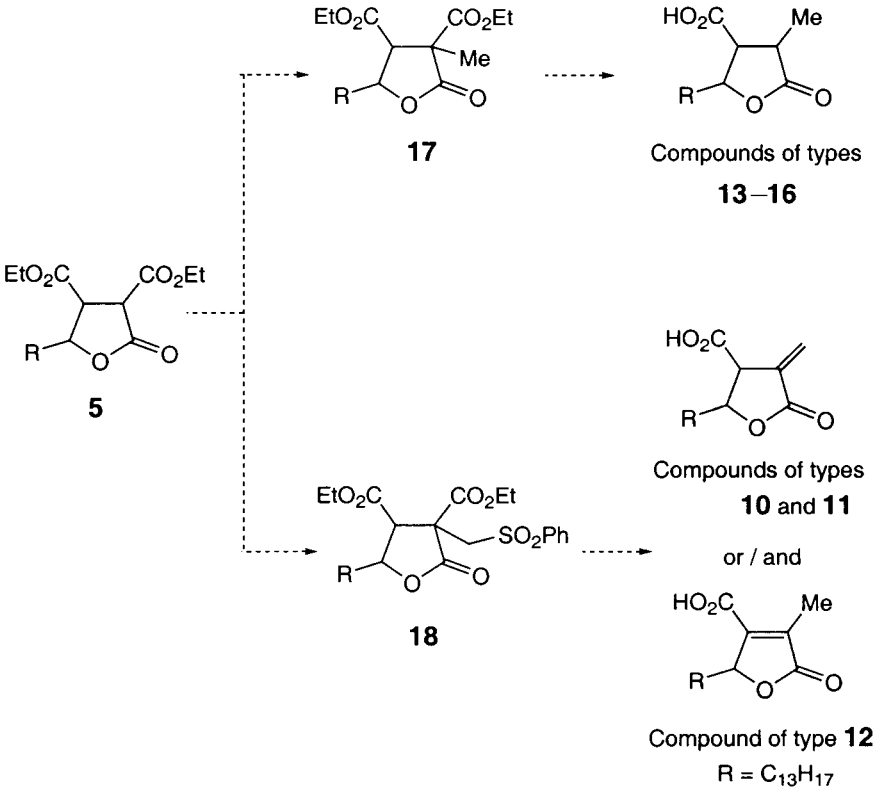
Scheme 3. *Proposed Transitions for the Stereochemical Course of the Addition Reactions of the Dianion* **2** *to Aldehydes*



these molecules either in racemic or pure enantiomeric form have been developed by a number of research groups over the past decade.

Since γ-lactones of type **5** could be readily obtained by the reaction of dianion **2** with aldehydes, we herein demonstrate the synthetic utility of this type of lactones for the syntheses of some naturally occurring α,β,γ-trisubstituted γ-lactones. As proposed in *Scheme 4*, we consider compounds **17** and **18** as important intermediates in the synthetic transformation of **5** into the corresponding natural products of types **13**–**16** and types **11** and **12**, respectively. Both γ-lactones **17** and **18** should be easily prepared from **5** by simple base-catalyzed methylation and (phenylthio)methylation followed by oxidation, respectively. Hydrolysis followed by decarboxylation of compound **17** would afford the desired compounds of types **13**–**16**. Similarly, compound **18** would be transformed into the corresponding compounds of types **10**–**12** by a tandem hydrolytic decarboxylative desulfonylation.

Scheme 4. *Proposed Synthetic Strategy to Natural Products* **10**–**16**

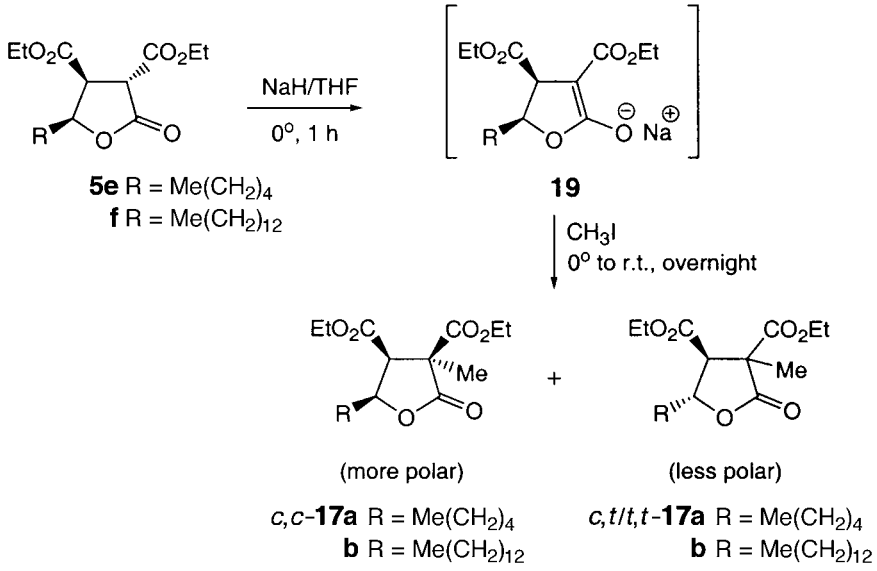


2.3. *α-Alkylation of α,β-Bis(ethoxycarbonyl)-Substituted γ-Lactones* **5e** *and* **5f**. Methylation of the diastereoisomer mixtures of **5e** or **5f** could be achieved by employing MeI/NaH in THF at 0°. Good yields of the α-methylated γ-lactones **17a** and **17b** were obtained. The diastereoisomer mixture of **5e** (*t,c*/(*t,t* + *c,c*)/*c,t* 70:27:3) provided compound *c,c*-**17a** (67% yield) and an inseparable mixture *c,t*/*t,t*-**17a** (60:40)

in 23% yield, while the diastereoisomer mixture of **5f** (*t,c*/(*t,t* + *c,c*) 63:34) gave compound *c,c*-**17b** (67% yield) and an iseparable mixture *c,t*/*t,t*-**17b** (51:49) in 25% yield.

The *c,c*-**17** was obtained as the major isomer. This can be rationalized by the assumption that methylation of the enolate anion **19** occurs from the less-hindered side avoiding the steric interaction with the ethoxycarbonyl group at C(4) (*Scheme 5*). The isomers *c,c*-**17a** and -**17b** could be easily separated from the isomer mixtures of *c,t*/*t,t*-**17a** and -**17b** respectively, by radial chromatography on silica-gel.

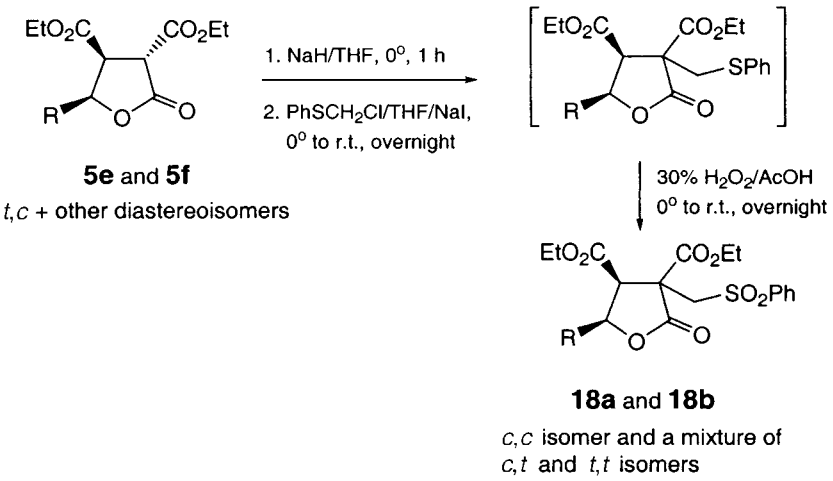
Scheme 5. *Base-Catalyzed Methylation of γ-Lactone* **5**



The relative configuration at the 4,5-positions of **17a** and **17b** could be assigned by the coupling constants observed for H–C(4), which appeared in the ^{1}H-NMR spectra as *d* at δ 3.30 (J_{cis} = 6.6–6.8 Hz) and 2.84–3.67 (J_{trans} = 9.7–9.9 Hz).

Having succeeded in preparing compounds **17**, we then prepared next α-(phenylsulfonyl)methyl-α,β-bis(ethoxycarbonyl)-substituted γ-lactones **18a** and **18b** by treatment of the γ-lactones **5e** and **5f** with $PhSCH_2Cl$/NaH in THF at 0° in the presence of NaI, followed by oxidation with H_2O_2/AcOH (*Scheme 6*). Thus, γ-lactone **5e** (*t,c*/*c,c*/*t,t*/*c,t* 82:6:11:trace) provided **18a** (98% yield) which contained mainly the *c,c* isomer and a small amount of other isomers. Similarly, γ-lactone **5f** containing mostly the *t,c* isomer and a small amount of other isomers afforded *c,c*-**18b** (88% yield) and an inseparable mixture *c,t*/*t,t*-**18b** (73:27; 5% yield) (*Scheme 6*). We assumed that the *c,c* isomer of **18** was obtained as the major isomer. This can be explained as discussed above for the formation of the *c,c* isomer of compound **17**.

Scheme 6. *Preparation of α-(Phenylsulfonyl)methylated γ-Lactone* **18**

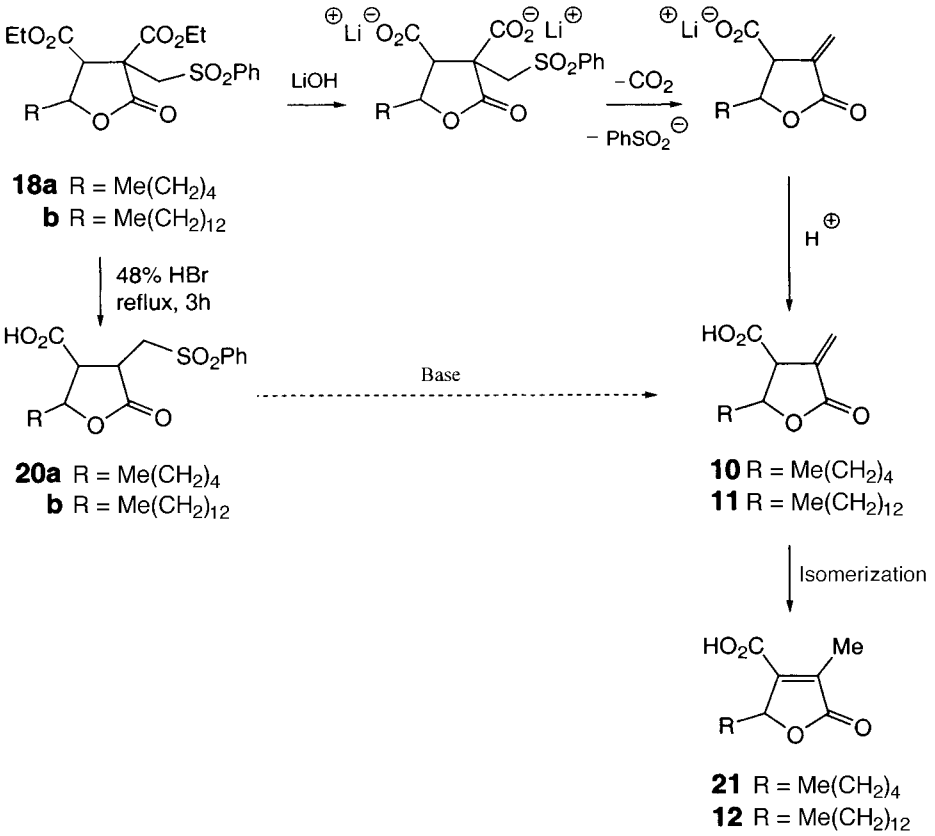


2.4. *Attempted Preparation of (±)-Methylenolactocin* (**10**) *and Preparation of (±)-Lichesterinic Acid* (**12**). As proposed in *Scheme 7*, hydrolysis of **18a** followed by base-catalyzed elimination of the expected product **20** should afford the desired methylenolactocin (**10**). Thus, treatment of **18a** containing mainly the *c,c* isomer with 48% HBr solution under reflux for 3 h provided the desired compound **20** in 48% yield, consisting of a *t,c*/*c,c*/*t,t* isomer mixture 32:64:4. Similarly, hydrolysis of a 41:59 mixture of *t,t*/*c,t*-**18a** gave **20** as a 85:15 mixture of *c,t*/*t,t* isomers in 65% yield. Attempts to convert compound **20** to the expected methylenolactocin (**10**) under various conditions, *e.g.*, LDA or DBU as a base in THF or CH_2Cl_2 as a solvent, were investigated. All experiments led to a complex mixture of unidentified products besides a small amount of **10** and compound **21** ($R = C_5H_{11}$) as revealed by the ^{1}H-NMR spectra.

During our investigation for the hydrolysis of **18a** to compound **20**, we found that the reaction of a diastereoisomer mixture of **18a** with LiOH (4 equiv.) in THF/H_2O under reflux for 3 h followed by stirring overnight provided butenolactone **21** ($R = Me(CH_2)_4$) in 69% yield. The formation of butenolactone **21** ($R = Me(CH_2)_4$) resulted from a tandem ester hydrolysisdecarboxylative elimination of the phenylsulfonyl group followed by isomerization of the initially formed exocyclic methylene group. By employing this advantage, (±)-lichesterinic acid (**12**) could be synthesized in 26% yield from γ-lactone **18b** (*Scheme 7*).

2.5. *Syntheses of (±)-Phaseolinic Acid* (**13**), *(±)-Nephromopsinic Acid* (**14**), *(±)-Rocellaric Acid* (**15**), *and (±)-Dihydroprotolichesterinic Acid* (**16**). The facile accessibility of γ-lactones *c,c*-**17a** and *c,c*-**17b** prompted us to try to convert them into the desired paraconic acids **13**–**16** by sequential hydrolysis and decarboxylation, expecting to be able to control the configurations at the 3-, 4-, and 5-positions. Thus, hydrolysis of γ-lactone *c,c*-**17a** by refluxing with 48% HBr solution for 5 h afforded an inseparable 62:38 mixture of paraconic acid **22** and (±)-phaseolinic acid (**13**) in 89% yield (*Scheme 8*). The same results were obtained when *c,c*-**17b** was treated with 48%

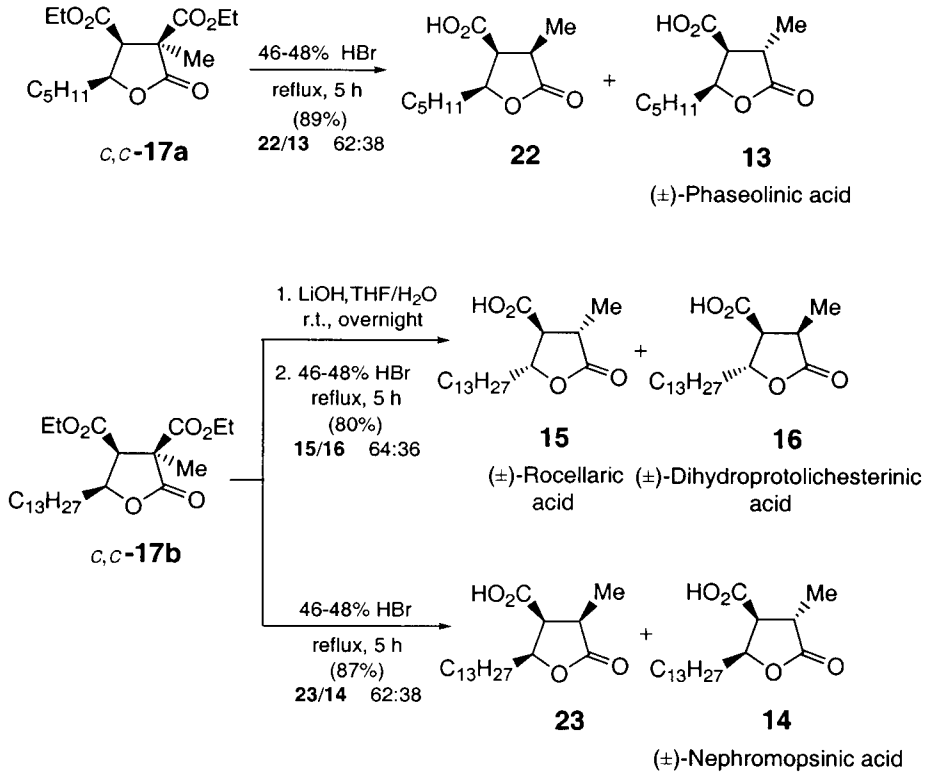
Scheme 7. *Preparation of (±)-Lichesterinic Acid* (**12**)



HBr solution under the same conditions; an inseparable 62:38 mixture of paraconic acid **23** and (±)-nephromopsinic acid (**14**) was obtained in 87% yield. It should be noted that under the hydrolytic conditions with 48% HBr solution, there was no isomerization at C(4) and C(5). Both (±)-phaseolinic acid (**13**) and (±)-nephromopsinic acid (**14**) could be separated from paraconic acids **22** and **23**, respectively, as their methyl ester derivatives formed by dicyclohexylcarbodiimide/MeOH treatment.

Hydrolysis of *c,c*-**17b** under basic conditions was also studied using LiOH/THF/H_2O at room temperature. The reaction led to incomplete hydrolysis as revealed by the ^{1}H-NMR spectrum of the crude product obtained. It was found that one ethoxycarbonyl group still remained. However, when the crude product was further treated with 48% HBr solution under reflux for 5 h, a 64:36 mixture of (±)-rocellaric acid (**15**) and (±)-dihydroprotolichesterinic acid (**16**) was obtained in 80% yield (*Scheme 8*). The results indicated that *c,c*-**17b** was isomerized to the thermodynamically more stable 4,5-*trans* isomer by LiOH during the hydrolysis in the first step, before the ethoxycarbonyl group was hydrolyzed. Good yield (72%) of a mixture **15**/**16** with the same ratio was obtained when a 73:27 mixture *c,t*/*t,t*-**17b** was hydrolyzed under the same conditions (LiOH and then 48% HBr solution under reflux).

Scheme 8. *Preparation of Natural Products* **13**–**16**



The separation of paraconic acids **15** and **16** from each other by chromatography was unsuccessful. Isomerization of (±)-dihydroprotolichesterinic acid (**16**) to (±)-rocellaric acid (**15**) was investigated. It was anticipated that this isomerization was successful by treatment of a 66 : 34 mixture **15**/**16** with 2 equiv. of LDA in THF at 0° for 1 h, followed by quenching with AcOH. The resulting product was a 89 : 11 mixture **15**/**16**. The major isomer, (±)-rocellaric acid (**15**), was separated by fractional crystallization (AcOEt) in 72% yield, whereas the minor (±)-dihydroprotolichesterinic acid (**16**) could not be separated in pure form. However, **16** could be isolated as its methyl ester.

3. Conclusions. – We demonstrated that the reaction of dianion **2** with carbonyl compounds afforded the expected paraconic acids **5a**–**k** as mixtures of diastereoisomers containing the *t,c*-isomer as the major isomer. Moreover, paraconic acids **5e** and **5f** could be used as starting materials for the syntheses of the natural products (±)-lichesterinic acid (**12**), (±)-phaseolinic acid (**13**), (±)-nephromopsinic acid (**14**), (±)-rocellaric acid (**15**), and (±)-dihydroprotolichesterinic acid (**16**). The desired natural compounds **13**–**16** could be prepared with retention of configuration at C(4) and C(5) by hydrolysis of the corresponding paraconic acid **17** (*c,c* isomer) and **17** (*c,t*/*t,t* isomers) (obtained by methylation of **5e** and **5f**) in refluxing 48% HBr solution. The products

13 – **16** were separated as their methyl esters. (±)-Lichesterinic acid (**12**) was prepared by treatment of α-[(phenylsulfonyl)methyl]-γ-lactone **18b** with LiOH in THF/H_2O. However, attempted synthesis of (±)-methylenolactocin (**10**) by elimination of the phenylsulfonyl group from compound **18a** was unsuccessful.

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Experimental Part

1. *General.* THF was distilled from sodium-benzophenone ketyl (sodium oxidodiphenylmethyl). The molarity of BuLi (in hexane) was determined by titration with diphenylacetic acid in THF at 0°. $^{i}Pr_2NH$ was distilled over CaH_2; CH_2Cl_2 and acetone were distilled over P_2O_5. All glasswares and syringes were oven-dried and kept in a dessicator before use. Radial chromatography: plates prepared with *Merck* silica-gel PF_{254} containing $CaSO_4 \cdot 1/2\,H_2O$ type *60* (TLC Art. 7749), prep. plates with *Merck* silica-gel *60* (PF_{254}, Art. 7747). FC = flash column chromatography. M.p.: *Büchi 501* melting-point apparatus, uncorrected. IR Spectra: *Jasco A-302* or *Perkin-Elmer 683* spectrometer; in cm^{-1}. NMR Spectra: *Bruker DPX-300* (^1H at 300 MHz, ^{13}C at 75 MHz) or *Bruker DPX-400* (^1H at 400 MHz) spectrometer; in $CDCl_3$ with $SiMe_4$ as internal standard; chemical shifts δ in ppm downfield from $SiMe_4$, *J* in Hz. MS: *Finnigan MAT* mass spectrometer; in m/z (rel. %). Elemental analyses: *Perkin-Elmer* elemental analyzer *2400 CHN.*

2. *Generation and Reactions of Dianion* **2** *with Carbonyl Compounds. Diethyl 2-(1,3-Benzodioxol-5-yl)tetrahydro-5-oxofuran-3,4-dicarboxylate* (**5a**): *General Procedure* (*G.P.*). A soln. of triethyl 1,1,2-ethanetricarboxylate (493 mg, 2.0 mmol) in THF (2 ml) was added dropwise at −78° to a THF soln. of lithium diisopropylamide (LDA) under Ar (prepared by reacting $^{i}Pr_2NH$ (0.7 ml, 5 mmol) in THF (8 ml) with 1.25M BuLi in hexane (3.5 ml, 4.4 mmol) at −78° for 30 min). After stirring at −78° for 1 h, a THF (2 ml) soln. of piperonal (1.3813 g, 2.5 mmol) was added dropwise to the pale yellow soln. of the dianion **2**. Stirring was continued at −78° for 2 h, then the reaction was quenched with AcOH (4 ml). The resulting mixture was warmed to r.t., and TsOH (monohydrate) was added as a catalyst. After stirring overnight, the mixture was diluted with H_2O (50 ml) and extracted with AcOEt (3 × 30 ml). The combined org. layer was washed with 10% $NaHCO_3$ soln., H_2O, and brine, dried (Na_2SO_4), and evaporated, and the crude product purified by prep. TLC (SiO_2, 20% AcOEt/hexane; double runs) to give two bands of **5a** (*Fr. 1* and *2*).

Fr. 1 (less polar) yielded a yellow viscous liquid: *c,t/t,t*-**5a** 11:89 (96 mg, 14%). IR (neat): 2984*m*, 2939*m*, 2907*m*, 1789*s*, 1738*s*, 1633*w*, 1612*m*, 1506*s*, 1493*s*, 1449*s*, 1398*m*, 1374*m*, 1303*s*, 1253*s*, 1197*s*, 1160*s*, 1038*s*, 929*m*, 859*m*, 815*m*, 705*m*. ^1H-NMR (300 MHz, $CDCl_3$): 6.88–6.70 (*m*, 3 arom. H); 5.92 (*t,t*) and 5.91 (*c,t*) (each *s*, OCH_2O); 5.79 (*c,t*), 5.37 (*t,t*) (each *d*, *J* = 9.25 and 8.9, resp., OC*H*Ar); 4.24 (*q*, *J* = 7.2, OCH_2Me of *t,t*); 4.20–4.05 (*m*, 2 OCH_2Me of *c,t* and OCH_2Me of *t,t*); 3.98 (*t,t*) and 3.92 (*c,t*) (each *d*, *J* = 10.7 and 9.4, resp., O_2CCHCO_2); 3.76 (*dd*, *J* = 10.7, 8.9, C*H*CO_2Et of *t,t*); 3.45 (app. *t*, *J* = 9.4, C*H*CO_2Et of *c,t*); 1.27 (app. *t*, *J* = 7.2, OCH_2*Me*); 1.16 (app. *t*, *J* = 7.2, OCH_2*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 169.1 (C=O); 168.9 (C=O); 166.2 (C=O); 148.3 (C); 148.1 (C); 130.6 (C, *c,t*) and 130.4 (C, *t,t*); 120.5 (CH, *c,t*), 120.4 (CH, *t,t*); 108.2 (CH, *t,t*) and 108.1 (CH, *c,t*); 106.6 (CH, *c,t*), 106.5 (CH, *t,t*); 101.4 (OCH_2O, *t,t*) and 101.3 (OCH_2O, *c,t*); 63.6 (OCH_2, *c,t*), 62.6 (OCH_2, *t,t*); 62.0 (OCH_2, *t,t*), 61.6 (OCH_2, *c,t*); 51.9 (CH, *t,t*), 51.5 (CH, *c,t*); 50.6 (CH, *t,t*), 50.5 (CH, *c,t*); 13.9 (Me, *t,t*) and 13.8 (Me, *c,t*); 13.88 (Me).

Fr. 2 (more polar) yielded a pale yellow solid: *t,c/c,c*-**5a** 86:14 (448 mg, 64%). ^1H-NMR (300 MHz, $CDCl_3$): 6.82–6.63 (*m*, 3 arom. H); 5.91 (*t,c*) and 5.90 (*c,c*) (each *s*, OCH_2O); 5.73 (*t,c*), 5.37 (*c,c*) (each *d*, *J* = 7.5 and 5.7, resp., OC*H*Ar); 4.24 (app. *q*, *J* = 7.2, OCH_2Me of *t,c* and *c,c*); 4.11 (*d*, *J* = 7.3, O_2CCHCO_2 of *t,c*); 4.07 (app. *t*, *J* = 7.5, C*H*CO_2Et of *t,c*); 3.91–3.71 (*m*, OCH_2Me of *t,c* and OCH_2Me, COCHCO, and C*H*CO_2Et of *c,c*); 1.28 (*t,c*) and 1.27 (*c,c*) (each *t*, *J* = 7.2 and 7.4, resp., OCH_2*Me*); 0.95 (*t,c*) and 0.94 (*c,c*) (each *t*, *J* = 7.2 and 7.7, resp., OCH_2*Me*).

The pale yellow solid obtained from the *Fr. 2* (diastereoisomer mixture) was recrystallized from AcOEt/hexane to give pure *t,c*-**5a**. White solid. M.p. 84–85°. IR (nujol): 3071*w*, 3046*w*, 2989*s*, 1797*s*, 1728*s*, 1610*w*, 1505*s*, 1486*m*, 1448*s*, 1413*m*, 1369*s*, 1324*s*, 1261*s*, 1238*s*, 1213*s*, 1199*s*, 1141*s*, 1043*s*, 1018*s*, 939*m*, 908*m*, 871*m*, 805*m*. ^1H-NMR (400 MHz, $CDCl_3$): 6.80 (*d*, *J* = 8.0, 1 arom. H); 6.74 (*d*, *J* = 8.0, 1 arom. H); 6.72 (*s*, 1 arom. H); 5.99 (*s*, OCH_2O); 5.82 (*d*, *J* = 8.0, OC*H*Ar); 4.32 (*q*, *J* = 7.2, 1 OCH_2Me); 4.19 (*d*, *J* = 7.2, O_2CCHCO_2); 4.15 (app. *t*,

$J = 7.6$, C*H*CO_2Et); 3.98–3.81 (*m*, 1 OCH_2Me); 1.37 (*t*, $J = 7.2$, OCH_2*Me*); 1.04 (*t*, $J = 7.2$, 1 OCH_2*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 169.8 (C=O); 168.1 (C=O); 166.1 (C=O); 148.1 (C); 147.8 (C); 128.3 (C); 119.7 (CH); 108.1 (CH); 106.2(CH); 101.3 (OCH_2O); 79.9 (OC*H*Ar); 62.7 (CH_2O); 61.6 (CH_2O); 49.8 (CH); 48.4 (CH); 13.9 (Me); 13.6 (Me). EI-MS: 350 (100, M^+), 321 (0.83), 304 (13), 287 (2), 275 (9), 259 (10), 247 (4), 230 (19), 215 (4), 203 (27), 190 (12), 173 (17), 149 (85), 127 (79), 99 (69), 93 (6), 71 (4), 65 (10), 53 (8), 45 (4). Anal. calc. for $C_{17}H_{18}O_8$ (350.33): C 58.29, H 5.18; found: C 58.20, H 5.13.

Diethyl Tetrahydro-2-(4-methoxyphenyl)-5-oxofuran-3,4-dicarboxylate (**5b**). According to the *G.P.*, with dianion **2** (2.0 mmol) in THF (10 ml) and the THF (5 ml) soln. of anisaldehyde (384 mg, 2.8 mmol). The crude product was purified by prep. TLC (SiO_2, 20% AcOEt/hexane; double runs): 79 : 4 : 14 : 3 mixture *t,c*/*c,c*/*t,t*/*c,t*-**5b** (545 mg, 81%). Pale yellow solid. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.37–7.24 (*m*, 2 arom. H of *c,t*, *c,c*, and *t,t*); 7.16 (*d*, $J = 8.7$, 2 arom. H of *t,c*); 6.93, 6.87 (each app. *d*, $J = 8.7$, 2 arom. H); 5.90 (*c,t*), 5.84 (*t,c*), 5.58 (*c,c*), 5.47 (*t,t*) (each *d*, $J = 9.3$, 7.8, 5.7, and 9.1, resp., OC*H*Ar); 4.30 (*q*, $J = 7.2$, OCH_2Me of *t,c*); 4.35–4.10 (*m*, 2 OCH_2Me of *c,t* and *t,t*, OCH_2Me of *c,c*); 4.20 (*t,c*), 4.06 (*t,t*), 3.99 (*c,t*) (each *d*, $J = 7.6$, 10.8, and 9.3, resp., COCHCO); 4.15 (*t,c*), 3.53 (*c,t*) (each app. *t*, $J = 7.7$ and 9.3, resp., C*H*CO_2Et); 3.95–3.69 (*m*, OCH_2Me of *t,c*, OCH_2Me, COC*H*CO and C*H*CO_2Et of *c,c*, C*H*CO_2Et of *t,t*, OMe of *c,t*, *c,c*, and *t,t*); 3.79 (*s*, OMe of *t,c*); 1.35 (*t,c*), 1.34 (*c,t* and *t,t*), 1.29 (*c,c*) (each *t*, $J = 7.2$, OCH_2*Me*); 1.24 (*c,t*), 1.22 (*t,t*), 0.95 (*t,c*), 0.92 (*c,c*) (each *t*, $J = 7.2$, 7.2, 7.2, and 7.6, resp., OCH_2*Me*).

The pale yellow solid of diastereoisomer mixture **5b** was recrystallized from AcOEt/hexane: pure *t,c*-**5b**. White solid. M.p. 82–83°. IR (nujol): 1801*s*, 1740*s*, 1693*w*, 1614*m*, 1581*w*, 1516*m*, 1454*m*, 1326*s*, 1304*m*, 1257*m*, 1241*m*, 1215*m*, 1181*m*, 1137*m*, 1015*m*, 968*m*, 847*m*, 806*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.18 (*d*, $J = 8.8$, 1 arom. H); 6.90 (*d*, $J = 8.8$, 1 arom. H); 5.87 (*d*, $J = 8.0$, OC*H*Ar); 4.33 (*q*, $J = 7.2$, OCH_2Me); 4.22 (*d*, $J = 7.2$, O_2CCHCO_2); 4.18 (app. *t*, $J = 7.8$, C*H*CO_2Et); 3.94–3.72 (*m*, OCH_2Me); 3.82 (*s*, ArOMe); 1.37 (*t*, $J = 7.2$, OCH_2*Me*); 0.98 (*t*, $J = 7.2$, OCH_2*Me*). ^{13}C NMR (75 MHz, $CDCl_3$): 170.0 (C=O); 168.3 (C=O); 166.3 (C=O); 160.1 (C); 127.3 (CH, 2 peaks merged); 126.6 (C) ; 113.9 (CH, 2 peaks merged); 80.0 (OCHAr); 62.7 (OCH_2); 61.5 (OCH_2), 55.2 (OMe); 49.8 (CH); 48.5 (CH); 13.6 (Me). EI-MS: 336 (29, M^+), 318 (2), 307 (1), 289 (8), 273 (1), 263 (9), 245 (5), 233 (2), 216 (10), 200 (40), 189 (17), 173 (22), 154 (32), 145 (18), 135 (81), 127 (100), 99 (93), 92 (7), 77 (22), 63 (6), 55 (13), 43 (6). Anal. calc. for $C_{17}H_{20}O_7$ (336.35): C 60.71, H 5.99; found: C 60.38, H 5.78.

Diethyl Tetrahydro-2-oxo-5-phenylfuran-3,4-dicarboxylate (**5c**). According to the *G.P.* with dianion **2** (2.0 mmol) in THF (10 ml) and a THF (2 ml) soln. of benzaldehyde (0.3 ml, 2.97 mmol). The crude product, a 71 : 6 : 19 : 4 mixture *t,c*/*c,c*/*t,t*/*c,t*-**5c**, was purified by radial chromatography (SiO_2, 8% AcOEt/hexane): 68 : 11 : 18 : 3 mixture *t,c*/*c,c*/*t,t*/*c,t*-**5c** (478 mg, 78%). Pale yellow liquid. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.48–7.24 (*m*, 5 arom. H); 5.97 (*c,t*), 5.91 (*t,c*), 5.65 (*c,c*) and 5.56 (*t,t*) (each *d*, $J = 8.9$, 7.0, 5.7, and 8.9, resp., OC*H*Ar); 4.33 (*q*, $J = 7.1$, OCH_2Me of *t,c*); 4.31–4.12 (*m*, COCHCO and C*H*CO_2Et of *t,c*, 2 OCH_2Me of *c,t* and *t,t*, and OCH_2Me of *c,c*); 4.09 (*t,t*), 4.02 (*c,t*), 3.95 (*c,c*) (each *d*, $J = 10.6$, 9.3, and 7.2, resp., COCHCO); 3.92–3.67 (*m*, OCH_2Me of *t,c*, OCH_2Me and C*H*CO_2Et of *c,c*, C*H*CO_2Et of *t,t*); 3.57 (*t*, C*H*CO_2Et of *c,t*); 1.37 (*t,c*), 1.35 (*c,t* and *t,t*), 1.32 (*c,c*) (each *t*, $J = 7.2$, 7.2, and 7.2, resp., OCH_2*Me*); 1.28 (*c,t*), 1.25 (*t,t*), 0.92 (*t,c*), and 0.87 (*c,c*) (each *t*, $J = 7.0$, 7.1, 7.2, and 7.2, resp., OCH_2*Me*).

Attempted separation of the diastereoisomers was made by prep. TLC (SiO_2, 20% AcOEt/hexane; double runs) to give two bands of **5c** (*Fr. 1* and *2*).

Fr. 1 (less polar) yielded *c,t*/*t,t*-**5c** (9 : 91) contaminated with a small amount of *t,c*-**5c**. IR (neat): 3067*m*, 3038*m*, 2985*m*, 2940*m*, 2909*m*, 1789*s*, 1738*s*, 1498*m*, 1458*m*, 1372*m*, 1354*m*, 1305*s*, 1256*s*, 1213*s*, 1199*s*, 1157*s*, 1020*s*, 976*m*, 918*m*, 857*m*, 760*m*, 701*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.46–7.35 (*m*, 5 arom. H); 5.96 (*c,t*), 5.54 (*t,t*) (each *d*, $J = 9.0$ and 8.8, resp., OC*H*Ar); 4.34–4.15 (*m*, 2 OCH_2Me); 4.07 (*t,t*), 4.00 (*c,t*) (each *d*, $J = 10.8$ and 9.4, resp., COCHCO); 3.87 (*dd*, $J = 10.4$, 8.9, C*H*CO_2Et of *t,t*); 3.55 (app. *t*, $J = 9.1$, C*H*CO_2Et of *c,t*); 1.33 (app. *t*, $J = 7.2$, OCH_2*Me*); 1.24 (app. *t*, $J = 7.2$, OCH_2*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$; major isomer *t,t*-**5c**): 169.2 (C=O); 169.1 (C=O); 166.2 (C=O); 136.8 (C); 129.2 (CH); 128.7 (CH); 126.1 (CH); 80.8 (OCH); 62.6 (OCH_2); 62.0 (OCH_2); 51.9 (CH); 50.6 (CH); 13.92 (Me); 13.89 (Me).

Fr. 2 (more polar) yielded a 95 : 5 mixture of the major *t,c*-**5c** contaminated with a small amount of *c,c*- and *t,t*-**5c**. Pale yellow liquid. IR (neat): 3066*w*, 3036*w*, 2985*m*, 2940*m*, 2907*m*, 1791*s*, 1733*s*, 1607*w*, 1498*m*, 1457*m*, 1400*m*, 1382*m*, 1372*m*, 1314*s*, 1214*s*, 1159*s*, 1097*m*, 1020*s*, 964*m*, 855*m*, 752*m*, 700*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.41–7.20 (*m*, 5 arom. H); 5.89 (*d*, $J = 7.6$, OC*H*Ar); 4.31 (*q*, $J = 7.1$, OCH_2Me); 4.20–4.13 (*m*, COCHCO, C*H*CO_2Et); 3.89–3.64 (*m*, OCH_2Me); 1.35 (*t*, $J = 7.2$, OCH_2*Me*); 0.90 (*t*, $J = 7.2$, OCH_2*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$; major isomer *t,c*-**5c**): 169.9 (C=O); 168.1 (C=O); 166.1 (C=O); 134.6 (C); 129.0 (CH); 128.3 (CH, 2 peaks merged); 125.7 (CH, 2 peaks merged); 80.0 (O*C*HAr); 62.6 (OCH_2); 61.4 (OCH_2); 49.7 (CH); 48.9 (CH); 13.8 (Me); 13.2 (Me). EI-MS: 306 (15, M^+), 278 (0.33), 260 (22), 243 (1), 232 (29), 215 (5), 203 (4),

186 (32), 173 (47), 159 (33), 145 (13), 127 (70), 115 (65), 105 (100), 99 (97), 91 (12), 82 (16), 77 (52), 63 (8), 51 (19), 45 (7). Anal. calc. for $C_{16}H_{18}O_6$ (306.32): C 62.74, H 5.92; found: C 62.56, H 5.90.

*Diethyl 2-(*tert*-Butyl)tetrahydro-5-oxofuran-3,4-dicarboxylate* (**5d**). According to the *G.P.*, with dianion **2** (2.0 mmol) in THF (10 ml) and a THF (2 ml) soln. of pivaldehyde (231 mg, 2.7 mmol). The crude product, a 80:20 mixture of two diastereoisomers, was purified by prep. TLC (SiO_2, 20% AcOEt/hexane; multiple runs): **5d** (305 mg, 53%) as a 79:21 mixture of two diastereoisomers. Colorless liquid. IR (neat): 2981*s*, 2910*m*, 2879*m*, 1792*s*, 1737*s*, 1482*m*, 1448*m*, 1407*m*, 1385*m*, 1371*s*, 1330*s*, 1275*s*, 1249*s*, 1196*s*, 1180*s*, 1159*s*, 1095*m*, 1029*s*, 1001*s*, 931*m*, 861*m*, 682*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.51 (app. *d*, $J = 7.2$, CHO of the major diastereoisomer); 4.34–4.06 (*m*, 2 OCH_2Me and C*H*O of the minor diastereoisomer); 3.97 (major), 3.76 (minor) (each *d*, $J = 6.0$ and 6.5, resp., COCHCO); 3.80 (app. *t*, $J = 6.6$, C*H*CO_2Et of the major diastereoisomer); 3.54 (*dd*, $J = 6.5$, 4.6, C*H*CO_2Et of the minor diastereoisomer); 1.35–1.23 (*m*, 2 OCH$_2$*Me*); 1.05 (minor), 1.02 (major) (each *s*, *t*Bu). ^{13}C-NMR (75 MHz, $CDCl_3$): 169.8 (C=O); 169.7 (C=O); 166.1 (C=O); 87.3 (OCH, major), 86.1 (OCH, minor); 62.5 (OCH$_2$, major), 61.8 (OCH$_2$, minor); 61.7 (OCH$_2$, major), 61.3 (OCH$_2$, minor); 50.7 (CH, major), 50.3 (CH, minor); 46.7 (CH, major), 46.4 (CH, minor); 34.7 (C, major), 33.3 (C, minor); 25.5 (Me); 13.9 (Me); 13.6 (Me, major), 13.5 (Me, minor). EI-MS: 287 (1.3, $[M+1]^+$), 271 (1), 253 (0.37), 241 (15), 230 (85), 213 (11), 201 (17), 195 (7), 183 (49), 173 (32), 157 (65), 137 (6), 127 (47), 111 (17), 99 (44), 84 (18), 71 (17), 57 (100), 41 (66). Anal. calc. for $C_{14}H_{22}O_6$ (286.33): C 58.73, H 7.75; found: C 58.68, H 8.05.

Diethyl Tetrahydro-2-oxo-5-pentylfuran-3,4-dicarboxylate (**5e**). According to the *G.P.*, with dianion **2** (5.0 mmol) in THF (25 ml) and a THF (5 ml) soln. of hexanal (0.76 ml, 6.2 mmol). The crude product, a 79:6:15:trace mixture *t,c*/*c,c*/*t,t*/*c,t*-**5e**, was purified by FC (SiO_2, 10% AcOEt/hexane): 82:6:11:trace mixture *t,c*/*c,c*/*t,t*/*c,t*-**5e** (826 mg, 55%). Colorless liquid. IR (neat): 2958*s*, 2936*s*, 2873*m*, 1790*s*, 1738*s*, 1468*m*, 1371*m*, 1305*s*, 1256*s*, 1177*s*, 1021*s*, 858*m*, 730*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.74–4.67 (*m*, CHO of *t,c*); 4.41 (*dt*, $J =$ 4.1, 8.4, CHO of *t,t*); 4.40–4.35 (*m*, CHO of *c,c*); 4.24–4.08 (*m*, 2 OCH_2Me); 3.89 (*t,t*); 3.88 (*t,c*), 3.67 (*c,c*) (each *d*, $J = 10.1$, 8.0, and 7.3, resp., COCHCO); 3.81 (app. *t*, $J = 8.0$, C*H*CO_2Et of *t,c*); 3.48–3.41 (*m*, C*H*CO_2Et of *c,c* and *t,t*); 1.84–1.14 (*m*, $(CH_2)_4$, 2 OCH$_2$*Me*); 0.82–0.77 (*m*, $(CH_2)_4$*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$, major isomer *t,c*-**5e**): 169.8 (C=O); 168.9 (C=O); 166.4 (C=O); 79.1 (OCH); 62.5 (OCH$_2$); 61.8 (OCH$_2$); 48.7 (CH); 47.7 (CH); 31.3 (CH_2); 31.2 (CH_2); 25.1 (CH_2); 22.3 (CH_2); 14.0 (Me); 13.9 (Me); 13.8 (Me). EI-MS: 301 (1.4, $[M+1]^+$), 300 (0.89, M^+), 285 (0.55), 273 (0.32), 254 (28), 237 (9), 227 (57), 218 (1.4), 209 (12), 201 (27), 183 (100), 173 (72), 169 (69), 155 (48), 145 (17), 137 (20), 127 (98), 109 (31), 99 (92), 81 (28), 71 (19), 67 (20), 55 (48), 43 (36), 32 (14). Anal. calc. for $C_{15}H_{24}O_6$ (300.36): C 59.99, H 8.05; found: C 59.96, H 7.99.

Attempted separation of the diastereoisomers was made by FC (SiO_2, 8% AcOEt/hexane) to provide *Fr. 1* and *2* of **5e**.

Fr. 1 (less polar) yielded a 5:29:3:63 mixture *c,t*/*t,c*/*c,c*/*t,t*-**5e** contaminated with a small amount of the starting material. Pale yellow liquid. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.94 (*c,t*), 4.52 (*t,t*) (each *dt*, $J = 3.2$, 9.0, and 4.1, 8.4, resp., CHO); 4.81 (*t,c*), 4.47 (*c,c*) (each *m*, CHO); 4.35–4.14 (*m*, 2 OCH_2Me); 4.00 (*t,c*), 3.99 (*t,t*), 3.86 (*c,t*), 3.75 (*c,c*) (each *d*, $J = 8.4$, 10.1, 8.0, and 7.3, resp., COCHCO); 3.93 (*t,c*), 3.23 (*c,t*) (each *t*, $J = 7.9$ and 9.2, C*H*CO_2Et); 3.56 (app. *dd*, $J = 10.2$, 8.6, C*H*CO_2Et of *c,c* and *t,t*); 2.00–1.20 (series of *m*, $(CH_2)_4$, 2 OCH$_2$*Me*); 0.90 (*m*, $(CH_2)_4$*Me*).

Fr. 2 (more polar) yielded the major diastereoisomer *t,c*-**5e** contaminated with a small amount of *c,c*- and *t,t*-**5e**. Colorless liquid. ^{1}H-NMR (400 Hz, $CDCl_3$): 4.81 (*m*, CHO); 4.29 (*q*, $J = 7.2$, OCH_2Me); 4.24 (*dq*, $J = 1.4$, 7.1, OCH_2Me); 3.99 (*d*, $J = 8.3$, COCHCO); 3.92 (*t*, $J = 7.9$, C*H*CO_2Et); 1.96–1.24 (series of *m*, $(CH_2)_4$, 2 OCH$_2$*Me*); 0.90 (*m*, $(CH_2)_4$*Me*).

Diethyl Tetrahydro-2-oxo-5-tridecylfuran-3,4-dicarboxylate (**5f**). According to the *G.P.*, with dianion **2** (2.0 mmol) in THF (10 ml) and a THF (2 ml) soln. of tetradecanal (571 mg, 2.7 mmol). The crude product, a 86:3:11:trace mixture *t,c*/*c,c*/*t,t*/*c,t*-**5f**, was purified by FC (SiO_2, 10% AcOEt/hexane): 87:3:10:trace mixture *t,c*/*c,c*/*t,t*/*c,t*-**5f** (513 mg, 62%). Colorless liquid. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.83–4.77 (*m*, CHO of *t,c*); 4.51 (*t,t*), 4.46 (*c,c*) (each *dt*, $J = 4.0$, 8.4, and 5.2, 8.7, resp., CHO); 4.34–4.18 (*m*, 2 OCH_2Me); 3.99 (app. *d*, $J = 8.0$, COCHCO of *t,c* and *t,t*); 3.92 (app. *t*, $J = 7.9$, C*H*CO_2Et of *t,c*); 3.76 (*d*, $J = 7.3$, COCHCO of *c,c*); 3.59–3.52 (*m*, C*H*CO_2Et of *c,c* and *t,t*), 1.95–1.18 (*m*, $(CH_2)_{12}$, 2 OCH$_2$*Me*); 0.89 (app. *t*, $J = 6.8$, $(CH_2)_{12}$*Me*).

Attempted separation of the diastereoisomers was performed by FC (SiO_2, 5% AcOEt/hexane) to provide *Fr. 1* and *2* of **5f**.

Fr. 1 (less polar) yielded a 92:8 mixture of *t,t*/*c,t*-**5f**. Colorless liquid. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.92 (*m*, CHO of *c,t*); 4.50 (*dt*, $J = 4.0$, 8.2, CHO of *t,t*); 4.30 (*q*, $J = 7.2$, OCH_2Me); 4.23 (*q*, $J = 7.2$, OCH_2Me); 3.98 (*t,t*),

3.84 (*c,t*) (each *d*, $J = 10.2$ and 9.5, resp., COCHCO); 3.54 (*dd*, $J = 10.2$, 8.7, C*H*CO_2Et of *t,t*); 3.22 (*t*, $J = 9.4$, C*H*CO_2Et of *c,t*); 1.94–1.20 (series of *m*, $(CH_2)_{12}$, 2 OCH_2*Me*); 0.88 (app. *t*, $J = 6.6$, $(CH_2)_{12}$*Me*).

Fr. 2 (more polar) yielded a colorless liquid of a mixture of the starting material and the desired *t,c*/(*c,c* + *t,t*)-**5f** as a 81:19 diastereoisomer mixture, which could not be separated by FC. However, the product could be separated from the starting material by distillation at 126°/0.5 Torr. The same diastereoisomer ratio *t,c*/(*c,c* + *t,t*)-**5f** was obtained as prior to the distillation. IR (neat): 2925*s*, 2854*s*, 1790*s*, 1738*s*, 1467*m*, 1371*m*, 1303*m*, 1258*m*, 1177*s*, 1097*m*. ^{1}H-NMR (400 MHz, $CDCl_3$; major isomer *t,c*-**5f**): 4.81 (*m*, CHO); 4.33–4.18 (*m*, 2 OCH_2Me); 3.98 (*d*, $J = 8.0$, COCHCO); 3.91 (*t*, $J = 7.8$, C*H*CO_2Et); 1.62–1.22 (*m*, $(CH_2)_{12}$, 2 OCH_2*Me*); 0.88 (*m*, $(CH_2)_{12}$*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$; the major isomer *t,c*-**5f**): 169.8 (C=O); 168.9 (C=O); 166.4 (C=O); 79.1 (OCH); 62.6 (OCH_2); 61.8 (OCH_2); 48.7 (CH); 47.8 (CH); 31.9 (CH_2); 31.4 (CH_2); 29.7 (CH_2); 29.6 (CH_2, 2 peaks merged); 29.5 (CH_2); 29.4 (CH_2); 29.3 (CH_2, 2 peaks merged); 29.1 (CH_2); 25.5 (CH_2); 22.7 (CH_2); 14.1 (Me, 2 peaks merged); 14.0 (Me). EI-MS: 412 (2, M^+), 367 (7), 339 (100), 311 (1), 293 (6), 281 (39), 247 (2), 229 (7), 218 (4), 201 (6), 183 (16), 173 (17), 155 (8), 145 (9), 127 (22), 109 (7), 99 (20), 95 (11), 81 (13), 69 (13), 55 (27), 43 (31), 32 (40). Anal. calc. for $C_{23}H_{40}O_6$ (412.58): C 66.96, H 9.77; found: C 66.93, H 10.04.

Diethyl Tetrahydro-2,2-dimethyl-5-oxofuran-3,4-dicarboxylate (**5g**). According to the *G.P.*, with dianion **2** (2.0 mmol) in THF (10 ml) and a soln. of 1.0M acetone in THF (3.0 ml, 3.0 mmol). The crude product was purified by prep. TLC (SiO_2, 30% AcOEt/hexane): **5g** (230 mg, 45%). Colorless liquid. IR (neat): 2985*s*, 2941*m*, 1784*s*, 1738*s*, 1467*m*, 1448*m*, 1378*s*, 1323*s*, 1292*s*, 1220*s*, 1183*s*, 1162*s*, 1115*s*, 1030*s*, 953*m*, 907*m*, 858*m*, 693*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.19–4.03 (*m*, 2 OCH_2Me); 4.03 (*d*, $J_{trans} = 11.6$, COCHCO); 3.58 (*d*, $J_{trans} = 11.6$, C*H*CO_2Et); 1.56 (*s*, MeC), 1.21 (*t*, $J = 7.4$, OCH_2*Me*), 1.19 (*s*, MeC), 1.18 (*t*, $J = 7.4$, OCH_2*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 168.5 (C=O); 168.2 (C=O); 166.3 (C=O); 82.9 (OC); 62.2 (OCH_2); 61.7 (OCH_2); 53.5 (CH); 49.0 (CH); 27.9 (CH); 23.2 (Me); 13.8 (Me); 13.78 (Me). EI-MS: 259 (11, $[M+1]^+$), 243 (17), 230 (0.6), 213 (17), 197 (54), 185 (9), 169 (18), 151 (8), 141 (100), 127 (30), 113 (34), 99 (23), 82 (4), 67 (8), 55 (5), 43 (13), 30 (1). Anal. calc. for $C_{12}H_{18}O_6$ (258.28): C 55.81, H 7.03; found: C 55.82, H 7.35.

Diethyl 2-Oxo-1-oxaspiro[4,5]decane-3,4-dicarboxylate (**5h**). According to the *G.P.*, with dianion **2** (2.0 mmol) in THF (10 ml) and a THF (2 ml) soln. of cyclohexanone (263 mg, 2.7 mmol). The crude product was purified by FC (SiO_2, 8% AcOEt/hexane): **5h** (344 mg, 58%). M.p. 47–48° (from Et_2O/hexane). White solid. IR (neat): 2983*m*, 2940*s*, 1784*s*, 1738*s*, 1465*m*, 1450*m*, 1376*s*, 1322*s*, 1299*s*, 1265*s*, 1219*s*, 1186*s*, 1125*s*, 1029*s*, 960*s*, 921*m*, 863*m*, 720*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.30–4.19 (*m*, 2 OCH_2Me); 4.18 (*d*, $J_{trans} = 11.5$, COCHCO); 3.59 (*d*, $J_{trans} = 11.5$, C*H*CO_2Et); 2.03–1.90, 1.80–1.58 (2 sets of *m*, $(CH_2)_5$); 1.34 (*t*, $J = 7.0$, OCH_2*Me*) 1.32 (*t*, $J = 7.2$, OCH_2*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 168.6 (C=O); 168.2 (C=O); 166.4 (C=O), 84.4 (O–C); 62.1 (OCH_2); 61.6 (OCH_2); 53.9 (CH); 48.7 (CH); 36.7 (CH_2); 32.1 (CH_2), 24.5 (CH_2); 22.2 (CH_2); 21.1 (CH_2); 13.9 (Me); 13.8 (Me). EI-MS: 298 (7, M^+), 252 (100), 234 (28), 224 (29), 206 (60), 181 (84), 167 (23), 161 (13), 151 (24), 135 (40), 127 (70), 107 (20), 99 (66), 91 (13), 79 (21), 69 (16), 55 (23), 41 (10). Anal. calc. for $C_{15}H_{22}O_6$ (298.34): C 60.39, H 7.43; found: C 60.18, H 7.72.

Diethyl Tetrahydro-5-oxo-2,2-diphenylfuran-3,4-dicarboxylate (**5i**). According to the *G.P.*, with dianion **2** (2.0 mmol) in THF (10 ml) and a THF (2 ml) soln. of benzophenone (457 mg, 2.5 mmol). The crude product was purified by prep. TLC (SiO_2, 8% AcOEt/hexane; double runs) to give a pale yellow viscous liquid of **5i** (307 mg, 41%) as a 86:14 *trans*/*cis* mixture, which was crystallized from AcOEt/hexane to afford a white solid (115 mg) as a 66:34 *trans*/*cis* mixture. M.p. 95–96°. IR (neat): 3060*m*, 3025*m*, 2955*s*, 1806*s*, 1747*s*, 1727*s*, 1599*w*, 1494*m*, 1448*s*, 1377*s*, 1349*m*, 1310*s*, 1250*s*, 1235*s*, 1219*s*, 1183*s*, 1165*s*, 1110*m*, 1083*m*, 1045*s*, 1026*s*, 988*s*, 966*m*, 928*w*, 917*w*, 905*w*, 892*m*, 848*w*, 823*w*, 755*s*, 726*m*, 697*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.68–7.64 (*trans*), 7.52–7.48 (*cis*) (each *m*, 2 arom. H); 7.39–7.05 (*m*, 8 arom. H); 4.65 (*trans*), 4.33 (*cis*) (each *d*, $J = 9.3$ and 6.6, resp., COCHCO); 4.26 (*trans*), 3.62 (*cis*) (each *d*, $J = 9.3$ and 6.6, resp., C*H*CO_2Et); 4.24–4.02 (*m*, OCH_2Me of *cis* isomer); 4.11 (*q*, $J =$ 7.3, OCH_2Me of *trans* isomer); 3.90–3.63 (*m*, OCH_2Me); 1.21 (*cis*), 1.17 (*trans*) (each *t*, $J = 7.0$ and 7.3, resp., OCH_2*Me*); 0.94 (*trans*), 0.80 (*cis*) (each *t*, $J = 7.0$ and 7.3, resp., OCH_2*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 168.9 (C=O, *trans*), 168.8 (C=O, *cis*); 168.0 (C=O, *trans*), 167.8 (C=O, *cis*); 165.8 (C=O, *trans*), 164.7 (C=O, *cis*); 141.0 (C, *trans*), 140.7 (C, *cis*); 139.4 (C, *trans*), 139.0 (C, *cis*); 129.0 (CH); 128.6 (CH); 128.4 (CH); 128.3 (CH); 128.1 (CH); 128.0 (CH); 127.9 (CH); 127.1 (CH); 125.9 (CH); 125.3 (CH); 125.1 (CH); 89.4 (OC, *trans*), 87.5 (OC, *cis*); 62.5 (OCH_2, *trans*), 62.0 (OCH_2, *cis*); 61.9 (OCH_2, *trans*), 61.2 (OCH_2, *cis*); 53.5 (CH, *trans*), 53.1 (CH, *cis*); 49.3 (CH, *trans*), 49.0 (CH, *cis*); 13.9 (Me, *cis*), 13.8 (Me, *trans*); 13.5 (Me, *trans*), 13.3 (Me, *cis*). EI-MS: 382 (2, M^+), 337 (3), 309 (0.8), 291 (2), 273 (0.7), 259 (3), 247 (2), 231 (2), 219 (2), 200 (100), 191 (16), 183 (40), 165 (6), 154 (36), 127 (65), 115 (3), 105 (37), 99 (37), 77 (17), 51 (4). Anal. calc. for $C_{22}H_{22}O_6$ (382.43): C 69.10, H 5.80; found: C 69.46, H 5.53.

Diethyl Tetrahydro-2-methyl-5-oxo-2-phenylfuran-3,4-dicarboxylate (**5j**). According to the *G.P.*, with dianion **2** (2.0 mmol) in THF (10 ml) and a THF (2 ml) soln. of acetophenone (0.3 ml, 2.56 mmol). The crude product was purified by prep. TLC (SiO_2, 10% AcOEt/hexane; multiple runs): **5j** (252 mg, 39%). Yellow liquid containing mainly one diastereoisomer (by ^{1}H- and ^{13}C-NMR (strong peaks due to *C*H and 2 other small signals, presumably arising from *C*H of the other 2 diastereoisomers)). IR (neat): 3063*w*, 2985*m*, 2940*m*, 2907*m*, 1789*s*, 1738*s*, 1604*w*, 1498*m*, 1466*m*, 1448*m*, 1380*m*, 1322*s*, 1284*s*, 1212*s*, 1176*s*, 1125*m*, 1028*s*, 907*m*, 859*m*, 793*m*, 754*m*, 700*s*. ^{1}H-NMR (300 MHz, $CDCl_3$; major isomer): 7.40–7.23 (*m*, 5 arom. H); 4.34–4.23 (*m*, OCH_2Me); 4.14 (*d*, $J = 11.0$, COCHCO); 3.94 (*d*, $J = 11.0$, $CHCO_2$Et); 4.01–3.82 (*m*, OCH_2Me); 2.07 (*s*, MeC); 1.33 (*t*, $J = 7.2$, 2 OCH_2Me). ^{13}C-NMR (75 MHz, $CDCl_3$; major isomer): 169.4 (C=O); 167.4 (C=O); 166.2 (C=O); 138.8 (C); 128.4 (CH); 128.3 (CH); 124.7 (CH); 85.5 (O–C); 62.4 (OCH_2); 61.6 (OCH_2); 55.8 (CH); 48.8 (CH); 27.9 (Me); 13.8 (Me); 13.6 (Me). EI-MS: 320 (5, M^+), 305 (5), 275 (3), 259 (33), 247 (1), 231 (12), 213 (7), 200 (100), 189 (3), 173 (2), 154 (26), 145 (3), 127 (84), 115 (8), 105 (37), 99 (41), 77 (15), 43 (5). Anal. calc. for $C_{17}H_{20}O_6$ (320.35): C 63.74, H 6.29; found: C 63.84, H 6.63.

Diethyl 2-Ethyltetrahydro-2-methyl-5-oxofuran-3,4-dicarboxylate (**5k**). According to the *G.P.*, with dianion **2** (2.0 mmol) in THF (10 ml) and a THF (2 ml) soln. of butan-2-one (0.23 ml, 2.7 mmol). The crude product, a 53:10:16:21 mixture of 4 diastereoisomers, was purified by FC (SiO_2, 8% AcOEt/hexane): colorless liquid of **5k** (202 mg, 37% yield) as a mixture of 4 diastereoisomers. The ratio of diastereoisomers was determined by integration of the $MeCH_2C$ signals, *i.e.*, 4 sets of *t* at δ 0.91 ($J = 7.4$), 0.99 ($J = 7.4$), 1.069 ($J = 7.3$), and 1.073 ($J = 7.3$). However, only the ^{1}H-NMR data of two isomers (*trans* at the 3,4-positions) could be assigned, whereas the remaining two isomers (*cis* at the 3,4-positions) could not clearly be identified. IR (neat; diastereoisomer mixture): 2983*s*, 2943*m*, 1784*s*, 1737*s*, 1466*m*, 1384*s*, 1311*s*, 1271*s*, 1223*s*, 1180*s*, 1118*s*, 1029*s*, 951*m*, 904*m*, 861*m*, 708*m*. ^{1}H-NMR (300 MHz, $CDCl_3$; 2 3,4-*trans* isomers): 4.34–4.17 (*m*, 2 OCH_2Me, and COCHCO of the minor isomer); 4.16 (*d*, $J = 11.7$, COCHCO of the major isomer); 3.78 (minor), 3.76 (major) (each *d*, $J = 11.1$ and 11.7, resp., $CHCO_2$Et); 2.02 (minor), 1.60 (major) (each *m*, CCH_2Me); 1.65 (*s*, MeC of the major isomer); 1.37–1.29 (*m*, 2 OCH_2Me and MeC of the minor isomer); 1.07 (minor), 0.99 (major) (each *t*, $J = 7.3$ and 7.4, resp., CCH_2Me). ^{13}C-NMR (75 MHz, $CDCl_3$; major isomer: 168.6 (C=O); 168.1 (C=O); 166.4 (C=O); 85.1(O–C); 62.1 (OCH_2); 61.5 (OCH_2); 53.9 (CH); 49.1 (CH); 29.0 (CH_2); 24.8 (Me); 13.7 (Me, two peaks merged); 7.3 (Me). EI-MS: 273 (0.92, $[M+1]^+$), 257 (3), 243 (50), 227 (8), 209 (8), 197 (100), 181 (9), 169 (29), 155 (33), 141 (16), 127 (30), 109 (12), 99 (18), 81 (7), 69 (3), 55 (4), 43 (9). Anal. calc. for $C_{13}H_{20}O_6$ (272.31): C 57.34, H 7.40; found: C 57.30, H 7.73.

When the colorless liquid of **5k** was left standing at r.t., it crystallized. Upon addition of hexane, a white solid of the major isomer was obtained as a single diastereoisomer. M.p. 49.5–51°. IR (nujol): 1781*s*, 1730*s*, 1384*s*, 1374*s*, 1312*s*, 1272*s*, 1221*s*, 1198*s*, 1180*s*, 1160*s*, 1118*s*, 1028*s*, 952*m*, 906*m*, 862*m*, 802*m*, 710*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.31 (*q*, $J = 7.1$, OCH_2Me); 4.24 (*m*, ABX_3, OCH_2Me); 4.17 (*d*, $J = 11.7$, COCHCO); 3.76 (*d*, $J = 11.7$, $CHCO_2$Et); 1.68, 1.55 (2 sets of *sext.*, ABX_3, CCH_2Me); 1.66 (*s*, MeC); 1.35 (*t*, $J = 7.1$, OCH_2Me); 1.32 (*t*, $J = 7.1$, OCH_2Me); 1.00 (*t*, $J = 7.4$, CCH_2Me).

3. *Preparation of* **17a**,**b**. *Diethyl Tetrahydro-3-methyl-2-oxo-5-pentylfuran-3,4-dicarboxylate* (**17a**). A THF (5 ml) soln. of a 70:27:3 mixture *t,c*/(*t,t* + *c,c*)/*c,t*-**5e** (1.50 g, 5.0 mmol) was added dropwise at 0° to a suspension of NaH (153 mg, 5.10 mmol; 80% dispersion in oil) in THF (10 ml). After stirring at 0° for 1 h, MeI (0.5 ml, 0.80 mmol) was added. The mixture was slowly warmed from 0° to r.t. overnight (15 h), then quenched with 0.5M HCl (0.5 ml), diluted with H_2O (50 ml), and extracted with AcOEt (3 × 30 ml). The combined extracts were washed with 5% $Na_2S_2O_5$ soln., H_2O, and brine, dried (Na_2SO_4), and evaporated. The crude product was purified by radial chromatography (SiO_2, 5% AcOEt/hexane) to give *Fr. 1* and *2* of **17a**.

Fr. 1 (less polar) yielded an inseparable 60:40 mixture *c,t*/*t,t*-**17a** (368 mg, 23%). Colorless liquid. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.85 (*dt*, $J = 9.1$, 3.2, CHO of *c,t*); 4.69 (*ddd*, $J = 9.7$, 8.5, 4.1, CHO of *t,t*); 4.30 (*q*, $J = 7.1$, OCH_2Me of *t,t*); 4.27–4.10 (*m*, 2 OCH_2Me of *c,t*, and OCH_2Me of *t,t*); 3.67 (*t,t*), 2.84 (*c,t*) (each *d*, $J = 9.7$ and 9.8, resp., $CHCO_2$Et); 1.96–1.24 (*m*, $(CH_2)_4$, 2 OCH_2Me); 1.65 (*c,t*), 1.44 (*t,t*) (each *s*, Me); 0.93–0.87 (*m*, $(CH_2)_4Me$).

Fr. 2 (more polar) yielded pure *c,c*-**17a** (1.0453 g, 67%). Colorless liquid. IR (neat): 2982*s*, 2957*s*, 2937*s*, 2873*m*, 1799*s*, 1743*s*, 1732*s*, 1464*m*, 1375*m*, 1348*m*, 1327*m*, 1296*s*, 1234*s*, 1203*s*, 1125*s*, 1097*s*, 1063*m*, 1018*s*, 949*m*, 858*m*, 773*m*, 731*m*, 693*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.63–4.55 (*m*, CHO); 4.27–4.13 (*m*, 2 OCH_2Me); 3.30 (*d*, $J = 6.8$, $CHCO_2$Et); 1.80–1.22 (*m*, $(CH_2)_4$, $(CH_2)_4Me$); 1.65 (*s*, MeC); 0.91–0.87 (*m*, $(CH_2)_4Me$). ^{13}C-NMR (75 MHz, $CDCl_3$): 172.3 (C=O); 169.1 (C=O); 168.8 (C=O); 77.0 (CH); 61.8 (OCH_2); 61.2 (OCH_2); 54.5 (CH); 53.0 (C); 31.3 (CH_2); 30.8 (CH_2); 25.5 (CH_2); 22.3 (CH_2); 21.5 (Me); 13.9 (Me); 13.8 (Me). EI-MS: 315 (20, $[M+1]^+$), 269 (27), 251 (1), 241 (10), 223 (9), 215 (4), 197 (45), 169 (100), 151 (19), 141 (36), 123 (29), 113

(45), 95 (19), 81 (11), 69 (8), 55 (8), 41 (10). Anal. calc. for $C_{16}H_{26}O_6$ (314.39): C 61.13, H 8.34; found: C 61.04, H 8.39.

Diethyl Tetrahydro-3-methyl-2-oxo-5-tridecylfuran-3,4-dicarboxylate (**17b**). As described for **17a**, with a THF (3 ml) soln. of a 66:34:trace mixture *t,c*/(*t,t* + *c,c*)/*c,t*-**5f** (1.24 g, 3.0 mmol), a THF (6 ml) suspension of NaH (80% dispersion in oil, 93 mg, 3.10 mmol), and MeI (0.32 ml, 5.10 mmol). The crude product, a 75:13:12 mixture of three diastereoisomers, was purified by radial chromatography (SiO_2, 5% AcOEt/hexane) to give *Fr. 1* and *2* of **17b**.

Fr. 1 (less polar) yielded an inseparable 51:49 mixture *c,t*/*t,t*-**17b** (353 mg, 25%). Colorless liquid. IR (neat): 2925*s*, 2854*s*, 1785*s*, 1741*s*, 1465*m*, 1380*m*, 1353*m*, 1300*m*, 1208*s*, 1106*m*, 1021*m*, 980*m*, 860*m*, 722*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.84 (*dt*, *J* = 3.3, 9.1, CHO of *c,t*); 4.69 (*ddd*, *J* = 9.5, 8.2, 4.2, CHO of *t,t*); 4.34–4.40 (*m*, 2 OCH_2Me); 3.67 (*t,t*), 2.86 (*c,t*) (each *d*, *J* = 9.9, C*H*CO_2Et); 1.95–1.20 (*m*, $(CH_2)_{12}$, 2 OCH$_2$*Me*); 1.64 (*c,t*), 1.44 (*t,t*) (each *s*, Me); 0.88 (app. *t*, *J* = 6.6, $(CH_2)_{12}$*Me*).

Fr. 2 (more polar) yielded pure *c,c*-**17b** (851 mg, 67%). White solid. M.p. 48–49° (from hexane). IR (nujol): 1788*s*, 1738*m*, 1721*s*, 1472*s*, 1326*m*, 1237*m*, 1210*s*, 1132*m*, 1121*m*, 1094*m*, 1030*m*, 1008*m*, 995*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.58 (*ddd*, *J* = 9.2, 6.6, 4.2, CHO); 4.25 (*q*, *J* = 7.1, OCH_2Me); 4.20 (*q*, *J* = 7.1, OCH_2Me); 3.30 (*d*, *J* = 6.6, C*H*CO_2Et); 1.80–1.24 (*m*, $(CH_2)_{12}$, 2 OCH$_2$*Me*); 1.66 (*s*, Me); 0.90 (app. *t*, *J* = 6.9, $(CH_2)_{12}$*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 172.4 (C=O); 169.2 (C=O); 169.0 (C=O); 77.1 (CH); 62.0 (OCH_2); 61.3 (OCH_2); 54.7 (CH); 53.1 (C); 31.9 (CH_2); 31.0 (CH_2); 29.7 (CH_2); 29.6 (CH_2); 29.6 (CH_2); 29.5 (CH_2); 29.4 (CH_2); 29.3 (CH_2); 29.2 (CH_2); 26.0 (CH_2); 22.7 (CH_2); 21.7 (Me); 14.1 (Me); 14.0 (Me); 13.9 (Me). EI-MS: 427 (2, [*M* + 1]$^+$), 381 (13), 353 (9), 336 (7), 309 (19), 281(100), 253 (2), 235 (8), 197 (4), 187 (17), 169 (7), 141 (24), 123 (6), 113 (31), 95 (12), 81 (10), 69 (10), 57 (14), 43 (23). Anal. calc. for $C_{24}H_{42}O_6$ (426.61): C 67.57, H 9.92; found: C 67.73, H 9.82.

4. *Preparation of* **18a**,**b**. *Diethyl Tetrahydro-2-oxo-5-pentyl-3-[(phenylsulfonyl)methyl]furan-3,4-dicarboxylate* (**18a**). A THF (8 ml) soln. of a 82:6:11:trace mixutre *t,c*/*c,c*/*t,t*/*c,t*-**5e** (2.61 g, 8.6 mmol), was added dropwise at 0° to a suspension of NaH (80% dispersion in oil; 264 mg, 8.78 mmol) in THF (18 ml). After stirring at 0° for 1 h, a THF (10 ml) soln. of chloromethyl phenyl sulfide (2.064 g, 13.0 mmol) was added, followed by the addition of a THF (10 ml) soln. of NaI (2.004 g, 13.0 mmol). The mixture was stirred and slowly warmed from 0° to r.t. overnight (15 h), then quenched with 0.5M HCl (5 ml), diluted with H_2O (50 ml), and extracted with AcOEt (3 × 50 ml). The combined extract was washed with 5% $Na_2S_2O_5$ soln., H_2O, and brine, dried (Na_2SO_4), and evaporated. The crude product was purified by FC (SiO_2, 5% AcOEt/hexane) to give *Fr. 1* and *2* of the corresponding sulfide.

Fr. 1 (less polar) yielded an inseparable 70:30 mixture of *c,t* and *t,t* sulfide (149 mg, 4%). Colorless liquid. IR (neat): 3060*w*, 2958*m*, 2934*m*, 2862*m*, 1783*s*, 1743*s*, 1583*m*, 1467*m*, 1440*m*, 1390*m*, 1370*m*, 1353*m*, 1300*m*, 1271*m*, 1231*s*, 1197*s*, 1115*m*, 1097*m*, 1025*s*, 944*m*, 859*m*, 745*m*, 692*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.47–7.39 (*m*, 2 arom. H); 7.34–7.21 (*m*, 3 arom. H); 4.98 (*t,t*), 4.88 (*c,t*) (each *dt*, *J* = 3.7, 8.6 and 3.2, 8.7, resp., CHO); 4.31–4.00 (*m*, 2 OCH_2Me); 3.88, 3.64 (each *d*, *AB*, *J* = 14.4, CH_2SPh of *c,t*); 3.84 (*t,t*), 3.61 (*c,t*) (each *d*, *J* = 9.0 and 9.3, resp., C*H*CO_2Et); 3.73, 3.69 (each *d*, *AB*, *J* = 13.6, CH_2SPh of *t,t*); 1.92, 1.71 (2 sets of *m*, CH_2); 1.62–1.18 (*m*, 2 OCH$_2$*Me*, $(CH_2)_3$); 0.93 (m, Me).

Fr. 2 (more polar) yielded pure *c,c* sulfide (3.36 g, 92 %). Pale yellow liwuid. IR (nujol): 3059*w*, 2957*m*, 2933*m*, 2872*m*, 1781*s*, 1739*s*, 1583*m*, 1469*m*, 1440*m*, 1370*m*, 1306*m*, 1191*s*, 1125*m*, 1096*m*, 1066*m*, 1017*s*, 946*m*, 860*m*, 746*m*, 692*m*. ^{1}H-NMR (400 Hz, $CDCl_3$): 7.43–7.39 (*m*, 2 arom. H); 7.32–7.20 (*m*, 3 arom. H); 4.59 (*ddd*, *J* = 9.8, 7.5, 4.1, CHO); 4.14 (*q*, *J* = 7.1, OCH_2Me); 4.07 (*m*, *ABX*$_3$, OCH_2Me); 3.86 (*d*, *J* = 7.5, C*H*CO_2Et); 3.68 (*d*, *J* = 14.1, 1 H, CH_2SPh); 3.50 (*d*, *J* = 14.1, 1 H, CH_2SPh); 1.79, 1.66 (2 sets of *m*, CH_2); 1.51, 1.37 (2 sets of *m*, CH_2); 1.29 (*m*, CH_2); 1.22 (*t*, *J* = 7.1, OCH$_2$*Me*); 1.21 (*t*, *J* = 7.1, OCH$_2$*Me*); 0.88 (app. *t*, *J* = 6.7, $(CH_2)_4$*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 170.7 (C=O); 168.5 (C=O); 166.9 (C=O); 134.4 (S–C); 130.8 (CH); 129.1 (CH); 127.4 (CH); 78.0 (CH); 62.3 (OCH_2); 61.2 (OCH_2); 58.5 (C); 49.9 (CH); 38.4 (CH_2); 31.2 (CH_2); 30.8 (CH_2); 25.5 (CH_2); 22.3 (CH_2); 13.9 (Me); 13.8 (Me); 13.6 (Me). EI-MS: 422 (37, M^+), 399 (1), 393 (0.25), 377 (3), 365 (0.27), 348 (4), 331 (5), 313 (0.53), 299 (66), 287 (1), 275 (9), 253 (24), 225 (8), 207 (5), 175(4), 158 (11), 147 (9), 135 (5), 123 (100), 109 (33), 99 (20), 77 (12), 65 (15), 55 (16), 43 (22). Anal. calc. for $C_{22}H_{30}O_6S$ (422.55): C 62.54, H 7.16; found: C 62.78, H 7.18.

The crude sulfide, obtained from the reaction of a 82:6:11:trace mixture *t,c*/*c,c*/*t,t*/*c,t*-**5e** (1.21 g, 4.0 mmol) with chloromethyl phenyl sulfide (1.01 g, 6.3 mmol) and NaI (900 mg, 6.0 mmol) under the conditions described above, was dissolved in AcOH (25 ml) and cooled to 0°. Aq. H_2O_2 (30% soln., 6.0 ml, 60 mmol) was added dropwise, then the mixture was stirred and slowly warmed from 0° to r.t. overnight (15 h). After usual workup, the crude product, mainly one diastereoisomer (by ^{1}H-NMR), was purified by radial chromatography (SiO_2,

8% AcOEt/hexane): **18a** (1.76 g, 97%) as a mixture of diastereoisomers containing mainly the *c,c* isomer and trace amounts of the other isomers. Colorless viscous liquid. IR (neat): 3066*m*, 2957*s*, 2934*s*, 2872*m*, 1784*s*, 1745*s*, 1585*m*, 1467*m*, 1448*m*, 1394*m*, 1371*m*, 1327*s*, 1311*s*, 1246*s*, 1196*s*, 1155*s*, 1085*s*, 1070*s*, 1017*s*, 949*m*, 861*m*, 804*m*, 750*m*, 723*m*, 690*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.92 (app. *d*, *J* = 7.3, 2 arom. H); 7.70 (app. *t*, *J* = 7.4, 1 arom. H); 7.60 (app. *t*, *J* = 7.6, 2 arom. H); 4.95 (*m*, CHO); 4.67 (*d*, *J* = 8.9, C*H*CO_2Et); 4.20 (m, 2 OC*H*$_2$CH$_3$); 3.93, 3.88 (each *d*, *AB*, *J* = 14.8, C*H*$_2$$SO_2$Ph); 1.93, 1.84 (2 sets of *m*, CH_2); 1.35 (*m*, $(CH_2)_2$); 1.30 (*t*, *J* = 7.1, OCH$_2$*Me*); 1.26 (*t*, *J* = 7.2, OCH$_2$*Me*); 0.91 (*m*, $(CH_2)_4$*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 171.2 (C=O); 168.5 (C=O); 166.7 (C=O); 140.6 (SO_2C), 135.0 (CH); 130.1 (CH); 130.0 (CH); 79.7 (OCH); 63.8 (OCH$_2$), 62.4 (OCH$_2$); 58.3 (CH$_2$$SO_2$Ph); 55.4 (C); 49.4 (CH); 32.0 (CH_2); 31.7 (CH_2); 26.5 (CH_2); 23.1 (CH_2); 14.64 (Me); 14.59 (Me); 14.31 (CH_2). EI-MS 455 (2, M^+), 437 (0.63), 409 (14), 381 (21), 363 (2), 337 (11), 317 (3), 281 (2), 269 (8), 253 (7), 239 (5), 223 (45), 195 (25), 169 (33), 141 (44), 125 (41), 111 (11), 95 (16), 77 (100), 67 (27), 51 (37), 43 (53).

Diethyl Tetrahydro-2-oxo-3-[(phenylsulfonyl)methyl]-5-tridecylfuran-3,4-dicarbocylate (**18b**). A THF (3 ml) soln. of a diastereoisomer mixture containing mainly *t,c*-**5f** and a small amount of the others isomers (825 mg, 2.0 mmol) was added dropwise at 0° to a suspension of NaH (80% dispersion in oil; 64 mg, 2.1 mmol) in THF (4 ml). After stirring at 0° for 1 h, a THF (6 ml) soln. of chloromethyl phenyl sulfide (478 mg, 3.0 mmol) was added, followed by the addition of NaI (450 mg, 3.0 mmol). The mixture was stirred and slowly warmed from 0° to r.t. overnight (15 h).

The crude product obtained from this reaction was dissolved in AcOH (12 ml) and cooled to 0°. Aq. H_2O_2 (30% soln.; 3.0 ml, 30 mmol) was added dropwise, then the mixture was stirred and slowly warmed from 0° to r.t. overnight (15 h). After usual workup, the crude product was purified by radial chromatography (SiO_2, 8% AcOEt/hexane) to give *Fr. 1* and *2* of **18b**.

Fr. 1 (less polar) yielded an inseparable 73 : 27 mixture *c,t*/*t,t*-**18b** (55 mg, 5%). Pale yellow liquid. IR (neat): 3066*w*, 2925*s*, 2854*s*, 1785*s*, 1746*s*, 1585*w*, 1466*m*, 1448*m*, 1393*m*, 1371*m*, 1356*m*, 1323*s*, 1311*s*, 1203*s*, 1161*s*, 1086*m*, 1023*m*, 947*m*, 838*m*, 857*m*, 783*m*, 746*m*, 723*m*, 689*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.96 (*c,t*), 7.89 (*t,t*) (each app. *dd*, *J* = 8.3, 1.3 and 8.2, 1.4, resp., 2 arom. H); 7.74 – 7.55 (*m*, 3 arom. H); 5.02 (*t,t*), 4.97 (*c,t*) (each *dt*, *J* = 3.7, 8.0 and 3.2, 8.9, resp., CHO); 4.35 – 3.97 (*m*, 2 OC*H*$_2$Me and C*H*CO_2Et of *c,t* and *t,t*; and C*H*$_2$$SO_2$Ph of *t,t*); 4.10, 3.91 (each *d*, *AB*, *J* = 14.7, C*H*$_2$$SO_2$Ph of *c,t*); 2.10 – 1.20 (*m*, $(CH_2)_{12}$, 2 OCH$_2$*Me*), 0.88 (app. *t*, *J* = 6.6, $(CH_2)_{12}$*Me*).

Fr. 2 (more polar) yielded pure *c,c*-**18b** (1.0013 g, 88%). White solid. M.p. 73 – 74° (AcOEt/hexane). IR (neat): 3064*w*, 3002*m*, 1779*s*, 1721*s*, 1587*w*, 1471*m*, 1447*m*, 1404*m*, 1376*m*, 1345*m*, 1324*s*, 1298*m*, 1259*s*, 1244*s*, 1230*s*, 1159*s*, 1120*m*, 1088*m*, 1071*m*, 1023*m*, 1008*m*, 963*m*, 867*m*, 855*m*, 803*m*, 748*m*, 725*m*, 687*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.95 (app. *dd*, *J* = 7.9, 1.2, 2 arom. H); 7.70 (*t*, *J* = 7.4, 1 arom. H); 7.60 (*t*, *J* = 7.7, 2 arom. H); 4.95 (*m*, CHO); 4.68 (*d*, *J* = 8.9, C*H*CO_2Et); 4.29 – 4.12 (*m*, 2 OC*H*$_2$Me); 3.94, 3.88 (each *d*, *AB*, *J* = 14.8, C*H*$_2$$SO_2$Ph); 1.95, 1.85 (2 sets of *m*, CH_2); 1.63, 1.46 (2 sets of *m*, CH_2); 1.28 (*m*, $(CH_2)_{10}$, 2 OCH$_2$*Me*); 0.89 (m, $(CH_2)_4$*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 170.5 (C=O); 167.9 (C=O); 166.1 (C=O); 139.9 (SO_2C(arom.)); 134.3 (CH); 129.4 (CH, 2 peaks merged); 127.8 (CH, 2 peaks merged); 79.1 (OCH); 63.1 (OCH$_2$); 61.7 (OCH$_2$); 57.7 (*C*H$_2$$SO_2$Ar); 54.7 (C); 48.8 ($CH_2$); 31.9 ($CH_2$); 31.1 ($CH_2$); 29.62 ($CH_2$); 29.59 ($CH_2$, 2 peaks merged); 29.47 (CH_2); 29.40 (CH_2); 29.29 (CH_2); 29.20 (CH_2); 26.1 (CH_2); 22.6 (CH_2); 14.1 (Me); 14.0 (Me); 13.6 (Me). EI-MS: 567 (4, $[M+1]^+$), 551 (0.61), 520 (23), 493 (82), 477 (6), 447 (7), 419 (6), 397 (2), 381 (31), 365 (2), 351 (7), 335 (56), 307 (19), 281 (100), 261 (10), 233 (11), 206 (19), 193 (5), 165 (98), 141 (35), 125 (49), 109 (16), 95 (26), 77 (84), 67 (35), 57 (50), 43 (91). Anal. calc. for $C_{30}H_{46}O_8S$ (566.77): C 63.58, H 8.18; found: C 63.59, H 8.39.

5. *Preparation of* **20a** *and* **12**. *Tetrahydro-5-oxo-2-pentyl-4-[(phenylsulfonyl)methyl]furan-3-carboxylic Acid* (**20a**). γ-Lactone *c,c*-**18a** (1.5001 g, 3.30 mmol) containing a small amount of the other isomers was refluxed in 48% HBr soln. (20 ml) for 3 h. The resulting mixture was diluted with H_2O (50 ml) and extracted with CH_2Cl_2 (3 × 30 ml). The combined org. layers was washed with sat. aq. $NaHCO_3$ soln. (3 × 30 ml). The basic soln. was acidified to pH 2 with 6M HCl and extracted with CH_2Cl_2 (3 × 30 ml). The combined org. phase was washed with H_2O and brine, dried (Na_2SO_4), and evaporated and the residue recrystallized from AcOEt/hexane: 32 : 64 : 4 mixture *t,c*/*c,c*/*t,t*-**20a** (562 mg, 48%). White solid. M.p. 155 – 157°. IR (nujol): 3282*m*, 3069*w*, 1771*s*, 1717*s*, 1589*w*, 1308*m*, 1283*m*, 1220*m*, 1188*m*, 1163*m*, 1151*m*, 1087*m*, 994*m*, 984*m*, 931*m*, 836*m*, 790*m*, 742*m*, 720*m*, 685*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.99 – 7.92 (*m*, 2 arom. H); 7.75 – 7.68 (*m*, 1 arom. H); 7.65 – 7.58 (*m*, 1 arom. H); 6.00 (br. *s*, CO_2H); 4.85 (*m*, CHO of *t,c*); 4.59 (app. *q*, *J* = 6.4, CHO of *c,c*); 4.50 (*dt*, *J* = 3.7, 8.8, CHO of *t,t*); 3.89 (*t*, *J* = 9.1, C*H*CO_2H of *t,c*); 3.79 (*dd*, *J* = 6.7, 5.4, C*H*CO_2H of *c,c*); 3.77 – 3.55 (*m*, 2 H, C*H*$CH_2$$SO_2$Ph and C*H*$_2$$SO_2$Ph of *t,c* and *t,t*; and C*H*$_2$$SO_2$Ph of *c,c*); 3.46 (*ddd*, *J* = 10.8, 6.8, 3.7, C*H*$CH_2$$SO_2$Ph of

c,c); 3.35–3.25 (*m*, 2 H, C*H*CO_2H and C$H_2$$SO_2$Ph of *t,t*); 3.30 (*dd*, *J* = 14.4, 10.1, 1 H, C$H_2$$SO_2$Ph of *t,c*); 1.77 (*q*, *J* = 7.5, CH_2 of *c,c*); 2.00–1.25 (*m*, $(CH_2)_4$ of *t,c* and *t,t,* and 3 CH_2 of *c,c*); 0.93–0.85 (*m*, $(CH_2)_4$*Me*). EI-MS: 355 (3, $[M+1]^+$), 337 (2), 290 (2), 265 (9), 245 (1), 237 (6), 213 (46), 195 (8), 177 (7), 162 (21), 148 (58), 125 (42), 113 (15), 94 (22), 85 (77), 77 (100), 67 (34), 55 (30), 41 (42). Anal. calc. for $C_{17}H_{22}O_6S$ (354.43): C 57.61, H 6.26; found: C 57.52, H 6.43.

(±)-Lichesterinic Acid (**12**). To an aq. soln. of LiOH·H_2O (263 mg, 6.0 mmol, 1.5 ml) was added a THF (15 ml) soln. of *c,c/t,t*-**18b** (779 mg, 1.40 mmol). The mixture was refluxed for 3 h and then stirred at r.t. overnight. The resulting mixture was diluted with H_2O (50 ml) and extracted with AcOEt (3 × 30 ml) to remove the unhydrolyzed ester. The aq. phase was then acidified to pH 2 with 6M HCl and extracted with AcOEt (3 × 30 ml). The combined org. layer was washed with H_2O and brine, dried (Na_2SO_4) and evaporated. The white solid, a mixture of **12** and an unidentified compound (310 mg), was recrystallized from AcOEt: (114 mg, 26%). White solid. M.p. 117.5–118.5° ([23] m.p. 114–115° (AcOH)). IR (nujol): 2740*m*, 2632*m*, 2533*m*, 1732*s*, 1704*s*, 1527*w*, 1422*m*, 1341*m*, 1325*m*, 1206*s*, 1153*m*, 1134*m*, 1044*m*, 963*m*, 936*m*, 890*m*, 760*m*, 714*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.14 (*m*, CHO); 2.90 (br. *s*, CO_2H); 2.26 (*d*, *J* = 2.1, MeC=C); 2.14, 1.61 (2 sets of *m*, CH_2); 1.48–1.22 (*m*, 11 CH_2); 0.90 (app. *t*, $(CH_2)_{12}$*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 172.7 (C=O); 166.3 (C=O); 146.8 (C); 139.8 (C); 81.4 (OCH); 32.7 (CH_2); 31.9 (CH_2); 29.65 (CH_2); 29.62 (CH_2, 2 peaks merged); 29.58 (CH_2); 29.50 (CH_2); 29.37 (CH_2); 29.33 (CH_2); 29.22 (CH_2); 24.8 (CH_2); 22.7 (CH_2); 14.1 (Me); 11.0 (Me). Anal. calc. for $C_{19}H_{32}O_4$ (324.47): C 70.34, H 9.94; found: C 70.29, H 9.61.

6. *(±)-Rocellaric Acid* (**15**) *and (±)-Dihydroprotolichesterinic Acid* (**16**). To a soln. of LiOH·H_2O (188 mg, 4.50 mmol) in H_2O (0.5 ml) was added a THF (4.5 ml) soln. of the pure *c,c*-**17b** (473 mg, 1.10 mmol). The mixture was stirred at r.t. overnight. After usual workup as described before, the crude product obtained (464 mg) was treated with 48% HBr soln. (6 ml) and refluxed for 5 h. The resulting mixture was diluted with H_2O (20 ml) and extracted with AcOEt (3 × 30 ml). The combined org. layers were washed with H_2O and brine, dried (Na_2SO_4), and evaporated. The solid was crystallized from AcOEt/hexane: 64:36 mixture **15**/**16** (289 mg, 80%). White solid. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.70 (*q*, *J* = 6.4, CHO of the minor isomer); 4.48 (*dt*, *J* = 8.7, 3.8, CHO of the major isomer); 3.16 (minor), 2.70 (major) (each *dd*, *J* = 9.2, 6.4 and 11.1, 9.4, resp., C*H*CO_2H); 3.08–2.92 (*m*, C*H*Me); 1.88–1.63 (*m*, CH_2); 1.60–1.20 (*m*, 11 CH_2); 1.37 (major), 1.30 (minor) (each *d*, *J* = 7.0 and 7.4, CH*Me*); 0.88 (app. *t*, *J* = 6.6, $(CH_2)_{12}$*Me*).

Base-Catalyzed Isomerization of **16** *to* **15**. A soln. of 1.56M BuLi in hexane (1.5 ml, 2.34 mmol) was added dropwise to a soln. of ^{i}Pr_2NH (0.36 ml, 2.5 mmol) in THF (4 ml) at 0° under Ar. After stirring at 0° for 30 min, a THF (1.5 ml) soln. of a 64:36 mixture **15**/**16** (305 mg, 0.94 mmol) was added dropwise. The mixture was stirred at 0° for 1 h and then quenched with AcOH. The mixture was allowed to reach r.t. and acidified to pH 2 with 1M HCl. Usual workup gave a brownish crystalline 89:11 mixture **15**/**16**. Fractional crystallization from AcOEt afforded pure **15** (219 mg, 72%). Colorless crystals. M.p. 98–99° [24]. IR (nujol): 1747*s*, 1715*s*, 1471*s*, 1455*s*, 1434*m*, 1398*m*, 1361*m*, 1314*m*, 1256*m*, 1222*m*, 1206*m*, 1172*m*, 1146*m*, 1126*m*, 1103*m*, 1015*m*, 973*m*, 944*m*, 894*m*, 718*m*, 698*m*, 671*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.85 (br., CO_2H); 4.49 (*ddd*, *J* = 9.1, 8.6, 4.0, CHO), 2.99 (*dq*, *J* = 11.4, 7.1, C*H*Me); 2.71 (*dd*, *J* = 11.1, 9.5, C*H*CO_2H); 1.77 (*m*, CH_2); 1.60–1.21 (*m*, 11 CH_2); 1.37 (*d*, *J* = 7.2, CH*Me*); 0.88 (app. *t*, *J* = 6.6, $(CH_2)_{12}$*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 176.7 (C=O); 176.1 (C=O); 79.4 (OCH); 53.9 (CH); 39.8 (CH); 34.9 (CH_2); 31.9 (CH_2); 29.7 (CH_2); 29.6 (CH_2); 29.57 (CH_2); 29.47 (CH_2); 29.36 (CH_2); 29.32 (CH_2); 29.20 (CH_2); 25.3 (CH_2); 22.7 (CH_2); 14.5 (Me); 14.1 (Me). EI-MS: 326 (5, M^+), 308 (3), 290 (1), 281 (20), 263 (3), 253 (23), 235 (11), 207 (3), 194 (2), 168 (3), 154 (10), 143 (10), 132 (17), 123 (8), 114 (18), 97 (28), 87 (23), 81 (20), 69 (44), 55 (51), 41 (100), 32 (5). Anal. calc. for $C_{19}H_{34}O_4$ (336.57): C 69.90, H 10.50; found: C 70.09, H 10.42.

Compound **16** could not be separated from the residue in pure form.

Methyl Esters of (±)-Rocellaric Acid (**15**) *and (±)-Dihydroprotolichesterinic Acid* (**16**). To a soln. of a 64:36 mixture **15**/**16** (258 mg, 0.79 mmol) in dry MeOH (3 ml) was added a soln. of dicyclohexylcarbodiimide (DCC; 260 mg, 1.26 mmol) in dry MeOH (1 ml). The mixture was stirred at r.t. overnight. The precipitates were then filtered off. After evaporation, the crude product, a 80:20 mixture of methyl esters of **15** and **16**, was purified by radial chromatography (SiO_2, 2% AcOEt/hexane) to give *Fr. 1* and *2* of methyl esters of **15** and **16**.

Fr. 1 (less polar) yielded the methyl ester of **15** (180 mg, 67%). White solid. M.p. 40–41° (hexane) [23]. IR (nujol): 1783*s*, 1743*s*, 1435*m*, 1320*m*, 1281*m*, 1265*m*, 1252*m*, 1203*m*, 1171*m*, 1105*m*, 1122*m*, 1065*m*, 998*m*, 980*m*, 968*m*, 937*m*, 724*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.45 (app. *dt*, *J* = 4.1, 8.5, CHO); 3.78 (*s*, CO_2Me); 2.96 (*dq*, *J* = 11.5, 7.2, C*H*Me); 2.66 (*dd*, *J* = 11.1, 9.5, C*H*CO_2Me); 1.73 (*m*, CH_2); 1.58–1.20 (*m*, 11 CH_2); 1.32 (*d*, *J* = 7.2, C*H*Me); 0.88 (app. *t*, *J* = 6.6, $(CH_2)_{12}$*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 176.7(C=O); 171.1 (C=O); 79.5 (OCH); 54.1 (CH); 52.5 (OMe); 39.8 (CH); 34.8 (CH_2); 31.8 (CH_2); 29.60 (CH_2); 29.57 (CH_2, 2 peaks merged);

29.53 (CH_2); 29.42 (CH_2); 29.38 (CH_2); 29.36 (CH_2); 29.32 (CH_2); 29.28 (CH_2); 29.21 (CH_2); 29.15 (CH_2); 25.2 (CH_2); 22.6 (CH_2); 14.4 (Me); 14.0 (Me). EI-MS: 340 (6, M^+), 322 (4), 308 (8), 294 (14), 281 (60), 267 (80), 253 (4), 235 (15), 207 (9), 182 (6), 168 (15), 154 (44), 146 (40), 129 (82), 109 (28), 101 (77), 81 (30), 69 (100), 55 (53), 41 (89).

Fr. 2 (more polar) yielded the methyl ester of **16** (22 mg, 8%) [24]. White solid. M.p. 50.0–50.5° (hexane). IR (nujol): 1770*s*, 1724*s*, 1464*s*, 1345*m*, 1220*m*, 1205*m*, 1181*s*, 1126*m*, 1092*m*, 1071*m*, 1016*m*, 986*m*, 964*m*, 917*m*, 802*m*, 720*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.70 (*q*, $J = 6.4$, CHO); 3.75 (*s*, CO_2Me); 3.11 (*dd*, $J = 9.4$, 7.4, C*H*CO_2Me); 2.97 (*dq*, $J = 9.4$, 7.4, C*H*Me); 1.70–1.62 (*m*, CH_2); 1.57–1.20 (*m*, 11 CH_2); 1.22 (*d*, $J = 7.6$, CH*Me*); 0.88 (app. *t*, $J = 6.7$, $(CH_2)_{12}$*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 177.3 (C=O); 170.5 (C=O); 79.4 (OCH); 52.1 (CH); 50.0 (Me); 37.1(CH_2); 34.7 (CH_2); 31.9 (CH_2); 29.62 (CH_2); 29.59 (CH_2, 2 peaks merged); 29.55 (CH_2); 29.44 (CH_2); 29.35 (CH_2); 29.30 (CH_2); 29.17 (CH_2); 25.3 (CH_2); 22.6 (CH_2); 14.1 (Me); 11.9 (Me).

7. *(±)-Nephromopsinic Acid* (**14**). Pure *c,c*-**17b** (400 mg, 0.94 mmol) was refluxed in 48% HBr soln. (10 ml) for 5 h. The resulting mixture was diluted with H_2O (50 ml) and extracted with AcOEt (3 × 30 ml). The combined org. layer was washed with H_2O and brine, dried (Na_2SO_4), and evaporated. The residue was crystallized from AcOEt/hexane: 62:38 mixture **23**/**14** (265 mg, 87%). White solid. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.72 (*m*, CHO of the minor isomer); 4.46 (*dt*, $J = 5.1$, 8.7, CHO of the major isomer); 3.35 (major), 3.24 (minor) (each *dd*, $J = 7.4$, 5.2 and 9.8, 8.3, resp., C*H*CO_2H); 3.06 (*dq*, $J = 9.8$, 7.1, C*H*Me of the minor isomer); 2.96 (*m*, C*H*Me of the major isomer); 1.92–1.24 (series of *m*, 12 CH_2 of both isomers, and CH*Me* of the minor isomer); 1.34 (*d*, $J = 7.1$, CH*Me* of the major isomer); 0.90 (app. *t*, $J = 6.8$, 3 H, $(CH_2)_{12}$*Me*).

Methyl Ester of (±)-Nephromopsinic Acid (**14**). To a soln. of the 38:62 mixture **14**/**23** (258 mg, 0.79 mmol) in dry MeOH (4 ml) and dry CH_2Cl_2 (0.5 ml) was added a soln. of DCC (280 mg, 1.35 mmol) in dry MeOH (1 ml). After stirring at r.t. overnight, the precipitates were filtered off and washed with AcOEt. The filtrate was evaporated, and the crude product purified by FC (SiO_2, 5% AcOEt/hexane): methyl ester of (±)-rocellaric acid (**15**; 46 mg, 15%; the formation of (±)-rocellaric acid methyl ester may be due to the equilibration at C(α) and C(β) of the initiallly formed methyl ester of **23**) and methyl ester of **14** (85 mg, 28%). White solid. M.p. 62–62.5° (AcOEt/hexane) [19e]. IR (nujol): 1781*s*, 1734*s*, 1429*m*, 1385*m*, 1338*m*, 1249*m*, 1205*s*, 1168*m*, 1133*m*, 1094*m*, 1076*m*, 1005*s*, 982*m*, 930*m*, 739*m*, 723*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.65 (*m*, CHO); 3.77 (*s*, CO_2Me); 3.18 (*dd*, $J = 9.8$, 8.3, C*H*CO_2Me); 3.05 (*dq*, $J = 10.0$, 7.0, C*H*Me); 1.60–1.22 (*m*, $(CH_2)_{12}$*Me*); 1.29 (*d*, $J = 7.1$, CH*Me*); 0.88 (app. *t*, $J = 6.6$, $(CH_2)_{12}$*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 177.5 (C=O); 170.1 (C=O); 77.5 (OCH); 52.3 (CH); 51.7 (Me); 36.3 (CH); 31.9 (CH_2); 31.2 (CH_2); 29.63 (CH_2); 29.60 (CH_2, 2 peaks merged); 29.57 (CH_2); 29.55 (CH_2); 29.45 (CH_2); 29.37 (CH_2); 29.31 (CH_2); 29.16 (CH_2); 25.6 (CH_2); 22.6 (CH_2); 14.4 (Me); 14.1 (Me).

8. *(±)-Phaseolinic Acid* (**13**). Pure *c,c*-**17a** (746 mg, 2.37 mmol) was refluxed in 48% HBr soln. (12 ml) for 5 h. The resulting mixture was diluted with H_2O (30 ml) and extracted with AcOEt (3 × 30 ml). The combined org. layer was washed with H_2O and brine, dried (Na_2SO_4), and evaporated. The solid was recrystallized from AcOEt/hexane: 38:62 mixture **13**/**22** (450 mg, 89%). ^{1}H-NMR (300 MHz, $CDCl_3$): 4.70 (*m*, CHO of the minor isomer); 4.44 (*dt*, $J = 8.4$, 5.1, CHO of the major isomer); 3.50 (br., COOH); 3.33 (major), 3.22 (minor) (each *dd*, $J = 7.3$, 5.2 and 9.6, 8.3, resp., C*H*CO_2H); 3.03 (*dq*, $J = 9.9$, 7.1, C*H*Me of the minor isomer); 2.94 (*quint.*, $J = 7.2$, C*H*Me of the major isomer); 1.92–1.25 (*m*, $(CH_2)_4$, and CH*Me*); 0.89 (*m*, $(CH_2)_4$*Me*).

Methyl Ester of (±)-Phaseolinic Acid (**13**). To a soln. of a 38:62 mixture **13**/**22** (405 mg, 1.90 mmol) in dry MeOH (4 ml) was added a soln. of DCC (613 mg, 3.0 mmol) in dry MeOH (2 ml). After stirring at r.t. overnight, the precipitate was filtered off and washed with AcOEt. The filtrate was evaporated to give the crude product, which was purified by radial chromatography (SiO_2, 2% AcOEt/hexane): methyl ester of **13** (178 mg, 41%) as a colorless liquid and methyl ester of **22** (110 mg, 26% yield) as a colorless liquid. Methyl ester of **13** (less polar) [25]: IR (neat): 2956*s*, 2936*s*, 2861*m*, 1781*s*, 1740*s*, 1457*m*, 1438*m*, 1381*m*, 1340*m*, 1248*m*, 1205*s*, 1182*s*, 1133*m*, 1114*m*, 1075*m*, 1051*m*, 1004*s*, 929*m*, 738*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.66 (*ddd*, $J = 9.9$, 8.2, 3.3, CHO); 3.78 (*s*, CO_2*Me*); 3.19 (*dd*, $J = 10.0$, 8.2, C*H*CO_2Me); 3.06 (*dq*, $J = 10.0$, 7.1, C*H*Me); 1.60–1.48 (*m*, CH_2); 1.46–1.24 (*m*, 3 CH_2); 1.30 (*d*, $J = 7.1$, CH*Me*); 0.90 (app. *t*, $J = 6.8$, $(CH_2)_4$*Me*). ^{13}C-NMR (75 MHz, $CDCl_3$): 177.5 (C=O); 170.1 (C=O); 77.5 (OCH); 52.2 (OMe); 51.6 (CH); 36.3 (CH); 31.3 (CH_2); 31.1 (CH_2); 25.2 (CH_2); 22.3 (CH_2); 14.3 (Me); 13.8 (Me). EI-MS: 229 (0.92, $[M+1]^+$), 308 (3), 210 (0.86), 197 (4), 182 (5), 169 (12), 157 (34), 141 (4), 129 (77), 113 (13), 97 (39), 88 (10), 81 (10), 69 (100), 59 (35), 55 (31), 41 (52), 32 (5). Anal. calc. for $C_{12}H_{20}O_4$ (228.30): C 63.14, H 8.83; found: C 63.01, H 8.92.

Methyl ester of **22** (more polar): IR (neat): 2955*s*, 2862*m*, 1781*s*, 1738*s*, 1463*m*, 1439*m*, 1397*m*, 1380*m*, 1343*m*, 1271*m*, 1199*s*, 1177*s*, 1128*m*, 1099*m*, 1038*m*, 1016*m*, 995*m*, 931*m*, 879*m*, 797*m*, 772*m*, 729*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.40 (*m*, CHO); 3.70 (*s*, CO_2Me); 3.31 (*dd*, $J = 7.5, 5.3$, $CHCO_2Me$); 2.90 (*m*, $CHMe$); 1.75–1.22 (series of *m*, $(CH_2)_4Me$); 1.19 (*d*, $J = 7.2$, $CHMe$); 0.85 (*m*, $(CH_2)_4Me$). ^{13}C-NMR (75 MHz, $CDCl_3$): 177.0 (C=O); 170.0 (C=O); 78.8 (OCH); 51.4 (OMe); 50.3 (CH); 38.8 (CH); 31.2 (CH_2); 30.6 (CH_2); 25.3 (CH_2); 22.2 (CH_2); 13.7 (Me); 10.1 (Me). EI-MS: 229 (9, $[M+1]^+$), 211 (2), 197 (8), 184 (5), 169 (51), 157 (14), 141 (12), 129 (29), 113 (29), 101 (46), 97 (22), 85 (16), 81 (28), 69 (100), 59 (47), 55 (40), 41 (63).

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