Highly Enantiospecific Synthesis of 4-Alkyl and 4,5-Dialkyl Substituted 4,5-Dihydrofuran-2(3*H*)-ones from Optically Active (*E*)- and (*Z*)-Alk-1-enyl *p*-Tolyl Sulphoxides: Application to the Synthesis of Lignan Lactones

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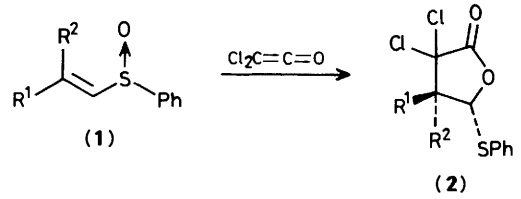
Stereochemically and optically pure 2-substituted ethylenic *p*-tolyl sulphoxides (*R*)-*E*-(**4**) and (*R*)-*Z*-(**4**) undergo readily and stereospecifically an additive Pummerer rearrangement reaction with dichloroketene to give *trans*- and *cis*-β-alkyl-α,α-dichloro-γ-*p*-tolylthio-γ-butyrolactone derivatives (**5**), respectively. Sequential reductive dechlorination and desulphurization lead to (−)-(*S*)-, from *trans*-(**5**), and (+)-(*R*)-β-alkyl-γ-butyrolactones [4-alkyl-4,5-dihydrofuran-2(3*H*)-ones] (**7**), from *cis*-(**5**), with a high optical purity, respectively. Reaction of the intermediate tolylthio derivatives (**6**) with allyltributylstannane gives β-alkyl-γ-allyl-γ-butyrolactones (**15**) and (**16**). These sequential reactions can be successfully applied to the synthesis of (+)-(*R*)-β-piperonylbutyrolactone (**20**), the key intermediate for the synthesis of antileukemic lignan lactones, in high chemical and optical yields. Acylation of compound (**20**) with 3,4,5-trimethoxybenzoyl chloride furnishes (+)-podorhizon (**21**).

Several years ago, Marino and Neisser[1] reported a stereospecific cyclisation (formally regarded as an additive Pummerer rearrangement)[2] of alkenyl sulphoxides (**1**) with dichloroketene to give β-substituted α,α-dichloro-γ-phenylthio-γ-butyrolactones (2) (Scheme 1). Recent publications by



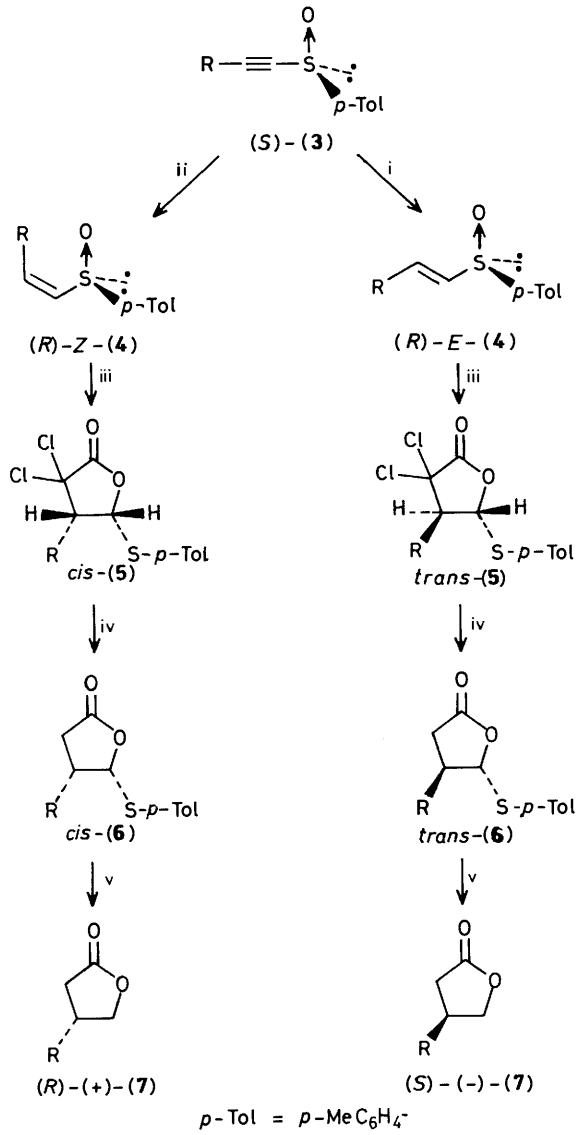
Scheme 1.

Marino and co-workers[3,4] and Posner and co-workers,[5] concerning the enantiospecificity of this lactonisation of chiral alkenyl sulphoxides, prompt us to report similar results obtained simultaneously and independently in our laboratory.[6] Marino and Posner, employed only (3*R*,*E*)-3-tolylsulphinyl-hept-2-ene (trisubstituted) as an acyclic sulphoxide for the reaction;[4] other sulphoxides were cyclo-olefinic.[3,5] We applied the reaction to enantiomerically and stereochemically pure 2-substituted (*E*)- and (*Z*)-ethylenic *p*-tolyl (*R*)-sulphoxides (**4**) (disubstituted), which were now readily available by stereoselective reduction of chiral acetylenic sulphoxides (**3**)[7] (Scheme 2).

This lactonization has usually been carried out in refluxing ether.[1,3–5] In the case of our compounds (**4**), however, the reaction in refluxing ether did not proceed cleanly, giving the desired lactones only in very low yields along with several by-products. We found that the highest yields of lactones were obtained when tetrahydrofuran (THF) was used as a solvent; the reaction proceeded even at low temperature. Thus, (*E*)-alkenyl sulphoxides (*R*)-*E*-(**4**) were treated with an excess of trichloroacetyl chloride and activated zinc in THF at −40 to −50 °C for 10 min to produce the desired *trans*-lactones *trans*-(**5**) in good yields (Scheme 2 and Table 1). The prolonged reaction time caused partial monodechlorination. In the case of the *Z*-isomers (*R*)-*Z*-(**4**), it was found that the yields of the products, *cis*-lactones *cis*-(**5**), were usually lower than the case of the *E*-isomers and very sensitive to reaction temperature. The reaction at −50 °C, suitable for the *E*-isomers, led to lower yields of the lactones and the run at −20 °C resulted in the formation of considerable amounts of the alkenyl sulphides and the additive Pummerer rearrangement product arising from the reaction with trichloroacetyl chloride itself. The most suitable temperature range was between −25 and −30 °C. A summary of these results is given in Table 2.

The relative stereochemistry shown in structures *trans*- and *cis*-(**5**) (Scheme 2) was established on the basis of their ^{1}H n.m.r. spectroscopic properties. In the lactones (**5**) derived from the *E*-isomers (*R*)-*E*-(**4**), the signals of H_β and H_γ appear at higher field, around δ 2.60 (H_β) and 5.23 (H_γ) (due to the shielding effects of the adjacent *cis* substituents), than those of the lactones (**5**) derived from the *Z*-isomers (*R*)-*Z*-(**4**)[8] which occur at δ 3.25 (H_β) and 5.78 (H_γ). Hence, the relative configuration of the alkyl and tolylthio groups in the former lactones is *trans* and in the latter *cis*. These results are consistent with those obtained previously.[1,3,4] Absolute configurations of the lactones (**5**) were confirmed by their conversion into (−)-(*S*)- and (+)-(*R*)-β-alkylbutyrolactones (**7**), respectively, as described below.

Transformation of the lactones (**5**) into the optically active β-alkylbutyrolactones (**7**), which are known to be useful chiral synthons in organic synthesis,[9] was achieved through two-step reductions. Thus, reductive dechlorination of the *trans*-lactones *trans*-(**5**) with activated zinc in acetic acid followed by reductive desulphurization of the resulting dechlorinated lactones *trans*-(**6**) with tributyltin hydride gave quantitatively the laevorotatory β-alkylbutyrolactones (−)-(*S*)-(**7**) (Table 1). In a similar manner, *cis*-(**5**) furnished the dextrorotatory enantiomers (+)-(*R*)-(**7**) with specific rotation values of almost equal magnitude to (−)-(**7**) (Table 2). One-step reductive dechlorination and desulphurization with Raney Ni resulted in lower yields (50—60%) without recovery of starting material. Among these optically active β-alkylbutyrolactones, one compound (+)-(*R*)-(**7a**) is known and reported to have the specific rotation value of $[\alpha]_D$ +6.7° (*c* 3.9 EtOH) [>90% enantiomer excess (e.e.)],[10] and hence, the absolute configuration in the laevorotatory lactones (**7**) would be *S* and in the dextrorotatory ones *R*, respectively. These results establish the absolute stereochemistries of the precursors *trans*- and *cis*-(**5**) and (**6**) as shown in Scheme 2. The optical purities of all compounds (*S*)- and (*R*)-(**7**)

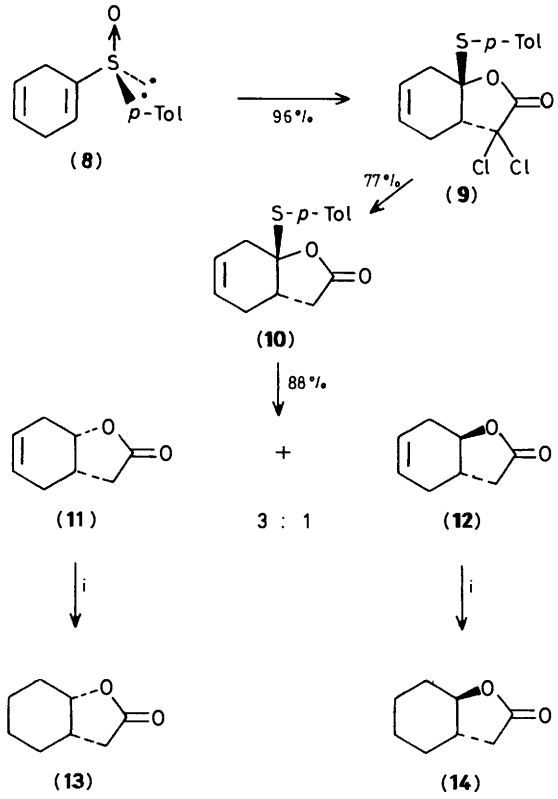


a: R = Pr
b: R = Bu
c: R = Pentyl
d: R = Hexyl

Scheme 2. *Reagents and conditions:* i, LAH, THF;[6] ii, H_2, $RhCl(Ph_3)_3$, benzene;[6] iii, Cl_3CCOCl, Zn, THF, −45 to −50 °C for (*R*)-*E*-(**4**) and −20 to −35 °C for (*R*)-*Z*-(**4**); iv, Zn–AcOH, room temp.; v, Bu_3SnH, AIBN, toluene, 90 °C

were determined by high-pressure liquid chromatographic analysis (h.p.l.c.) of the hydroxy amide derivatives, prepared by the reaction with (+)-(*R*)-phenylethylamine (Helmchen's method),[11] and high e.e. values were observed as shown in Tables 1 and 2. Thus, the reaction of alkenyl sulphoxides (**4**) with dichloroketene proceeded in a highly enantiospecific manner.

We also examined the reaction using the cyclohexadienyl sulphoxide (**8**) which was easily accessible from the cycloaddition of ethynyl *p*-tolyl (*R*)-sulphoxide[7] with butadiene. The reaction of compound (**8**) with dichloroketene under the same conditions as above also proceeded smoothly and selectively to give a single adduct (**9**), which was transformed into the dechlorinated lactone (**10**) in good yield (Scheme 3).



Scheme 3. *Reagent:* i, H_2, Pd, C, AcOEt

It was found that, in this case, the subsequent reductive desulphurization did not proceed stereoselectivity, giving rise to the *cis*- and *trans*-lactones (**11**) and (**12**) in a ratio of *ca.* 3:1. The absolute stereochemistry (shown in Scheme 3) and optical purity (100%) of these lactones (**11**) and (**12**) were confirmed by conversion into the known optically active saturated *cis*- and *trans*-lactones (**13**)[12,13] and (**14**),[12] respectively.

We then extended our study to conversion of β-alkyl-γ-

Table 1. (*S*)-4-Alkyl-4,5-dihydrofuran-2(3*H*)-ones (*S*)-(**7**) from (*E*)-alkenyl *p*-tolyl sulphoxides (*R*)-*E*-(**4**)

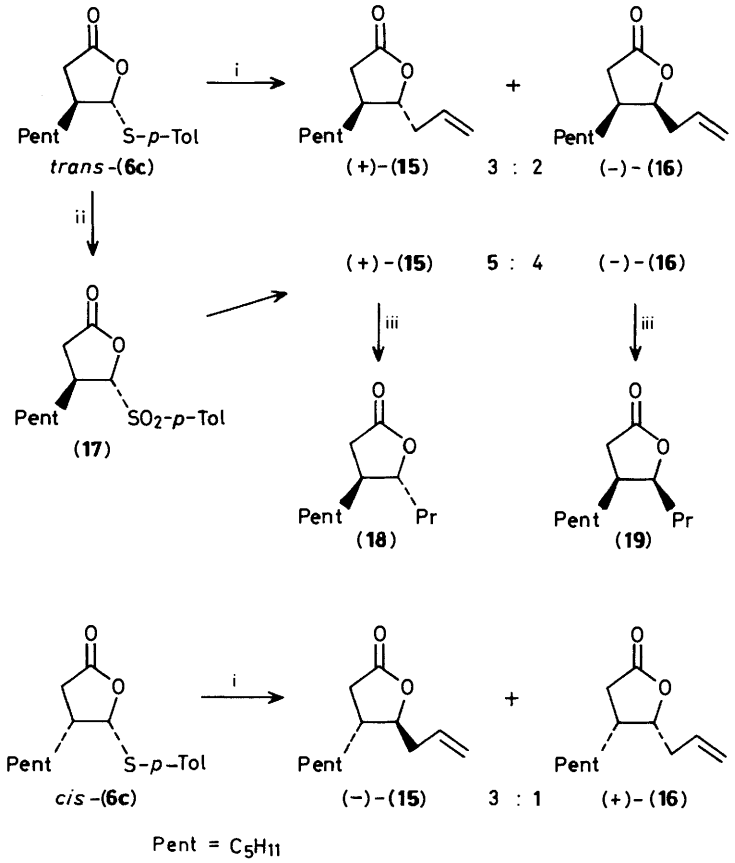
	Products					
Substrate (*R*)-*E*-(**4**)	*trans*-(**5**) Yield[a] (%)	*trans*-(**6**) Yield[a] (%)	(*S*)-(**7**) Yield[a] (%)	$[\alpha]_D$ (*c*)[b] (°)	Optical purity (% e.e)	Abs. config.
a; Pr	76	98	95	−6.4 (1.24)[d]	98.1	*S*
b; Bu	84	99	99	−6.0 (0.32)	100	*S*
c; Pentyl	84	98	99	−5.1 (2.07)	98.3	*S*
d; Hexyl	82	95	99	−4.2 (1.91)	98.3	*S*

[a] Yields are for the isolated pure products. [b] Measured in chloroform at 20 °C. [c] Determined by the Helmchen's method. [d] $[\alpha]_D$ −6.6° (*c* 1.54 EtOH).

Table 2. (*R*)-4-Alkyl-4,5-dihydrofuran-2(3*H*)-ones (*R*)-(**7**) from (*Z*)-alkenyl *p*-tolyl sulphoxides (*R*)-*Z*-(**4**)

Substrate (*R*)-*Z*-(**4**)	Reaction[a] temp. (°C)	Products: *cis*-(**5**) Yield[b] (%)	*cis*-(**6**) Yield[b] (%)	(*R*)-(**7**) Yield[b] (%)	$[\alpha]_D$ (*c*)[c] (°)	Optical purity[d] (% e.e)	Abs. config.
a; R = Pr	−35	50	96	92[e]	+6.4 (1.22)[e]	100	*R*
b; R = Bu	−25	68	97	97	+5.7 (1.73)	100	*R*
c; R = Pentyl	−20	49	98	92	+5.2 (1.45)	100	*R*
d; R = Hexyl	−25	62	95	99	+4.7 (1.69)	99.5	*R*
d; R = Hexyl	−50	45					

[a] For the reactions with dichloroketene. [b] Yields are for the isolated pure products. [c] Measured in chloroform at 20 °C. [d] Determined by the Helmchen's method. [e] Known compound, Ref. 10, lit. $[\alpha]_D^{26}$ +6.7 (*c* 3.9 EtOH) (>90% e.e).

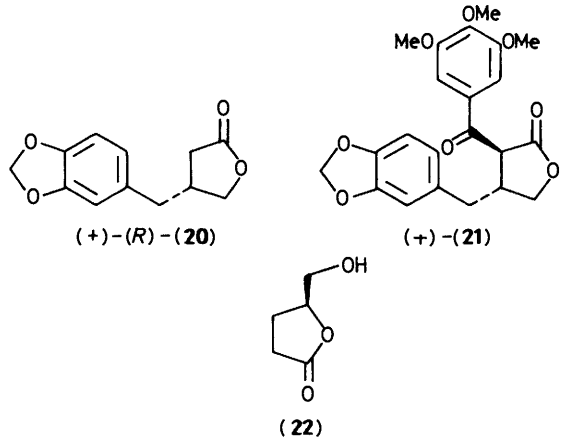


Scheme 4. *Reagents and conditions:* i, $Bu_3SnCH_2CH{=}CH_2$, $Bu_3SnOSO_2CF_3$ (0.3 equiv.), toluene, 110 °C; ii, *m*CPBA (2 equiv.), CH_2Cl_2, −80 °C; iii, H_2, Pd/C, AcOEt

tolylthiolactones (**6**) into β-alkyl-γ-allyl-lactones by substitution with allyltributylstannane (Scheme 4). The *trans* pentyl derivative *trans*-(**6c**) was chosen as a model substrate and the reaction examined by using a variety of catalyst–solvent systems. The best result was achieved when the reaction of *trans*-(**6c**) with allyltributylstannane was carried out with tributylstannyl triflate as catalyst in toluene. Thus, the *trans* and *cis* γ-allyl-substituted lactones (+)-(**15**) and (−)-(**16**) were obtained in 74% yield in a ratio of 3:2. Furthermore, it was found that the sulphonyl derivative (**17**) was superior to the sulphenyl one *trans*-(**6c**) as a substrate, giving compounds (+)-(**15**) and (−)-(**16**) quantitatively, although the selectivity was low (5:4). Catalytic hydrogenation of (**15**) and (**16**) gave the corresponding *trans* and *cis* saturated lactones (**18**) and (**19**), respectively. In the n.m.r. spectra, the signal due to the γ-methine proton in compounds (**15**) and (**18**) appeared at higher field [δ 4.15 in (**15**) and 4.09 in (**18**)] than that of the corresponding isomers (**16**) and (**19**) [δ 4.50 in (**16**) and 4.46 in (**19**)]. Thus, the former isomers (**15**) and (**18**) have *trans* stereochemistry, the latter (**16**) and (**19**) *cis* as discussed above.[8] The reaction of the isomeric *cis*-tolylthiolactone *cis*-(**6c**) under the same conditions gave a 76% yield of the corresponding enantiomers (−)-(**15**) and (+)-(**16**) in a ratio of 3:1.

As the results above show, the short steps, the simplicity of the operations, and the ready availability of both the starting stereoisomeric chiral alkenyl sulphoxides, this route should be more convenient than the previous one[10] for the synthesis of a variety of β-substituted γ-butyrolactones in a desired enantiomeric form and with a high optical purity. It can also be used in the synthesis of biologically and physiologically important lactonic compounds such as lignan lactones.

Synthesis of Lignan Lactones.—Recently, a number of pharmacologically interesting lignan lactones have been found in Nature, and some of them, such as steganacin, podophyllotoxin, deoxypodorhizon *etc.*, are known to exhibit antileukemic activity. These compounds possess in common a β-piperonyl-γ-butyrolactone entity having the same absolute configuration. The parent (+)-(*R*)-β-piperonyl-γ-butyrolactone (+)-(*R*)-(**20**), $[\alpha]_D$ +4.8° ($CHCl_3$), was first obtained as a degradation product from naturally occurring podorhizol-β-D-glucoside through (+)-podorhizon (+)-(**21**), $[\alpha]_D$ +79.5° ($CHCl_3$),[14]

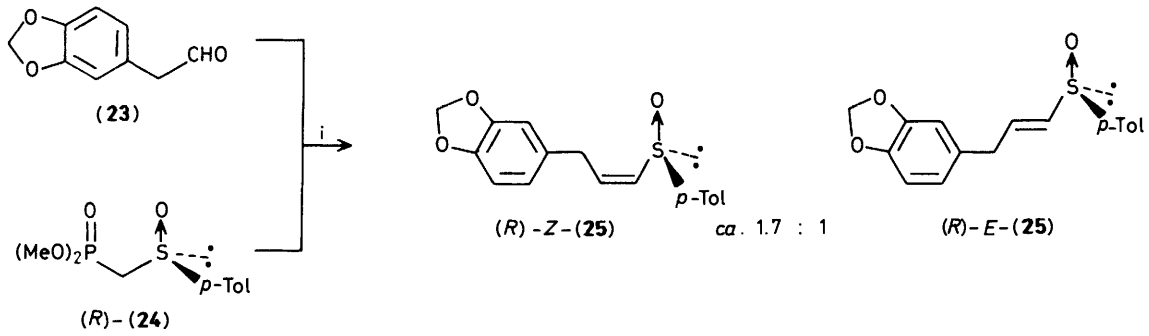


(+)-(*R*)-(**20**) (+)-(**21**) (**22**)

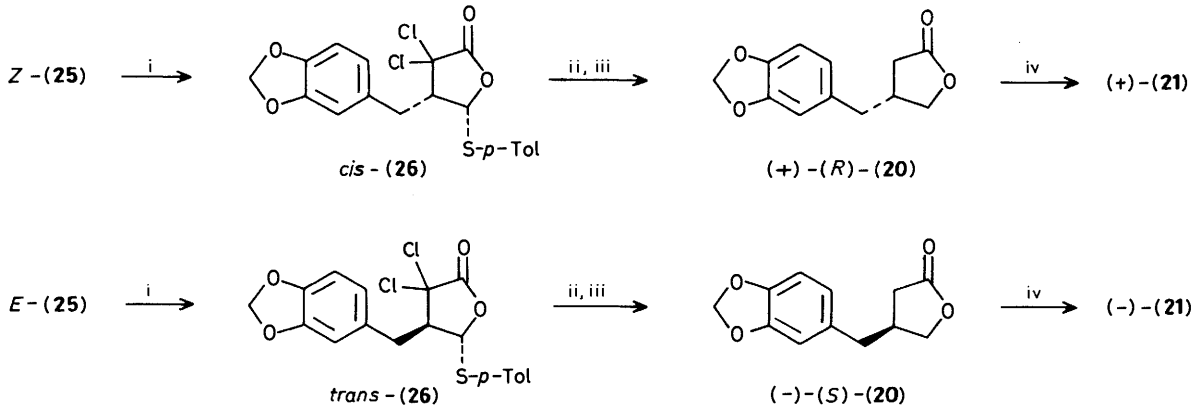
and later synthesized as the key intermediate for the synthesis of several lignan lactones in optically active form by Koga and coworkers.[15,16] The synthesis, however, was achieved *via* a multistep sequence involving the diastereoselective (58% diastereomeric excess) piperonylation of optically active γ-hydroxymethylbutyrolactone (**22**), which was prepared from L-glutamic acid, and a carbonyl transposition.[17,18] The present method for the β-alkylbutyrolactone synthesis would provide an alternative approach to the synthesis of compound (+)-(*R*)-(**20**) in a more straightforward manner and with higher enantiospecificity.

From the results discussed above, if seemed that the desired (*R*)-enantiomer of β-piperonylbutyolactone (*R*)-(**20**) could be obtained by applying the reaction with dichloroketene to *Z*-piperonylvinyl *p*-tolyl (*R*)-sulphoxide (*R*)-*Z*-(**25**). The requisite sulphoxide (*R*)-*Z*-(**25**) was prepared by the Horner–Wittig reaction of homopiperonal (**23**) with dimethyl (*R*)-*p*-tolylsulphinylmethanephosphonate (*R*)-(**24**).[19] Thus, treatment of homopiperonal (**23**) with the lithio derivative of (*R*)-(**24**) afforded a mixture of the *Z*- and *E*-ethylenic sulphoxides (*R*)-*Z*-(**25**) and (*R*)-*E*-(**25**), which could be separated by chromatography (Scheme 5). As expected, the reaction of compound (*R*)-*Z*-(**25**) with dichloroketene under the same conditions as described above gave the *cis*-β-piperonyl lactone *cis*-(**26**) in 94% yield as a single product (Scheme 6). Then, sequential reductive dechlorination and desulphurization furnished the desired β-piperonylbutyrolactone (+)-(*R*)-(**20**), $[\alpha]_D$ +4.5° ($CHCl_3$) (94% e.e.), in 80% yield. Acylation of this compound with 3,4,5-trimethoxybenzoyl chloride gave natural (+)-podorhizon (+)-(**21**), $[\alpha]_D$ +66.7° ($CHCl_3$), in a higher (90%) yield than the acylation by a mixed anhydride manner.[15,16] The observed lower optical purity in the product was due to contamination with chromatographically inseparable by-products, and simple recrystallization from methanol furnished optically pure (+)-podorhizon, $[\alpha]_D$ +78.7° ($CHCl_3$). In the exact same manner, the *E*-vinyl sulphoxide (*R*)-*E*-(**25**) gave in 86% overall yield (−)-podorhizon, (−)-(**21**) through the *trans* lactone *trans*-(**26**) and the antipodal β-piperonylbutyrolactone (−)-(*S*)-(**20**).

In view of the prior conversions of β-piperonyl-γ-butyrolactone (+)-(*R*)-(**20**) into (−)-deoxypodorhizon,[15,16] (−)-podor-



Scheme 5. *Reagent and conditions:* i, BuLi, THF, −70 to −75 °C, 30 min



Scheme 6. *Reagents and conditions:* i, Cl_3CCOCl, Zn, THF, −25 °C for *Z*-(**25**) and −45 °C for *E*-(**25**); ii, Zn–AcOH, room temp.; iii, Bu_3SnH, AIBN, toluene 90 °C; iv, LDA, THF, then 3,4,5-$(MeO)_3C_6H_2COCl$, −90 °C

hizoland(−)-*epi*-podorhizol,[15] (−)-hinokinin,[15] (−)-isodeoxypodophyllotoxin,[15] and (−)-attenuol,[15,20] and of (−)-deoxypodorhizon into (−)-steganacin,[21] the work described herein constitutes the formal and short total synthesis of these lignan lactones in high chemical and optical yields.

Experimental

All m.p.s were uncorrected. I.r. spectra were recorded for solutions in chloroform on a Jasco A-3 spectrophotometer. ^{1}H N.m.r. spectra were obtained for solutions in deuteriochloroform with a JEOL PMX-60 or 60SI (60 MHz) or PS-100 (100 MHz) instrument with tetramethylsilane as internal standard. High resolution mass spectra were run on a JEOL JMS-DX300 spectrometer. Optical rotations $[\alpha]_D$ were determined for solutions in chloroform at 20 °C, unless otherwise indicated, on a Jasco DIP-4S polarimeter. High-pressure liquid chromatography (h.p.l.c.) was carried out on a Jasco PRC-50 instrument with a silica gel packed column. Merck 60 GF-254 silica gel was used for preparative t.l.c. (p.l.c.). Microanalyses were carried out in the microanalytical laboratory of this Institute. Ether refers to diethyl ether.

Cyclohexa-1,4-*dienyl* p-*Tolyl* (−)-(R)-*Sulphoxide* (**8**).— Gaseous buta-1,3-diene was introduced into a solution of ethynyl *p*-tolyl (+)-(*R*)-sulphoxide[7] (2.9 g, 18 mmol) in toluene (120 ml) at room temperature for 10 min. Then, a solution of tin(IV) chloride in dichloromethane (0.8M; 10 ml, 0.4 equiv.) was added dropwise within 30 min with stirring, and the introduction of butadiene was continued for 22 h. After removal of excess of butadiene under reduced pressure, water was added, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with water and brine and evaporated to dryness. Chromatography of the residue on silica gel [eluant hexane–ethyl acetate (9:1)] gave the *adduct* (**8**) (2.5 g, 67%). An analytical sample was purified by recrystallization from hexane–ether (1:1) and had m.p. 74 °C; $[\alpha]_D^{23}$ −12.2° (*c* 1.79); $\nu_{max.}$ 3 000, 1 500, 1 090, and 1 040 cm^{-1}; δ 2.14—3.10 (4 H, m, 3- and 6-H_2), 2.34 (3 H, s, ArMe), 5.60 (2 H, br s, 4- and 5-H), 6.57 (1 H, m, 2-H), and 7.35 (4 H, AB type q, *J* 7 Hz, 4 × ArH) (Found: C, 71.8; H, 6.5. $C_{13}H_{14}OS$ requires C, 71.5; H, 6.5%).

General Procedure for the Reaction of Optically Active Alkenyl p-*Tolyl Sulphoxides* (**4**) *with Dichloroketene.*—A solution of the (*E*)-sulphoxide in THF [0.1M; 25 ml for *ca.* 2.5 mmol of (**4**)] was added to activated zinc powder[22] (10 equiv.) under nitrogen. To this stirred suspension at −45 °C was added a solution of trichloroacetyl chloride (0.85 ml, 3 equiv.) in THF (15 ml) dropwise, during 20 min. After 10 min, the remaining zinc powder was removed by filtration through Celite. The Celite was washed through with ether, the filtrate diluted with more ether, and the resulting solution was washed successively with saturated aqueous sodium hydrogen carbonate, water, and brine, and evaporated to dryness. The dichloro-lactonic product (**5**) was purified by chromatography on silica gel [eluant hexane–ethyl acetate (20:1)].

In the case of the (*Z*)-isomer, the reaction and work-up were carried out in the same manner, though the addition of trichloroacetyl chloride was carried out at −25 °C.

General Procedure for Reductive Dechlorination of Dichlorolactones (**5**).—To a solution of compound (**5**) in acetic acid [4 ml for 2.0 mmol of (**5**)] was added activated zinc powder (3 equiv.) portionwise at room temperature with vigorous stirring, and the reaction mixture was stirred for 30 min. The mixture was neutralized with saturated aqueous sodium hydrogen carbonate and then sodium carbonate, and extracted with ether. The combined extracts were washed with water and brine and evaporated to dryness. The tolylthiolactonic product (**6**) was purified by chromatography on silica gel [eluant hexane–ethyl acetate (5:1)].

General Procedure for Reductive Desulphurization of the Tolylthio Lactones (**6**).—To a solution of compound (**6**) in toluene [4 ml for 1.1 mmol of (**6**)] at 90 °C under nitrogen was added a solution of tributyltin hydride (3 equiv.) and azoisobutyronitrile (AIBN) (0.5 equiv.) in toluene (3—4 ml) dropwise during 30 min. The reaction mixture was stirred at 90—100 °C for 30 min and then allowed to cool to room temperature. It was then directly chromatographed on silica gel with pentane–ether (50:1) as eluant. After the toluene had been eluted, the chromatographic purification of the lactonic product (**7**) was carried out using a more polar solvent system [pentane–ether (5:1)]. The sample for measurement of the specific rotation was purified by evaporative short-path distillation at 20 mmHg and at a bath temperature of 105—110 °C for the propyl (**7a**), 120—125 °C for the butyl (**7b**), 135—140 °C for the pentyl (**7c**), and 145—150 °C for the hexyl derivatives (**7d**), respectively.

In the case of compounds (**11**) and (**12**), chromatographic separation was carried out using hexane–ethyl acetate (19:1).

(−)-(S)-4-*Propyl*-4,5-*dihydrofuran*-2(3H)-*one* (−)-(*S*)-(**7a**). —The reaction of the (*E*)-pentenyl sulphoxide *E*-(**4a**) (300 mg, 1.44 mmol) with dichloroketene gave 3,3-*dichloro*-4-*propyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2-(3H)-*one trans*-(**5a**) (668 mg, 76%); $\nu_{max.}$ 2 950, 1 805, 1 495, 1 180, and 970 cm^{-1}; δ 0.80—1.20 (3 H, t, *J* 6 Hz, *Me*CH_2), 1.40—2.20 (4 H, m, 2 × side chain CH_2), 2.36 (3 H, s, ArMe), 2.60 (1 H, m, 4-H), 5.23 (1 H, d, *J* 10 Hz, 5-H), and 7.07—7.60 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 318.0252. $C_{14}H_{16}Cl_2O_2S$ requires *M*, 318.0248).

The reductive dechlorination of compound *trans*-(**5a**) (659 mg, 2.06 mmol) gave 4-*propyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one trans*-(**6a**) (503 mg, 98%); $\nu_{max.}$ 2 940, 1 780, 1 495, 1 160, and 960 cm^{-1}; δ 0.70—1.10 (3 H, t-like, *Me*CH_2), 1.10—1.90 (4 H, m, 2 × side chain CH_2), 2.05—2.75 (3 H, m, 3-H_2 and 4-H), 2.31 (3 H, s, ArMe), 5.30 (1 H, d, *J* 6 Hz, 5-H), and 6.95—7.55 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 250.1028. $C_{14}H_{18}O_2S$ requires *M*, 250.1027). The reductive desulphurization of compound *trans*-(**6a**) (400 mg, 1.60 mmol) gave the *product* (−)-(*S*)-(**7a**) (195 mg, 95%); $[\alpha]_D$ −6.4° (*c* 1.24) and −6.6° (*c* 1.54 EtOH); $\nu_{max.}$ 2 940, 1 775, 1 180, and 1 020 cm^{-1}; δ 0.70—1.10 (3 H, t like, *Me*CH_2), 1.10—1.80 (4 H, m, 2 × side chain CH_2), 2.00—2.90 (3 H, m, 3-H_2 and 4-H), and 3.90 and 4.40 (1 H each, each dd, *J* 9 and 7 Hz, 5-H_2) (Found: C, 65.8; H, 9.7. $C_7H_{12}O_2$ requires C, 65.6; H, 9.4%).

(−)-(S)-4-*Butyl*-4,5-*dihydrofuran*-2(3H)-*one* (−)-(*S*)-(**7b**).— The reaction of the (*E*)-hexenyl sulphoxide *E*-(**4b**) (449 mg, 2 mmol) with dichloroketene gave 4-*butyl*-3,3-*dichloro*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one trans*-(**5b**) (560 mg, 84%); $\nu_{max.}$ 2 950, 1 805, 1 495, 1 180, and 970 cm^{-1}; δ 0.80—1.20 (3 H, t like, *Me*CH_2), 1.20—2.20 (6 H, m, 3 × side chain CH_2), 2.38 (3 H, s, ArMe), 2.50 (1 H, dt, *J* 10 and 6 Hz, 4-H), 5.10 (1 H, d, *J* 10 Hz, 5-H), and 7.00—7.55 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 332.0400. $C_{15}H_{18}Cl_2O_2S$ requires *M*, 332.0404). The reductive dechlorination of compound *trans*-(**5b**) (146 mg, 0.44 mmol) gave 4-*butyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one trans*-(**6b**) (113 mg, 99%); $\nu_{max.}$ 2 940, 1 780, 1 495, 1 160, and 960 cm^{-1}; δ 0.70—1.10 (3 H, t, like, *Me*CH_2), 1.10—1.90 (6 H, m, 3 × side chain CH_2), 2.05—2.75 (3 H, m, 3-H_2 and 4-H), 2.31 (3 H, s, ArMe), 5.30 (1 H, d, *J* 6 Hz, 5-H), and 6.95—7.55 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 264.1180. $C_{15}H_{20}O_2S$ requires *M*, 264.1183). The reductive desulphurization of compound *trans*-(**6b**) (100 mg, 0.38 mmol) gave the *product* (−)-(*S*)-(**7b**) (52 mg, 99%); $[\alpha]_D$ −6.0° (*c* 0.32); $\nu_{max.}$

2 940, 1 750, 1 180, and 1 020 cm^{-1}; δ 0.70—1.10 (3 H, t like, $MeCH_2$), 1.10—1.80 (6 H, br s, 3 × side chain CH_2), 2.00—2.90 (3 H, m, 3-H_2 and 4-H), and 3.90 and 4.40 (1 H each, each dd, *J* 9 and 7 Hz, 5-H_2) (Found: C, 67.7; H, 10.1 $C_8H_{14}O_2$ requires C, 67.6; H, 9.9%).

(−)-(S)-4-*Pentyl*-4,5-*dihydrofuran*-2(3H)-*one* (−)-(*S*)-(**7c**).—The reaction of the (*E*)-heptenyl sulphoxide *E*-(**4c**) (600 mg, 2.53 mmol) with dichloroketene gave 3,3-*dichloro*-4-*pentyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one trans*-(**5c**) (741 mg, 84%); $\nu_{max.}$ 2 950, 1 805, 1 495, 1 180, and 970 cm^{-1}; δ 0.70—1.15 (3 H, t like, $MeCH_2$), 1.15—2.20 (8 H, m, 4 × side chain CH_2), 2.35 (3 H, s, ArMe), 2.65 (1 H, dt, *J* 10 and 6 Hz, 4-H), 5.22 (1 H, d, *J* 10 Hz, 5-H), and 7.05—7.60 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 346.0550. $C_{16}H_{20}Cl_2O_2S$ requires *M*, 346.0560).

The reductive dechlorination of compound *trans*-(**5c**) (700 mg, 2.0 mmol) gave 4-*pentyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one trans*-(**6c**) (550 mg, 98%); $\nu_{max.}$ 2 940, 1 780, 1 495, 1 160, and 960 cm^{-1}; δ 0.70—1.10 (3 H, t like, $MeCH_2$), 1.10—1.90 (8 H, br s, 4 × side chain CH_2), 2.05—2.75 (3 H, m, 3-H_2 and 4-H), 2.32 (3 H, s, ArMe), 5.30 (1 H, d, *J* 6 Hz, 5-H), and 7.00—7.60 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 278.1336. $C_{16}H_{22}O_2S$ requires *M*, 278.1339). The reductive desulphurization of compound *trans*-(**6c**) (412 mg, 1.48 mmol) gave the *product* (−)-(*S*)-(**7c**) (230 mg, 99%); $[\alpha]_D$ −5.1° (*c* 2.07); $\nu_{max.}$ 2 940, 1 750, 1 180, and 1 020 cm^{-1}; δ 0.70—1.10 (3 H, t like, $MeCH_2$), 1.10—1.80 (8 H, br s, 4 × side chain CH_2), 2.00—2.90 (3 H, m, 3-H_2 and 4-H), and 3.90 and 4.40 (1 H each, each dd, *J* 9 and 7 Hz, 5-H_2) (Found: C, 69.5; H, 10.5. $C_9H_{16}O_2$ requires C, 69.2; H, 10.3%).

(−)-(S)-4-*Hexyl*-4,5-*dihydrofuran*-2(3H)-*one* (−)-(*S*)-(**7d**).—The reaction of the (*E*)-octenyl sulphoxide *E*-(**4d**) (380 mg, 1.5 mmol) with dichloroketene gave 3,3-*dichloro*-4-*hexyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one trans*-(**5d**) (446 mg, 82%); $\nu_{max.}$ 2 950, 1 805, 1 495, 1 180, and 970 cm^{-1}; δ 0.70—1.10 (3 H, t like, $MeCH_2$), 1.10—2.20 (10 H, m, 5 × side chain CH_2), 2.35 (3 H, s, ArMe), 2.60 (1 H, dt, *J* 10 and 6 Hz, 4-H), 5.22 (1 H, d, *J* 10 Hz, 5-H), and 7.05—7.60 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 360.0706. $C_{17}H_{22}Cl_2O_2S$ requires *M*, 360.0717). The reductive dechlorination of compound *trans*-(**5d**) (600 mg, 1.66 mmol) gave 4-*hexyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one trans*-(**6d**) (462 mg, 95%); $\nu_{max.}$ 2 940, 1 780, 1 495, 1 160, and 960 cm^{-1}; δ 0.70—1.05 (3 H, t like, $MeCH_2$), 1.05—1.95 (10 H, br s, 5 × side chain CH_2), 2.05—2.75 (3 H, m, 3-H_2 and 4-H), 2.34 (3 H, s, ArMe), 5.35 (1 H, d, *J* 6 Hz, 5-H), and 7.05—7.60 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 292.1493. $C_{17}H_{24}O_2S$ requires *M*, 292.1496). The reductive desulphurization of compound *trans*-(**6d**) (400 mg, 1.37 mmol) gave the *product* (−)-(*S*)-(**7d**) (230 mg, 99%); $[\alpha]_D$ −4.2° (*c* 1.91); $\nu_{max.}$ 2 940, 1 775, 1 180, and 1 020 cm^{-1}; δ 0.70—1.10 (3 H, t like, $MeCH_2$), 1.10—1.80 (10 H, br s, 5 × side chain CH_2), 2.00—2.90 (3 H, m, 3-H_2 and 4-H), and 3.90 and 4.40 (1 H, each, each dd, *J* 9 and 7 Hz, 5-H_2) (Found: C, 70.2; H, 10.6. $C_{10}H_{18}O_2$ requires C, 70.5; H, 10.7%).

(+)-(R)-4-*Propyl*-4,5-*dihydrofuran*-2(3H)-*one* (+)-(*R*)-(**7a**).—The reaction of the (*Z*)-pentenyl sulphoxide *Z*-(**4a**) (525 mg, 2.52 mmol) with dichloroketene gave 3,3-*dichloro*-4-*propyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one cis*-(**5a**) (404 mg, 50%); $\nu_{max.}$ 2 950, 1 805, 1 495, 1 180, and 970 cm^{-1}; δ 0.80—1.20 (3 H, t like, $MeCH_2$), 1.20—2.20 (4 H, m, 2 × side chain CH_2), 2.35 (3 H, s, ArMe), 3.25 (1 H, q, *J* 7 Hz, 4-H), 5.78 (1 H, d, *J* 8 Hz, 5-H), and 7.00—7.60 (4 H, AB, type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 318.0258. $C_{14}H_{16}Cl_2O_2S$ requires *M*, 318.0248).

The reductive dechlorination of compound *cis*-(**5a**) (404 mg, 1.26 mmol) gave 4-*propyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one cis*-(**6a**) (302 mg, 96%); $\nu_{max.}$ 2 940, 1 780, 1 495, 1 160, and 960 cm^{-1}; δ 0.70—1.20 (3 H, t like, $MeCH_2$), 1.20—1.85 (4 H, m, 2 × side chain CH_2), 2.20—2.68 (2 H, m), and 2.68—3.00 (1 H, m, 3-H_2 and 4-H), 2.33 (3 H, s, ArMe), 5.74 (1 H, d, *J* 7 Hz, 5-H), and 7.00—7.60 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 250.1028. $C_{14}H_{18}O_2S$ requires *M*, 250.1027). The reductive desulphurization of compound *cis*-(**6a**) (302 mg, 1.2 mmol) gave the *product* (+)-(*R*)-(**7a**) (142 mg, 92%); $[\alpha]_D$ +6.4° (*c* 1.22) {lit.,[10] $[\alpha]_D$ +6.7° (*c* 3.9 EtOH) for the >90% e.e. sample}. The i.r. and ^1H n.m.r. spectra were identical with those of (−)-(*S*)-(**7a**) (Found: C, 65.8; H, 9.7. $C_7H_{12}O_2$ requires C, 65.6; H, 9.4%).

(+)-(R)-4-*Butyl*-4,5-*dihydrofuran*-2(3H)-*one* (+)-(*R*)-(**7b**).—The reaction of the (*Z*)-hexenyl sulphoxide *Z*-(**4b**) (700 mg, 3.15 mmol) with dichloroketene gave 4-*butyl*-3,3-*dichloro*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one cis*-(**5b**) (718 mg, 68%); $\nu_{max.}$ 2 950, 1 805, 1 495, 1 180, and 970 cm^{-1}; δ 0.80—1.20 (3 H, t like, $MeCH_2$), 1.20—2.30 (6 H, m, 3 × side chain CH_2), 2.35 (3 H, s, ArMe), 3.23 (1 H, q, *J* 7 Hz, 4-H), 5.78 (1 H, d, *J* 8 Hz, 5-H), and 7.00—7.60 (4, H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 332.0397. $C_{15}H_{18}Cl_2O_2S$ requires *M*, 332.0404). The reductive dechlorination of compound *cis*-(**5b**) (600 mg, 1.8 mmol) gave 4-*butyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one cis*-(**6b**) (463 mg, 97%); $\nu_{max.}$ 2 940, 1 780, 1 495, 1 160, and 960 cm^{-1}; δ 0.70—1.10 (3 H, t like, $MeCH_2$), 1.10—1.90 (6 H, m, 3 × side chain CH_2), 2.20—3.30 (3 H, m, 3-H_2 and 4-H), 2.33 (3 H, s, ArMe), 5.75 (1 H, d, *J* 7 Hz, 5-H), and 7.00—7.60 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 264.1180. $C_{15}H_{20}O_2S$ requires *M*, 264.1183). The reductive desulphurization of compound *cis*-(**6b**) (380 mg, 1.43 mmol) gave the *product* (+)-(*R*)-(**7b**) (198 mg, 97%); $[\alpha]_D$ +5.7° (*c* 1.73). The i.r. and ^1H n.m.r. spectra were identical with those of (−)-(*S*)-(**7b**) (Found: C, 67.7; H, 10.2. $C_8H_{14}O_2$ requires C, 67.6; H, 9.9%).

(+)-(R)-4-*Pentyl*-4,5-*dihydrofuran*-2(3H)-*one* (+)-(*R*)-(**7c**).—The reaction of the (*Z*)-heptenyl sulphoxide *Z*-(**4c**) (700 mg, 2.96 mmol) with dichloroketene gave 3,3-*dichloro*-4-*pentyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one cis*-(**5c**) (500 mg, 49%); $\nu_{max.}$ 2 950, 1 805, 1 495, 1 180, and 970 cm^{-1}; δ 0.70—1.10 (3 H, t like, $MeCH_2$), 1.10—2.25 (8 H, m, 4 × side chain CH_2), 2.35 (3 H, s, ArMe), 3.23 (1 H, q, *J* 7 Hz, 4-H), 5.78 (1 H, d, *J* 8 Hz, 5-H), and 7.00—7.60 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 346.0559. $C_{16}H_{20}Cl_2O_2S$ requires *M*, 346.0560).

The reductive dechlorination of compound *cis*-(**5c**) (470 mg, 1.35 mmol) gave 4-*pentyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one cis*-(**6c**) (370 mg, 98%); $\nu_{max.}$ 2 940, 1 780, 1 495, 1 160, and 960 cm^{-1}; δ 0.70—1.10 (3 H, t like, $MeCH_2$), 1.10—1.90 (8 H, br s, 4 × side chain CH_2), 2.20—3.10 (3 H, m, 3-H_2 and 4-H), 2.33 (3 H, s, ArMe), 5.90 (1 H, d, *J* 7 Hz, 5-H), and 7.10—7.80 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 278.1339. $C_{16}H_{22}O_2S$ requires *M*, 278.1339). The reductive desulphurization of compound *cis*-(**6c**) (330 mg, 1.18 mmol) gave the *product* (+)-(*R*)-(**7c**) (170 mg, 92%); $[\alpha]_D$ +5.2° (*c* 1.45). The i.r. and ^1H n.m.r. spectra were identical with those of (−)-(*S*)-(**7c**) (Found: C, 69.1; H, 10.3. $C_9H_{16}O_2$ requires C, 69.2; H, 10.3%).

(+)-(R)-4-*Hexyl*-4,5-*dihydrofuran*-2(3H)-*one* (+)-(*R*)-(**7d**).—The reaction of the (*Z*)-octenyl sulphoxide *Z*-(**4d**) (529 mg, 2.11 mmol) with dichloroketene gave 3,3-*dichloro*-4-*hexyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one cis*-(**5d**) (473 mg, 62%); $\nu_{max.}$ 2 950, 1 805, 1 495, 1 180, and 970 cm^{-1}; δ 0.70—1.10 (3 H, t like, $MeCH_2$), 1.10—2.30 (10 H, m, 5 × side chain CH_2), 2.35 (3 H, s, ArMe), 3.23 (1 H, q, *J* 7 Hz, 4-H), 5.78 (1 H, d, *J* 8 Hz, 5-H), and 7.00—7.60 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 360.0724. $C_{17}H_{22}Cl_2O_2S$ requires *M*, 360.0717).

The reductive dechlorination of compound *cis*-(**5d**) (600 mg, 1.66 mmol) gave 4-*hexyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one cis*-(**6d**) (444 mg, 95%); $\nu_{max.}$ 2 940, 1 780, 1 495, 1 160, and 960 cm^{-1}; δ 0.70—1.10 (3 H, t like, $MeCH_2$), 1.10—1.90 (10 H, br

s, 5 × side chain CH_2), 2.16—3.00 (3 H, m, 3-H_2 and 4-H), 2.33 (3 H, s, ArMe), 5.75 (1 H, d, *J* 7 Hz, 5-H), and 7.00—7.60 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 292.1498. $C_{17}H_{24}O_2S$ requires *M*, 292.1496).

The reductive desulphurization of compound *cis*-(**6d**) 350 mg, 1.2 mmol) gave the *product* (+)-(*R*)-(**7d**) (203 mg, 99%); $[\alpha]_D$ +4.7° (*c* 1.69). The i.r. and ^1H n.m.r. spectra were identical with those of (−)-(*S*)-(**7d**) (Found: C, 70.7; H, 10.8. $C_{10}H_{18}O_2$ requires C, 70.5; H, 10.7%).

(−)-(3a*S*,7a*S*)- *and* (−)-(3a*S*,7a*R*)-3a,4,7,7a-*Tetrahydrobenzofuran*-2(3H)-*ones* (**11**) *and* (**12**).—The reaction of the cyclohexadienyl sulphoxide (**8**) (400 mg, 1.8 mmol) with dichloroketene gave 3,3-*dichloro*-7a-p-*tolylthio*-3a,4,7,7a-*tetrahydrobenzofuran*-2(3H)-*one* (**9**) (570 mg, 96%); $\nu_{max.}$ 3 040, 2 930, 1 800, 1 620, 1 600, 1 500, 1 115, and 1 060 cm^{-1}; δ 2.50—2.90 (4 H, m, 4- and 7-H_2), 2.33 (3 H, s, ArMe), 2.80 (1 H, m, 3a-H), 5.20—6.20 (2 H, m, 5- and 6-H), and 7.25 (4 H, AB type q, *J* 7 Hz, 4 × ArH) (Found: *m/z* 328.0052. $C_{15}H_{14}Cl_2O_2S$ requires *M*, 328.0091). The reductive dechlorination of compound (**9**) (530 mg, 1.3 mmol) gave 7a-p-*tolylthio*-3a,4,7,7a-*tetrahydrobenzofuran*-2(3H)-*one* (**10**) (260 mg, 77%); $\nu_{max.}$ 3 020, 1 775, 1 620, 1 495, 1 090, and 1 045 cm^{-1}; δ 1.70—2.90 (7 H, m, 3-, 4-, and 7-H_2, and 3a-H), 2.33 (3 H, s, ArMe), 5.50—6.00 (2 H, m, 5- and 6-H), and 7.26 (4 H, AB type q, *J* 7 Hz, 4 × ArH) (Found: *m/z* 260.0869. $C_{15}H_{16}O_2S$ requires *M*, 260.0870).

The reductive desulphurization of compound (**10**) (830 mg, 3.2 mmol) gave the *products* (**11**) (270 mg, 62%) and (**12**) (110 mg, 26%). Compound (**11**) had b.p. 80 °C (bath) at 0.2 mmHg; $[\alpha]_D$ −55.0° (*c* 0.629 MeOH); $\nu_{max.}$ 2 930, 1 770, 1 425, 1 150, and 1 030 cm^{-1}; δ 1.90—3.30 (7 H, m, 3-, 4-, and 7-H_2, and 3a-H), 4.72 (1 H, q, *J* 5 Hz, 7a-H), and 5.73 (2 H, m, 5- and 6-H) (Found: C, 69.2; H, 7.5. $C_8H_{10}O_2$ requires C, 69.6; H, 7.3%). Compound (**12**) had m.p. 62 °C; $[\alpha]_D$ −97.2° (*c* 0.473 MeOH); $\nu_{max.}$ 2 920, 1 780, 1 130, and 1 020 cm^{-1}; δ 1.50—3.00 (7 H, m, 3-, 4-, and 7-H_2, and 3a-H), 4.00 (1 H, m, 7a-H), and 5.63 (2 H, m, 5- and 6-H) (Found: C, 69.6; H, 7.5. $C_8H_{10}O_2$ requires C, 69.6; H, 7.3%).

(−)-(3a*S*,7a*S*)- *and* (+)-(3a*S*,7a*R*)-3a,4,5,6,7,7a-*Hexahydrobenzofuran*-2(3H)-*ones* (**13**) *and* (**14**).—A solution of the unsaturated lactone (**11**) or (**12**) (0.03M) in ethyl acetate was hydrogenated over 5% Pd–C (50 wt%) at room temperature under atmospheric pressure for 5 or 20 h, respectively. The reaction mixture was passed through a short column of Celite and silica gel and concentrated. Distillation of the residue at 80 °C (bath) and 0.1 mmHg gave quantitatively the known *saturated lactone* (**13**) or (**14**), respectively. Compound (**13**) had $[\alpha]_D$ −45.5° (*c* 0.548) and −45.8° (*c* 0.572 MeOH) {lit. $[\alpha]_D$ −40.3° (*c* 8 $CHCl_3$) for the (3a*S*,7a*S*)-isomer[12] and +41.9° (*c* 10.3 $CHCl_3$)[12] and +45.5° (*c* 0.43 MeOH)[13] for the (3a*R*,7a*R*)-isomer}. Compound (**14**) had $[\alpha]_D$ +80.8° (*c* 0.548) {lit.[12] $[\alpha]_D$ +78.5° (*c* 2.9 $CHCl_3$) for the (3a*S*,7a*R*)-isomer and −77.6° (*c* 4.6 $CHCl_3$) for the (3a*R*,7a*S*)-isomer}.

The i.r. and ^1H n.m.r. spectra of these compounds (**13**) and (**14**) were identical with those of the reported values,[12,13] respectively.

(4S,5R)-4-*Pentyl*-5-p-*tolylsulphonyl*-4,5-*dihydrofuran*-2(3H)-*one* (**17**).—To a solution of the pentyl-tolylthio-lactone *trans*-(**6c**) (160 mg, 0.56 mmol) in dichloromethane (3 ml) was added dropwise a solution of *m*-chloroperbenzoic acid (80%; 240 mg, 2 equiv.) in dichloromethane (3 ml) at room temperature under nitrogen, and the reaction mixture was stirred for 2 h. It was then washed with saturated aqueous sodium hydrogen carbonate until acidic materials were free from the organic solution. Evaporation of the solvent to dryness gave the *sulphonyl derivative* (**17**) (170 mg, 99%); $\nu_{max.}$ 1 800, 1 600, 1 325, and 1 155 cm^{-1}; δ 0.40—1.80 (11 H, m, C_5H_{11}), 2.00—3.20 (3 H, m, 3-H_2 and 4-H), 2.44 (3 H, s, ArMe), 4.77 (1 H, d, *J* 2 Hz, 5-H), and 7.20—7.90 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 310.1231. $C_{16}H_{22}O_4S$ requires *M*, 310.1238).

(+)-(S,5R)- *and* (−)-(4S,5S)-5-*Allyl*-4-*pentyl*-4,5-*dihydrofuran*-2(3H)-*ones* (+)-(**15**) *and* (−)-(**16**) *and the Enantiomers*.—To a solution of the *trans*-pentyl-tolylthiolactone *trans*-(**6c**) (150 mg, 0.55 mmol) and freshly prepared allyltributylstannane (340 mg, 2 equiv.)[23] in toluene (6 ml) was added dropwise a solution of tributylstannyl triflate in toluene (1M; 1.5 ml, 0.3 equiv.) at 60 °C under nitrogen, and the resulting mixture was heated under reflux for 15 h. The organotin compound and toluene were separated from the lactone mixture by chromatography on silica gel [eluant hexane–ethyl acetate (19:1)]. Preparative h.p.l.c. [eluant hexane–ethyl acetate (4:1)] of the mixture thus obtained gave the trans-*isomer* (+)-(**15**) (39 mg, 44%) and the cis-*isomer* (−)-(**16**) (27 mg, 30%). Analytical samples were purified by short-path distillation at 100 °C (bath) and 0.2 mmHg. Compound (+)-(**15**) had $[\alpha]_D^{18}$ +46.4° (*c* 1.5); $\nu_{max.}$ 2 940, 2 870, 1 770, 1 650, 1 470, 1 420, 980, and 930 cm^{-1}; δ 0.60—1.80 (11 H, m, C_5H_{11}), 1.80—3.10 (5 H, m, 3- and allylic-H_2, and 4-H), 4.15 (1 H, q, *J* 6 Hz, 5-H), and 4.90—5.40 (2 H, m), and 5.40—6.20 (1 H, m) (vinyl protons) (Found: C, 73.8; H, 10.1. $C_{12}H_{20}O_2$ requires C, 73.4; H, 10.3%). Compound (−)-(**16**) had $[\alpha]_D^{18}$ −33.8° (*c* 0.666); $\nu_{max.}$ 2 940, 2 860, 1 770, 1 645, 1 470, 1 420, 1 050, and 925 cm^{-1}; δ 0.60—1.70 (11 H, m, C_5H_{11}), 2.00—2.90 (5 H, m, 3- and allylic-H_2, and 4-H), 4.50 (1 H, q, *J* 6.6 Hz, 5-H), 4.90—5.30 (2 H, m), and 5.40—6.20 (1 H, m) (vinyl protons) (Found: C, 73.3; H, 10.4. $C_{12}H_{20}O_2$ requires C, 73.4; H, 10.3%).

The reaction of the sulphonyl derivative (**17**) under the same conditions gave compounds (+)-(**15**) (56%) and (−)-(**16**) (44%). The reaction of the *cis*-pentyl-tolylthio-lactone *cis*-(**6c**) under the same conditions gave the enantiomers (−)-(**15**) (55%), $[\alpha]_D^{17}$ −45.9° (*c* 0.344), and (+)-(**16**) (21%), $[\alpha]_D^{17}$ +33° (*c* 0.239), respectively. The i.r. and ^1H n.m.r. spectra of both compounds were identical with those of the corresponding enantiomers described above.

(4S,5R)- *and* (4S,5S)-4-*Pentyl*-5-*propyl*-4,5-*dihydrofuran*-2(3H)-*ones* (**18**) *and* (**19**).—A solution of the allylated lactone (+)-(**15**) or (−)-(**16**) (700 mg, 0.4 mmol) in ethyl acetate (10 ml) was hydrogenated over 5% Pd–C (50 wt%) at room temperature under atmospheric pressure for 6 h. The reaction mixture was passed through a short column of Celite and silica gel and evaporated under reduced pressure to give quantitatively the saturated lactone (**18**) or (**19**), respectively. Compound (**18**) had $[\alpha]_D^{23}$ +54.1° (*c* 0.194); $\nu_{max.}$ 1 770 and 1 190 cm^{-1}; δ 0.60—1.90 (18 H, m, C_5H_{11} and C_3H_7), 1.90—2.80 (3 H, m, 3-H_2 and 4-H), and 4.09 (1 H, q like, *J* 4 Hz, 5-H) (Found: C, 72.7; H, 11.4. $C_{12}H_{22}O_2$ requires C, 72.7; H, 11.2%). Compound (**19**) had $[\alpha]_D^{23}$ −19° (*c* 0.22); $\nu_{max.}$ 1 770 and 1 170 cm^{-1}; δ 0.70—1.90 (18 H, m, C_5H_{11} and C_3H_7), 1.90—2.80 (3 H, m, 3-H_2 and 4-H), and 4.46 (1 H, m, 5-H) (Found: C, 72.3; H, 11.2. $C_{12}H_{22}O_2$ requires C, 72.7; H, 11.2%).

(−)-(R)-(Z)- *and* (+)-(R)-(E)-1-[3-(3,4-*Methylenedioxyphenyl*)*propenyl*] p-*Tolyl Sulphoxides* (**25**).—A solution of butyl-lithium (1.45M hexane solution; 2 ml, 2.9 mmol) was added to a solution of dimethylphosphorylmethyl *p*-tolyl (*R*)-sulphoxide (**24**)[19] (847 mg, 3.2 mmol) in THF (10 ml) dropwise at −80 °C under nitrogen. After 15 min, a solution of freshly prepared 3,4-methylenedioxyphenylacetaldehyde (**23**) (504 mg, 3.0 mmol) in THF (10 ml) was added, and the reaction mixture was stirred at −75 to −70 °C for 30 min. The reaction mixture

was diluted with ethyl acetate, and the resulting solution was washed with water and brine, and evaporated to dryness. Chromatography of the residue (1.08 g) on silica gel (40 g) [eluant hexane–ethyl acetate (gradient)] gave *compounds Z*-(**25**) (565 mg, 61%) and *E*-(**25**) (328 mg, 35%). Compound *Z*-(**25**) had $[\alpha]_D$ −273° (*c* 0.18 acetone); $\nu_{max.}$ 3 000, 1 505, 1 490, 1 295, 1 040, and 930 cm^{-1}; δ 2.43 (3 H, s, Me), 3.80—4.00 (2 H, m, CH_2), 5.95 (2 H, s, OCH_2O), 6.20—6.50 (2 H, m, CH=CH), 6.73 (3 H, s, 3 × ArH), and 7.25—7.70 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: C, 67.9; H, 5.3. $C_{17}H_{16}O_3S$ requires C, 68.0; H, 5.4%). Compound *E*-(**25**) had m.p. 86—88 °C (from hexane–ether); $[\alpha]_D$ +152° (*c* 0.50 acetone); $\nu_{max.}$ 3 000, 1 505, 1 490, 1 440, 1 250, 1 040, and 930 cm^{-1}; δ 2.42 (3 H, s, Me), 3.47 (2 H, d, *J* 6 Hz, CH_2), 5.91 (2 H, s, OCH_2O), 6.08 (1 H, d, *J* 15.5 Hz, =CHS), 6.50 (1 H, dt, *J* 15.5 and 6 Hz, CH_2CH=), 6.60 (3 H, s, 3 × ArH), and 7.10—7.60 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: C, 68.2; H, 5.7. $C_{17}H_{16}O_3S$ requires C, 68.0; H, 5.4%).

(+)-(R)-4-(3,4-*Methylenedioxyphenyl*)*methyl*-4,5-*dihydrofuran*-2(3H)-*one* (+)-(*R*)-(**20**).—Reaction with dichloroketene, reductive dechlorination, and reductive desulphurization were carried out in the same manner as described in the general procedures. Different solvent systems for chromatographic separation are indicated. The reaction of the (*Z*)-olefinic sulphoxide *Z*-(**25**) (386 mg, 1.3 mmol) with dichloroketene and chromatographic purification [eluant hexane–ethyl acetate (7:1)] gave 3,3-*dichloro*-4-(3,4-*methylenedioxyphenyl*)*methyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one cis*-(**26**) (500 mg, 94%), m.p. 165—166 °C; $\nu_{max.}$ 3 000, 1 805, 1 505, 1 490, 1 445, and 1 250 cm^{-1}; δ 2.33 (3 H, s, Me), 2.90—3.75 (3 H, m, CH_2 and 4-H), 5.62 (1 H, d, *J* 7 Hz, 5-H), 5.93 (2 H, s, OCH_2O), 6.80—7.00 (3 H, m, 3 × ArH), and 7.00—7.50 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 410.0147. $C_{19}H_{16}Cl_2O_4S$ requires *M*, 410.0146). The reductive dechlorination of compound *cis*-(**26**) (543 mg, 1.32 mmol) gave 4-(3,4-*methylenedioxyphenyl*)*methyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one* (395 mg, 87%), m.p. 80—82 °C; $\nu_{max.}$ 3 000, 1 780, 1 505, 1 490, 1 445, 1 245, 1 160, 1 045, and 970 cm^{-1}; δ 2.30 (3 H, s, Me), 2.60—3.20 (5 H, m, CH_2, 3-H_2, and 4-H), 5.73 (1 H, d, *J* 6 Hz, 5-H), 5.86 (2 H, s, OCH_2O), 6.60—6.90 (3 H, m, 3 × ArH), and 7.00—7.60 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 342.0924. $C_{19}H_{18}O_4S$ requires *M*, 342.0925). The reductive desulphurization of this compound (385 mg, 1.12 mmol) and chromatographic purification [eluant hexane–ethyl acetate (3:1)] gave the *product* (+)-(*R*)-(**20**) (225 mg, 91%), b.p. 145—150 °C (bath) at 0.15 mmHg; $[\alpha]_D$ +4.5° (*c* 1.17) (*ca.* 94% e.e.) {lit.[14] $[\alpha]_D$ +4.8° (*c* 1.142 $CHCl_3$)}; $\nu_{max.}$ 2 900, 1 780, 1 505, 1 490, 1 240, 1 175, and 1 045 cm^{-1}; δ 2.13—3.00 (5 H, m, CH_2, 3-H_2, and 4-H), 3.90—4.60 (2 H, m, 5-H_2), 5.90 (2 H, s, OCH_2O), and 6.50—6.90 (3 H, m, 3 × ArH) (Found: C, 65.6; H, 5.2. $C_{12}H_{12}O_4$ requires C, 65.5; H, 5.5%). The spectral data were in good agreement with those of the reported degradation product of natural (+)-podorhizon (+)-(**21**).[14]

(−)-(S)-4-(3,4-*Methylenedioxyphenyl*)*methyl*-4,5-*dihydrofuran*-2(3H)-*one* (−)-(*S*)-**20**).—Reactions with dichloroketene, reductive dechlorination, and reductive desulphurization were carried out in the same manner as described in the general procedures. Different solvent systems for chromatographic separation are indicated. The reaction of the (*E*)-olefinic sulphoxide *E*-(**25**) (518 mg, 1.72 mmol) with dichloroketene and chromatographic purification [eluant hexane–ethyl acetate (10:1)] gave 3,3-*dichloro*-4-(3,4-*methylenedioxyphenyl*)*methyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one trans*-(**26**) (648 mg, 91%); $\nu_{max.}$ 3 000, 1 810, 1 505, 1 490, 1 445, 1 250, and 1 045 cm^{-1}; δ 2.37 (3 H, s, Me), 2.50—3.30 (3 H, m, CH_2 and 4-H), 5.38 (1 H, d, *J* 10 Hz, 5-H), 5.97 (2 H, s, OCH_2O), 6.60—7.00 (3 H, m, 3 × ArH), and 7.07—7.50 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 410.0144. $C_{19}H_{16}O_4SCl_2$ requires *M*, 410.0146). The reductive dechlorination of compound *trans*-(**26**) (744 mg, 1.8 mmol) and chromatographic purification [eluant hexane–ethyl acetate (7:1)] gave 4-(3,4-*methylenedioxyphenyl*)*methyl*-5-p-*tolylthio*-4,5-*dihydrofuran*-2(3H)-*one* (596 mg, 96%); $\nu_{max.}$ 3 000, 1 780, 1 505, 1 490, 1 445, 1 245, 1 155, 1 045, and 965 cm^{-1}; δ 2.30 (3 H, s, Me), 2.60—3.10 (5 H, m, CH_2, 3-H_2, and 4-H), 5.40 (1 H, d, *J* 3 Hz, 5-H), 5.91 (2 H, s, OCH_2O), 6.40—6.90 (3 H, m, 3 × ArH), and 7.00—7.60 (4 H, AB type q, *J* 8 Hz, 4 × ArH) (Found: *m/z* 342.0925. $C_{19}H_{18}O_4S$ requires *M*, 342.0925).

The reductive desulphurization of this compound (589 mg, 1.72 mmol) and chromatographic purification [eluant hexane–ethyl acetate (5:1)] gave the *product* (−)-(*S*)-(**20**) (370 mg, 98%), b.p. 150—155 °C (bath) at 0.6 mmHg; $[\alpha]_D$ −4.6° (*c* 1.98) (*ca.* 96% e.e) (Found: C, 65.8; H, 5.6. $C_{12}H_{12}O_4$ requires C, 65.5; H, 5.5%). The i.r. and ^1H n.m.r. spectra are identical with those of (+)-(*R*)-(**20**).

Natural (+)- *and Unnatural* (−)-*Podorhizon* (**21**).—To a solution of lithium di-isopropylamide (2 equiv.), prepared from butyl-lithium 1.45M hexane solution; 0.62 ml, 0.9 mmol) and di-isopropylamine (101 mg, 1 mmol) in THF (4 ml), was added a solution of the piperonyl-lactone (+)-(*R*)-(**20**) (99 mg, 0.45 mmol) in THF (3 ml) dropwise at −90 °C under nitrogen.

The mixture was stirred for 45 min after which a solution of freshly prepared 3,4,5-trimethoxybenzoyl chloride (125 mg, 1.2 equiv.) in THF (2 ml) was added at −70 °C, and stirring continued for 15 min. Saturated aqueous ammonium chloride was added, and the product was extracted with ethyl acetate. The combined extracts were washed with water and brine, and evaporated to dryness. P.l.c. of the residue [developer hexane–ethyl acetate (2:3)] gave (+)-*podorhizon* (+)-(**21**) (167 mg, 90%), $[\alpha]_D$ +66.7° (*c* 0.776). Recrystallization from methanol once gave the pure sample, m.p. 131—132 °C (lit.,[14] m.p. 129—130 °C); $[\alpha]_D$ +78.8° (*c* 0.57) {lit.[14] $[\alpha]_D$ +79.5° (*c* 0.588 $CHCl_3$)}; $\nu_{max.}$ 2 930, 1 775, 1 680, 1 590, 1 505, 1 495, 1 420, 1 340, 1 135, and 935 cm^{-1}; δ 2.77 (2 H, d, *J* 7 Hz, benzylic CH_2), 3.20—3.70 (1 H, m, β-H), 3.90 (6 H, s, 2 × OMe), 3.96 (3 H, s, OMe), 4.10—4.90 (3 H, m, γ-H_2 and α-H), 5.93 (2 H, s, OCH_2O), 6.50—6.90 (3 H, br s, 3 × ArH), and 7.22 (2 H, s, 2 × ArH), identical with the reported values[14] (Found: C, 63.6; H, 5.8. $C_{22}H_{22}O_8$ requires C, 63.8; H, 5.4%).

In the same manner, (−)-podorhizon (−)-(**21**), m.p. 130—131 °C; $[\alpha]_D$ −79.3° (*c* 0.74), was obtained in 95% yield (143 mg) from (−)-(*S*)-(**20**) (79 mg).

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