*Tetrahedron* Vol. 37, pp. 285 to 290
Pergamon Press Ltd., 1981 Printed in Great Britain

0040-4020/81/0155-0285 $02.00/0

# STUDIES ON THE CHEMICAL CONSTITUENTS OF RUTACEOUS PLANTS—XLI[1]

## ABSOLUTE CONFIGURATION OF RUTARETIN METHYL ETHER

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(*Received in Japan* 5 *March* 1980)

**Abstract**—The absolute configuration of rutaretin methyl ether (**1**) has been established by transformation of it into methyl hexahydrorutaretin methyl ether (**5**) which was independently derived from *S*-marmesin (**2**) via photo-Fries reaction as a key step.

In the course of studies on the chemical constituents of Rutaceous plants, we[2] occasionally isolated a new dihydrofurocoumarin (**1**) from *Xanthoxylum arnottianum* Maxim. (Rutaceae) together with other fourteen coumarins involving *S*-marmesin[3] (**2**) and *R*-columbianetin[4] (**3**). In 1967, Schneider *et al.*[5] isolated a phenolic coumarin, rutaretin (**4**), from *Ruta graveolens* L. (Rutaceae) and proposed a plain structure for it. Since our new coumarin was identified with Schneider's Me derivative of rutaretin (**4**) including the sign of the Cotton effect in the ORD curve, it should be rutaretin methyl ether (**1**) having the same absolute configuration. However, the absolute configuration of rutaretin (**4**) had not been established. In this paper, we report the absolute configuration of rutaretin methyl ether (**1**) by transformation of *S*-marmesin (**2**) having a known chiral center[3b] into a common derivative of rutaretin methyl ether, methyl hexahydrorutaretin methyl ether (**5**).

Initially, we found that *S*-marmesin (**2**) and *R*-columbianetin (**3**) show more levorotatory values of specific rotation in the protic solvent than in an aprotic solvent but the same negative Cotton effect, although the reported absolute configurations of these coumarins[3b,6] are not the same. This observation forced us to re-examine the absolute configurations of these coumarins. Ozonolysis of **2** and **3** resulted in hydroxylactones (**6a** and **b**) antipodal to each other (Scheme 1).

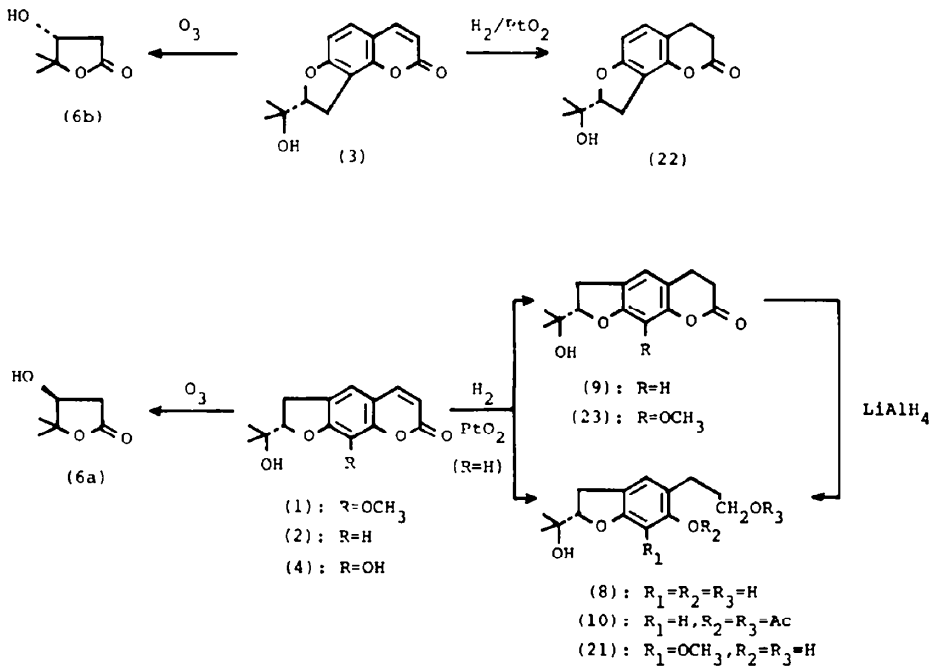
The absolute configuration of the (−)-hydroxylactone[6b] (**6a**) which was obtained from *S*-columbianetin (**7**) had been established and accepted as an *S*,[3b,6] leaving the determination of the absolute configuration of rutaretin methyl ether (**1**) which shows a negative Cotton effect in the CD curve.

Catalytic hydrogenation of *S*-marmesin (**2**) gave a mixture of a triol (hexahydromarmesin: **8**) and dihydromarmesin (**9**) in 36.1% and 38.2% yield.

Table 1. $[\alpha]_D$ and $[\theta]$ of some dihydrofuranocoumarins and their dihydrocoumarin derivatives

| solvent / coumarin | | MeOH | $CHCl_3$ | Δ (MeOH−$CHCl_3$) |
|---|---|---|---|---|
| R-columbianetin (3) | $[\alpha]_D$ | −262.0° | −188.3° | −73.7° |
| | $[\theta]_{335}$ | −15994 | −9180 | −6814 |
| S-marmesin (2) | $[\alpha]_D$ | −16.0° | +28.8° | −44.8° |
| | $[\theta]_{335}$ | −5405 | −918 | −4487 |
| S-rutaretin methyl ether (1) | $[\alpha]_D$ | −41.0° | +10.8° | −51.8° |
| | $[\theta]_{335}$ | −5226 | −865 | −4361 |
| R-dihydrocolumbianetin (22) | $[\alpha]_D^*$ | −85.9° | −63.9° | −22.0° |
| | $[\theta]_{283}$ | +907 | +225 | +682 |
| S-dihydromarmesin (9) | $[\alpha]_D^*$ | +37.5° | +39.8° | −2.4° |
| | $[\theta]_{288}$ | −2442 | −1224 | −1218 |
| S-dihydrorutaretin methyl ether (23) | $[\alpha]_D^*$ | +16.5° | +15.1° | +1.4° |
| | $[\theta]_{287}$ | −1471 | −869 | −609 |

* this value is at 589 nm in the ORD curve




Scheme 1.

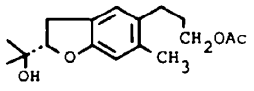
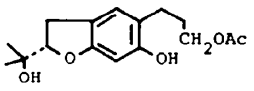
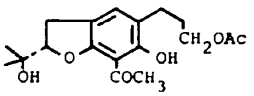
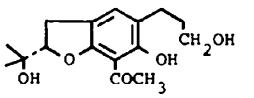
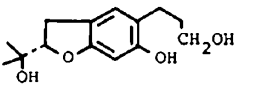
respectively. Treatment of **9** with LAH provided the triol **8** in 98% yield.

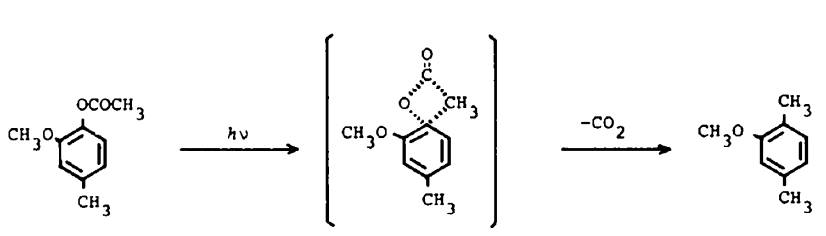
This (**8**) was treated with acetic anhydride-pyridine to give diacetyl triol (**10**) as an oily product. In the IR spectrum, **10** shows OH bands at 3670 and 3575 $cm^{-1}$, and phenolic and alcoholic acetate bands at 1750sh and 1730 $cm^{-1}$. In the NMR spectrum, it shows sharp 3H singlets due to two acetyl Me groups at 2.03 and 2.27 $\delta$, and a methylene signal at 4.04 $\delta$ which is shifted to the down field by 47 c/s when compared with the corresponding signals of the starting triol (**8**), indicating that acetylation took place at a primary alcohol of **8**. These data supported the structure of the diacetate (**10**).

Irradiation of an ethanolic 0.04 M solution of **10** with a medium pressure mercury lamp (200 W) afforded a mixture of five products (Table 2) with recovery of a small amount of the starting material (**10**). Each component was separated by column chromatography.

The first product (**11**) was obtained as a colourless oil. In the mass spectrum, the parent peak appeared at *m/e* 292 corresponding to the molecular formula $C_{17}H_{24}O_4$. The NMR spectrum disclosed the presence of an arylmethyl group in place of an acetoxy group of the starting diacetate (**10**) by the appearance of a 3H sharp singlet at 2.23 $\delta$. In 1968, Bradshaw[7] reported that the photo-reaction of creosol (**15**) gave 2-

Table 2. Photo-reaction products of diacetylhexahydromarmesin (10)

| Product | No | Yield(%) | Product | No | Yield(%) |
|---|---|---|---|---|---|
|  | 11 | 4.3 |  | 13 | 12.7 |
|  | 12 | 30.6 |  | 14 | 3.7 |
|  | 8 | 1.4 | | | |



(15) (16)

Scheme 2

methoxy-*p*-xylene (**16**) and proposed a mechanism shown in Scheme 2. Based on this, the arylmethyl product was depicted by the formula **11**.

The major product (**12**) was obtained as a yellow oil. In the high resolution mass spectrum of **12**, the observed value of the parent peak (*m/e* 336.159) coincides with the calculated value (*m/e* 336.157) for the molecular formula $C_{18}H_{24}O_6$. In the NMR spectrum, it shows an aromatic proton and an H-bonded OH proton at 7.07 and 12.86 $\delta$, respectively. Hydrolysis of **12** with 10% KOH aq gave an alcohol (**14**) which shows a CO band at 1625 $cm^{-1}$ in the IR spectrum. These data strongly indicated that **12** is a desired photo-Fries rearrangement product.

Other three products (**13**, **14** and **8**) were confirmed as de-acetylated products of the starting diacetate (**10**) or of the desired photo-Fries rearrangement product (**12**). Norrish type I reaction of **10** and **12** explained the formation of them.

Methylation of the photo-Fries rearrangement product (**12**) followed by Baeyer–Villiger oxidation provided an oily acetate (**18**). In the IR spectrum, this acetate (**18**) shows a newly born phenol-acetate band at 1765 $cm^{-1}$ together with an aliphatic acetate band at 1730 $cm^{-1}$ in a CO region. In the NMR spectrum, **18** shows a 3H singlet attributable to a phenol acetate group at 2.32 $\delta$, demonstrating the Baeyer Villiger reaction proceeded in the desired direction.

Hydrolysis of **18** followed by methylation gave a dimethoxy-diol (**5**) as an oily product which was characterized as a benzoate (**20**), m.p. 67.5–69°.

On the other hand, hexahydrorutaretin methyl ether (**21**) was prepared by the similar treatment of rutaretin methyl ether (**1**) in the case of *S*-marmesin (**2**). Methylation of the hexahydro-derivative (**21**) afforded methyl hexahydrorutaretin methyl ether (**5**) which was identical with a sample of the dimethoxy-diol (**5**) prepared from *S*-marmesin (**2**).

Since both the derivatives have the same negative Cotton effect in the CD curve, we may safely deduce that the absolute configuration of rutaretin methyl ether (**1**) should be depicted as *S*.

It should be noted here that *R*-dihydrocolumbianetin (**22**) and *S*-dihydromarmesin (**9**) [and *S*-dihydrorutaretin methyl ether (**23**)] has an opposite sign of Cotton effect in the CD although the parent coumarins of these derivatives have the same positive Cotton effect. These facts imply that the sign of the Cotton effect of a coumarin derivative does not reflect the absolute configuration but that of a dihydrocoumarin derivative would provide good diagnostic information about a chiral center (Table 1).

## EXPERIMENTAL

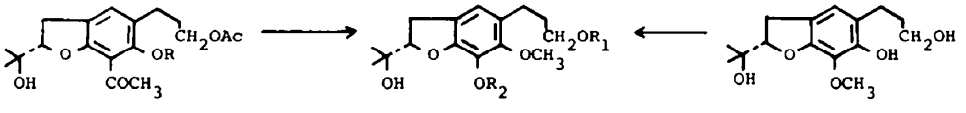
All m.ps were measured on a micro-melting hot-stage (Yanagimoto) and are uncorrected. IR, NMR with TMS as internal reference, and mass spectra (MS) were obtained with Hitachi EPI-G3, JEOL JNM-MH-100, and Hitachi RMU-6E spectrometers, respectively. Optical rotations were taken with JASCO DIP-SL polarimeter. ORD and CD measurements were carried out on JASCO J-20 spectropolarimeter. Irradiation was performed with medium pressure Hg lamp (Nitsuko Sekiei). For column chromatography, silicic acid (100 mesh, Mallinkrodt) and Kieselgel H nach Stahl (Merck) were used. For tlc, Kieselgel $GF_{254}$ nach Stahl (Merck) was used.

*Isolation of S-rutaretin methyl ether* (**1**), *S-marmesin* (**2**), *and R-columbianetin* (**3**). As reported,[2] **1**, **2** and **3** were isolated in 0.010%, 0.059%, and 0.007% yield from the root wood[2a] of *X. arnottianum*, and 0.105, 0.197 and 0.081% yield from the xylem[2b] of the same plant, respectively, together with a lot of miscellaneous compounds.

(*a*) *Rutaretin methyl ether* (**1**). Colourless prisms, m.p. 147–148° (lit.[5] m.p. 133°), $[\alpha]_D^{14}$ +10.8° (*c* 0.895, $CHCl_3$); $[\alpha]_D^{18}$ −41.0° (*c* 1.00, MeOH). CD (*c* 1.3 × $10^{-4}$, MeOH) $[\theta]_{335}$ −5226, $[\theta]_{255}$ −2576; CD (*c* 1.2 × $10^{-4}$, $CHCl_3$) $[\theta]_{335}$ −865, $[\theta]_{290}$ +865. The ORD curve of the coumarin gifted by Prof. Schneider was measured in our laboratory and identified with that of our sample.

(*b*) *S-Marmesin* (**2**). Colourless pillars, m.p. 192–193° (lit.[3a] m.p. 189.5°), $[\alpha]_D^{18}$ +28.8° (*c* 1.24, $CHCl_3$) (lit.[3a] $[\alpha]_D^{34}$ +26.8° ($CHCl_3$)]; $[\alpha]_D^{20}$ −16.0 (*c* 1.00, MeOH). CD (*c* 4.1 × $10^{-4}$, MeOH) $[\theta]_{335}$ −5405, $[\theta]_{252}$ −3003; CD (*c* 4.3 × $10^{-4}$, $CHCl_3$) $[\theta]_{335}$ −918, $[\theta]_{290}$ +1263.

(*c*) *R-Columbianetin* (**3**). Colourless needles, m.p. 166–166.5° (m.p. 164.5–165°[4a] reported for *S*-columbianetin).



(12) : R=H
(17) : R=$CH_3$

(18) : $R_1$=$R_2$=Ac
(19) : $R_1$=$R_2$=H
(5) : $R_1$=H, $R_2$=$CH_3$
(20) : $R_1$=$COC_6H_5$, $R_2$=$CH_3$

(21)

Scheme 3.

$[\alpha]_D^{15}$ −185.3° (c 0.973, dioxane), $[\alpha]_D^{11}$ −188.3° (c 1.04, $CHCl_3$), $[\alpha]_{365}^{16.5}$ −262.0° (c 1.01, MeOH). CD (c 4.2 × 10⁻⁴, MeOH) $[\theta]_{333}$ −15994; CD (c 4.3 × 10⁻⁴, $CHCl_3$) $[\theta]_{333}$ −9180, $[\theta]_{320}$ +1148.

*Ozonolysis of* R-*columbianetin* (**3**). [R-*dihydro*-4-*hydroxy*-5,5-*dimethyl*-2(3H)*furanone* (**6b**)]: $O_3$ was bubbled through a soln of **3** (300 mg) in anhyd $CHCl_3$ (15 ml) for 1.5 hr at a flow rate of 600 l/hr. The mixture was evaporated to dryness *in vacuo*. The residue was dissolved into $H_2O$ (12 ml) and heated at 80–100° for 30 min. After addition of 2N KOH (4 ml) and 35% $H_2O_2$ aq. (500 mg), the mixture was kept at room temp for 1 hr, heated at 50° for 30 min, and diluted with water (10 ml). Excess of $H_2O_2$ was decomposed by bubbling $SO_2$ gas until the soln became acidic to Congo Red. After removal of a soluble fraction in $CHCl_3$, the mixture was extracted with $Et_2O$ for 10 days. The ethereal soln was dried over $K_2CO_3$ and evaporated to give a colourless oil (25 mg). IR $\nu_{max}^{CHCl_3}$ cm⁻¹: 3610, 3410 (OH), 1773 (CO). NMR ($CDCl_3$) δ: 1.39, 1.45 (each 3H, s, C-$CH_3$), 2.00 (1H, br s, OH), 2.52 (1H, d.d, J = 18.0, 3.5 Hz, >CH $CH_AH_B$CO), 2.96 (1H, d.d, J = 18.0, 6.5 Hz, >CH $CH_AH_B$CO), 4.20 (1H, d.d, J = 6.5, 3.5 Hz, $-C(OH)CH_2$). ORD (c 9.49 × 10⁻⁴, $CHCl_3$) $[\phi]_{650}$ +41°, $[\phi]_{400}$ +71°, $[\phi]_{360}$ +200°. *3,5-Dinitrobenzoate*: A mixture of **6b** (57.6 mg), pyridine (1.5 ml), 3,5-dinitrobenzoyl chloride (240 mg) in abs benzene (1 ml) was heated at 65° for 2 min, cooled, and diluted with benzene (12 ml). The mixture was washed with 1N HCl and then a soln of $NaHCO_3$ (300 mg) in half-sat NaCl aq (12 ml). The mixture was dried over $K_2CO_3$ and evaporated to dryness. Preparative tlc of the residue on $SiO_2$ [$CHCl_3$–AcOEt = 5:1 (v/v), $R_f$ = 0.50] gave pale yellow fine needles (23.5 mg), m.p. 150° (lit.[8] m.p. 150–151.5°), which were recrystallized from $Et_2O$–benzene. IR $\nu_{max}^{CHCl_3}$ cm⁻¹: 1780, 1740 (CO). NMR ($CDCl_3$) δ: 1.55 (6H, s, C-$CH_3$ × 2), 2.77 (1H, d.d, J = 20.0, 2.5 Hz, >CH $CH_AH_B$CO), 3.26 (1H, d.d, J = 6.5, 20.0 Hz, >CHCH$_A$H$_B$CO), 5.53 (1H, d.d, J = 6.5, 2.5 Hz, $-CHCH_2$), 9.05–9.20 (2H, m, arom. H), 9.20–9.30 (1H, m, arom. H).

*Ozonolysis of* S-*marmesin* (**2**). [S-*dihydro*-4-*hydroxy*-5,5-*dimethyl*-2(3H)*furanone* (**6a**)]. Treatment of **2** (300 mg) with $O_3$ according to the above method gave a colourless oil (180 mg) which shows the same physical data as **6b** except ORD (c 1.0 × 10⁻³, $CHCl_3$) $[\phi]_{650}$ −18°, $[\phi]_{400}$ −33°, $[\phi]_{360}$ −123°]. *3,5-Dinitrobenzoate*: A mixture of **6a** (77.5 mg), pyridine (1.5 ml) and 3,5-dinitrobenzoyl chloride (250 mg) in abs benzene (1 ml) was treated as the corresponding hydroxylactone obtained from **3** to give pale yellow prisms (22.1 mg), m.p. 153°, which shows the same physical data with the benzoate prepared from **6b**.

*Catalytic reduction of* S-*marmesin* (**2**). A soln of **2** (2.00 g) in EtOH (100 ml) was hydrogented over $PtO_2$ (0.71 g) under 30 atm pressure and room temp for 46 hr. The catalyst was filtered off and the filtrate was evaporated to dryness *in vacuo*. The residue was dissolved in $CHCl_3$ and chromatographed on $SiO_2$.

(*a*) S-*Dihydromarmesin* (**9**). Elution with $CHCl_3$ gave a colourless solid (0.77 g), which was recrystallized from benzene–hexane to give colourless prisms, m.p. 131–131.5° (lit.[9] m.p. 135°). IR $\nu_{max}^{CHCl_3}$ cm⁻¹: 3570 (OH), 1740 (CO). CD (c 8.4 × 10⁻⁴, MeOH) $[\theta]_{288}$ −2442; CD (c 8.3 × 10⁻⁴, $CHCl_3$) $[\theta]_{294}$ −1224.

(*b*) S-*Hexahydromarmesin* (*triol*) (**8**). Elution with EtOAc gave a slightly yellow oil (0.74 g), which was distilled to give a colourless oil, b.p. 160° (1.6 × 10⁻⁴ mmHg). IR $\nu_{max}^{CHCl_3}$ cm⁻¹: 3580, 3340 (OH). NMR ($CDCl_3$) δ: 1.20, 1.30 (each 3H, s, C-$CH_3$), 1.77 (2H, dif. t, J = 6.5 Hz, $CH_2CH_2CH_2$), 2.61, 3.57 (each 2H, t, J = 6.5 Hz, $ArCH_2CH_2CH_2O$), 2.99 (2H, d, J = 10.0 Hz, >CHC$H_2$Ar), 4.53 (1H, t, J = 10.0 Hz, $OCHCH_2$), 6.31, 6.77 (each 1H, s, arom. H). MS *m/e*: 252 ($M^+$, 64.7%), 83 (100%). CD (c 4.3 × 10⁻³, MeOH) $[\theta]_{292}$ −2435.

When the mixture formed by catalytic reduction of **2** was directly treated with LAH, this material (**8**) could be obtained in 97.6% yield from starting marmesin (**2**).

*Reduction of* S-*dihydromarmesin* (**9**) *with LAH*. A soln of **9** (0.249 g) in abs THF (5 ml) was added to a suspension of LAH (0.1895 g) in dry $Et_2O$ (6 ml) with stirring under ice-cooling. The mixture was stirred at room temp for 1 hr and, then, refluxed for 2 hr. After decomposition of excess LAH by addition of EtOAc and wet $Et_2O$ followed by 10% $H_2SO_4$ aq., the mixture was extracted with $Et_2O$. The ethereal soln was dried over $MgSO_4$, and evaporated to give a colourless oil (0.248 g) which was identical with **8**.

S-*Diacetyldehydromarmesin* (**10**). To a soln of **8** (5.947 g) in dry $Et_2O$ (59.4 ml) was added $Ac_2O$ (18.063 g) and pyridine (18.869 g). The mixture was allowed to stand at room temp for 3 hr, poured into ice-water, and then, extracted with $Et_2O$. The ethereal extract was washed with sat $CuSO_4$ aq, dried over $K_2CO_3$, and evaporated to dryness to give colourless oil (6.550 g). IR $\nu_{max}^{CHCl_3}$ cm⁻¹: 3670, 3575 (OH), 1750 sh, 1730 (CO). NMR ($CDCl_3$) δ: 1.19, 1.31 (each 3H, s, C-$CH_3$), 1.80 (2H, m, $CH_2CH_2CH_2$), 2.03, 2.27 (each 3H, s, $COCH_3$), 2.47–4.04 (each 2H, t, J = 7.0 Hz, $ArCH_2CH_2CH_2O$), 3.08 (2H, d, J = 8.5 Hz, >CHC$H_2$Ar), 4.59 (1H, t, J = 8.5 Hz, $OCHCH_2$), 6.42, 6.96 (each 1H, s, arom. H). MS *m/e*: 336 ($M^+$, 23.6%), 176 (100%). This material was used for the next reaction without further purification.

*Photo-Fries rearrangement of the diacetate* (**10**). A soln of **10** (6.257 g) in 95% EtOH (465 ml) was irradiated for 10.7 hr under $N_2$ with ice-cooling. Evaporation of the solvent under reduced pressure gave a brown oil (6.485 g), which was dissolved in a mixed solvent, $CHCl_3$–benzene (1:1 (v/v)] and chromatographed on $SiO_2$.

(*a*) S-3-[2,3-*Dihydro*-2-(1-*hydroxy*-1-*methylethyl*)-6-*methyl*-5-*benzofuranyl*]-1-*propanol acetate* (**11**). The first elution with $CHCl_3$–benzene [1:1 (v/v)] gave a colourless oil (0.255 g) which was purified by repeating column chromatography on $SiO_2$. IR $\nu_{max}^{CHCl_3}$ cm⁻¹: 3575, 3450 (OH), 1725 (CO). NMR ($CDCl_3$) δ: 1.20, 1.31 (each 3H, s, C-$CH_3$), 1.83 (2H, m, $CH_2CH_2CH_2$), 2.04 (3H, s, $OCOCH_3$), 2.23 (3H, s, Ar $CH_3$), 2.58, 4.09 (each 2H, t, J = 7.0 Hz, $ArCH_2CH_2CH_2O$), 3.07 (2H, d, J = 9.0 Hz, >CHC$H_2$Ar), 4.55 (1H, t, J = 9.0 Hz, $OCHCH_2$), 6.56, 6.90 (each 1H, s, arom. H). MS *m/e*: 292 ($M^+$, 22.6%), 147 (100%).

(*b*) S-3-[2,3-*Dihydro*-6-*hydroxy*-2-(1-*hydroxy*-1-*methylethyl*)-7-*methylcarbonyl*-5-*benzofuranyl*]-1-*propanol acetate* (**12**). The second elution with $CHCl_3$–benzene (1:1 (v/v)] gave a yellow oil (1.915 g) which was purified by repeating column chromatography on $SiO_2$. High resolution MS: 336.159 ($M^+$) ($C_{18}H_{24}O_6$ requires: 336.157). IR $\nu_{max}^{CHCl_3}$ cm⁻¹: 3690, 3600 (OH), 1735, 1635 (CO). NMR ($CDCl_3$) δ: 1.26, 1.37 (each 3H, s, C-$CH_3$), 1.82 (1H, s, OH, exchangeable), 1.90 (2H, m, $CH_2CH_2CH_2$), 2.05, 2.65 (each 3H, s, $COCH_3$), 2.61–4.07 (each 2H, t, J = 7.0 Hz, $ArCH_2CH_2CH_2O$), 3.09 (2H, d, J = 9.0 Hz, >CHC$H_2$Ar), 4.72 (1H, t, J = 9.0 Hz, $OCHCH_2$), 7.07 (1H, s, arom. H), 12.86 (1H, s, OH, exchangeable). MS *m/e*: 336 ($M^+$, 96.1%), 190 (100%).

Hydrolysis of **12** (0.0470 g) with 10% KOH aq (1 ml) in EtOH (1 ml) afforded **14**, as a yellow oil (0.0295 g) which was identical with the other photo-Fries reaction product (**14**) *vide infra*.

(*c*) *Recovery of the starting diacetate* (**10**). Subsequent elution with the same mixed solvent afforded the starting **10** (0.142 g).

(*d*) S-3-[2,3-*Dihydro*-6-*hydroxy*-2-(1-*hydroxy*-1-*methylethyl*)-5-*benzofuranyl*]-1-*propanol acetate* (**13**). Elution with $CHCl_3$ gave a colourless oil (0.674 g). Purification of the oily product due to column chromatography on $SiO_2$ yielded fine needles (0.390 g), m.p. 97–98°, which were recrystallized from benzene–$Et_2O$–hexane. IR $\nu_{max}^{CHCl_3}$ cm⁻¹: 3670, 3585, 3370 (OH), 1728 (CO). NMR ($CDCl_3$) δ: 1.19, 1.29 (each 3H, s, C-$CH_3$), 1.84 (2H, m, $CH_2CH_2CH_2$), 2.03 (3H, s, $COCH_3$), 2.43, 6.57 (each 1H, s, OH, exchangeable), 2.57–4.07 (each 2H,

t, J = 7.5 Hz, $ArCH_2CH_2CH_2O$), 3.01 (2H, d, J = 8.5 Hz, $>CHCH_2Ar$), 4.55 (1H, t, J = 8.5 Hz, $OCHCH_2$), 6.25, 6.81 (each 1H, s, arom H). MS *m/e*: 294 ($M^+$, 37.4%), 176 (100%). (Found: C, 65.24; H, 7.63. $C_{16}H_{22}O_5$ requires: C, 65.29; H, 7.53).

(*e*) S-3-[2,3-*Dihydro*-6-*hydroxy*-2-(1-*hydroxy*-1-*methylethyl*)-7-*methylcarbonyl*-5-*benzofuranyl*]-1-*propanol* (**14**). Elution with $CHCl_3$–EtOAc [1:1 (v/v)] gave a yellow oil (0.219 g), which was purified by repeating column chromatography. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3680, 3600 (OH), 1625 (CO). NMR ($CDCl_3$) $\delta$: 1.24, 1.36 (each 3H, s, C–$CH_3$), 1.77 (2H, m, $CH_2CH_2CH_2$), 2.17 (2H, br. s, OH × 2), 2.63, 3.56 (each 2H, t, J = 7.0 Hz, $ArCH_2CH_2CH_2O$), 2.65 (3H, s, $COCH_3$), 3.09 (2H, d, J = 9.0 Hz, $>CHCH_2Ar$), 4.71 (1H, t, J = 9.0 Hz, $OCHCH_2$), 7.09 (1H, s, arom H), 13.01 (1H, s, OH).

(*f*) *The triol* (**8**). The subsequent elution with $CHCl_3$–EtOAc [1:1 (v/v)] gave a colourless oil (66 mg) which was identical with an authentic sample of **8** with respect to IR spectrum.

S-3-[2,3-*Dihydro*-2-(1-*hydroxy*-1-*methylethyl*)-6-*methoxy*-7-*methylcarbonyl*-5-*benzofuranyl*]-1-*propanol acetate* (**17**). To a soln of **12** (292 mg) in dry acetone (30 ml) was added anhydr $K_2CO_3$ (480 mg) and MeI (0.54 ml) and then the mixture was refluxed for 11 hr and then for a further 10 hr. Inorganic substance was filtered off and the solvent was evaporated under reduced pressure. The residue was dissolved in water and extracted with $Et_2O$. The ethereal soln was washed with $H_2O$, dried over $K_2CO_3$, and evaporated to dryness to give a pale yellow oil (335 mg). IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3650, 3590, 3450 (OH), 1725, 1680 (CO). NMR ($CDCl_3$) $\delta$: 1.21, 1.31 (each 3H, s, C–$CH_3$), 1.87 (2H, m, $CH_2CH_2CH_2$), 2.04, 2.56 (each 3H, s, $COCH_3$), 2.43 (1H, s, OH, exchangeable), 2.59, 4.08 (each 2H, t, J = 7.0 Hz, $ArCH_2CH_2CH_2O$), 3.08 (2H, dif. d, J = 9.0 Hz, $>CHCH_2Ar$), 3.71 (3H, s, $OCH_3$), 4.63 (1H, t, J = 9.0 Hz, $OCHCH_2$), 7.00 (1H, s, arom. H). MS *m/e*: 350 ($M^+$, 100%).

S-3-[2,3-*Dihydro*-7-*hydroxy*-2-(1-*hydroxy*-1-*methylethyl*)-6-*methoxy*-5-*benzofuranyl*]-1-*propanol diacetate* (**18**). To an ice-cooled HCOOH (10 g) was added 35% $H_2O_2$ aq (1 g) and then the mixture was allowed to stand at room temp for 1 hr. The performic acid soln prepared above was added to a soln of **17** (50 mg) in HCOOH (1 g) under ice-cooling. The mixture was allowed to stand at room temp for 8 hr. After decomposition of excess of the peracid by addition of $Na_2SO_3$ (100 mg), the mixture was poured into $H_2O$ and extracted with $Et_2O$. The ethereal soln was dried over $K_2CO_3$ and evaporated to dryness to give a yellow oil (35 mg). High resolution MS: 336.170 ($M^+$) ($C_{19}H_{26}O_5$ requires: 336.168). IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3600 (OH), 1765 sh, 1730 (CO). NMR ($CDCl_3$) $\delta$: 1.17, 1.29 (each 3H, s, C–$CH_3$), 1.85 (2H, m, $CH_2CH_2CH_2$), 2.03, 2.32 (each 3H, s, $COCH_3$), 2.59, 4.08 (each 2H, t, J = 7.0 Hz, $ArCH_2CH_2CH_2O$), 3.14 (2H, d, J = 9.0 Hz, $>CHCH_2Ar$), 3.76 (3H, s, $OCH_3$), 4.63 (1H, t, J = 9.0 Hz, $OCHCH_2$), 6.80 (1H, s, arom H). MS *m/e*: 366 ($M^+$, 28.2%), 266 (100%).

S-3-[2,3-*Dihydro*-7-*hydroxy*-2-(1-*hydroxy*-1-*methylethyl*)-6-*methoxy*-5-*benzofuranyl*]-1-*propanol* (**19**). A soln of **18** (268 mg) in EtOH (13 ml) involving 10% NaOH aq (1 ml) was allowed to stand at room temp for 10 hr. The mixture was made slightly acidic with 10% HCl aq and repeatedly extracted with EtOAc. The organic layer was dried over $MgSO_4$ and evaporated to dryness to give a yellowish brown oil (215 mg). IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3700, 3550 (OH). NMR ($CDCl_3$) $\sigma$: 1.20, 1.33 (each 3H, s, C–$CH_3$), 1.80 (2H, m, $CH_2CH_2CH_2$), 2.63, 3.58 (each 2H, t, J = 7.0 Hz, $ArCH_2CH_2CH_2O$), 3.07 (2H, d, J = 9.0 Hz, $>CHCH_2Ar$), 3.80 (3H, s, $OCH_3$), 4.64 (1H, t, J = 9.0 Hz, $OCHCH_2$), 6.48 (1H, s, arom. H). MS *m/e*: 282 ($M^+$, 100%). This material was used for the following step without purification.

S-3-[2,3-*Dihydro*-6,7-*dimethoxy*-2-(1-*hydroxy*-1-*methylethyl*)-5-*benzofuranyl*]-1-*propanol* (*dimethoxy-diol*) (**5**). A mixture of **19** (50 mg), anhydr $K_2CO_3$ (100 mg), and MeI (0.1 ml) in dry acetone (4 ml) was refluxed for 4 hr, poured into $H_2O$, and extracted with EtOAc. The EtOAc soln was dried over $K_2CO_3$ and evaporated to dryness *in vacuo*. Preparative tlc of the residue on $SiO_2$ [$CHCl_3$:EtOAc = 1:1 (v/v), $R_f$ = 0.45] gave a colourless oil (38 mg). High resolution MS: 296.165 ($M^+$) ($C_{16}H_{24}O_5$ requires: 296.162). IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3675, 3580, 3470 (OH). NMR ($CDCl_3$) $\delta$: 1.23, 1.35 (each 3H, s, C–$CH_3$), 1.79 (2H, m, $CH_2CH_2CH_2$), 2.62, 3.58 (each 2H, t, J = 7.0 Hz, $ArCH_2CH_2CH_2O$), 3.09 (2H, d, J = 9.0 Hz, $>CHCH_2Ar$), 3.84, 3.96 (each 3H, s, $OCH_3$), 4.64 (1H, t, J = 9.0 Hz, $OCHCH_2$), 6.64 (1H, s, arom. H). MS *m/e*: 296 ($M^+$, 100%). CD (c 7.1 × 10$^{-4}$, MeOH) $[\theta]_{284}$ −2064.

*Dimethoxy-diol benzoate* (**20**). A mixed soln of **5** (69 mg) and benzoyl chloride (0.5 ml) in pyridine (0.7 ml) was kept at room temp for 3.5 hr, poured onto ice-water, and extracted with $Et_2O$. The ethereal soln was washed with sat $CuSO_4$ aq and dried over $K_2CO_3$ and evaporated to dryness. Preparative tlc [$CHCl_3$–EtOAc = 5:1 (v/v), $R_f$ = 0.21] of the residue gave colourless needles (69 mg), m.p. 67.5–69°, which were recrystallized from $Et_2O$–hexane. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3580 (OH), 1705 (CO). NMR ($CDCl_3$) $\delta$: 1.20, 1.33 (each 3H, s, C–$CH_3$), 2.00 (2H, m, $CH_2CH_2CH_2$), 2.68, 4.32 (each 2H, t, J = 6.5 Hz, $ArCH_2CH_2CH_2O$), 3.08 (2H, d, J = 9.0 Hz, $>CHCH_2Ar$), 3.81, 3.93 (each 3H, s, $OCH_3$), 4.60 (1H, t, J = 9.0 Hz, $OCHCH_2$), 6.64 (1H, s, arom. H), 7.30–7.60 (3H, m, arom. H), 7.96–8.08 (2H, m, arom. H). CD (c 5.0 × 10$^{-4}$, MeOH) $[\theta]_{300}$ +199, $[\theta]_{284}$ −1572. (Found: C, 68.95; H, 7.15. $C_{23}H_{28}O_6$ requires: C, 68.98; H, 7.05%).

This material was identical with an authentic sample of the benzoate which was prepared from the Me derivative of **21**.

*Dihydrorutaretin methyl ether*[a] (**23**). A soln of **1** (2.00 g) in EtOH (100 ml) was hydrogenated over $PtO_2$ (1.00 g) under 30 atm pressure and at room temp for 12 hr. After removal of the catalyst by filtration, the filtrate was evaporated to dryness *in vacuo*. Purification of the residue by column chromatography on $SiO_2$ gave colourless oily product (1.791 g). IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3670, 3580, 3510 (OH), 1770 (CO). NMR ($CDCl_3$) $\delta$: 1.23, 1.35 (each 3H, s, C–$CH_3$), 1.82 (1H, s, OH, exchangeable), 2.60–3.00 (4H, m, $ArCH_2CH_2CO$), 3.14 (2H, d, J = 9.0 Hz, $>CHCH_2Ar$), 3.97 (3H, s, $OCH_3$), 4.66 (1H, t, J = 9.0 Hz, $OCHCH_2$), 6.65 (1H, s, arom H). CD (c 8.2 × 10$^{-4}$, MeOH) $[\theta]_{289}$ −1471.

*Hexahydrorutaretin methyl ether* (**21**). A soln of **23** (910 mg) in dry THF (18 ml) was gradually added to an ice-cooled suspension of LAH (500 mg) in $Et_2O$ (20 ml) with stirring. The mixture was stirred at room temp for 1 hr and then refluxed for 1 hr. After decomposition of the excess LAH with EtOAc the mixture was acidified with 10% $H_2SO_4$ aq and extracted with $Et_2O$ and then EtOAc. The organic solns were combined, dried over $MgSO_4$, and evaporated to dryness. The residue was chromatographed on $SiO_2$ to give colourless prisms (714 mg), m.p. 96.5–97.5°, which was recrystallized from benzene. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3640 sh, 3550 sh, 3490, 3390 (OH). NMR ($CDCl_3$) $\delta$: 1.23, 1.34 (each 3H, s, C–$CH_3$), 1.80 (2H, m, $CH_2CH_2CH_2$), 2.65, 3.60 (each 2H, t, J = 7.0 Hz, $ArCH_2CH_2CH_2O$), 3.07 (2H, d, J = 9.0 Hz, $>CHCH_2Ar$), 3.32 (3H, br. s, OH, exchangeable), 3.99 (3H, s, $OCH_3$), 4.64 (1H, t, J = 9.0 Hz, $OCHCH_2$), 6.60 (1H, s, arom. H).

*Methylation of hexahydrorutaretin methyl ether* (**21**) [methyl hexahydrorutaretin methyl ether (**5**)]. A mixture of **21** (250 mg), anhydr $K_2CO_3$ (497 mg), and MeI (0.55 ml) in dry acetone (20 ml) was refluxed for 5 hr, poured into $H_2O$, and

[a] In the cases of **1** and **3**, catalytic hydrogenation under the same condition used by us afforded a dihydro derivative as a sole product.

extracted with EtOAc. The EtOAc soln was dried over $K_2CO_3$ and evaporated to dryness *in vacuo*. The residual oily product (235 mg) was identified with a sample of **5** prepared from **2**. CD ($c$ $6.4 \times 10^{-4}$, MeOH) $[\theta]_{284} -1873$. *The benzoate* (**20**). The above **5** (50 mg) was treated with benzoyl chloride (0.06 ml) as the corresponding product prepared from **2** to give colourless needles, m.p. 69–70° (42.7 mg) identical with a sample of **20**. CD ($c$ $5.2 \times 10^{-4}$, MeOH) $[\theta]_{300} +154$, $[\theta]_{283.5} -1574$.

R-*Dihydrocolumbianetin*[a] (**22**). A soln of **3** (200 mg) in EtOH (50 ml) was hydrogenated over $PtO_2$ (100 mg) under 30 atm pressure and at room temp for 14 hr. After removal of catalyst by filtration, the filtrate was evaporated to dryness *in vacuo*. Purification of the residue by column chromatography on $SiO_2$ gave colourless cottony needles (129 mg), m.p. 115.5–117° (lit. m.p. 112–113°,[a] m.p. 111.5–112.5°,[4b] m.p. 113.7–114.5°[4c]) which were recrystallized from $Et_2O$-hexane-benzene. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3505 (OH), 1740 (CO). NMR ($CDCl_3$) $\delta$: 1.20, 1.32 (each 3H, s, C-$CH_3$), 1.86 (1H, s, OH, exchangeable), 2.64–3.00 (4H, m, $ArCH_2CH_2CO$), 3.16 (2H, d, $J = 9.0$ Hz, $OCHCH_2Ar$), 4.64 (1H, t, $J = 9.0$ Hz, $OCHCH_2$), 6.49, 6.90 (each 1H, d, $J = 8.0$ Hz, arom. H). CD ($c$ $8.3 \times 10^{-4}$, MeOH) $[\theta]_{283} +907$. CD ($c$ $8.0 \times 10^{-4}$, $CHCl_3$) $[\theta]_{292} -75$, $[\theta]_{283} +225$. (Found: C, 67.71; H, 6.58. $C_{14}H_{16}O_4$ requires: C, 67.73; H, 6.50%).

*Acknowledgements*—We with to thank Prof. J. Lemmich of the Royal Danish School of Pharmacy for sending a detail experimental data for preparation of dihydro-4-hydroxy-5,5-dimethyl-2 (3H) furanone 3,5-dinitrobenzoate. We also wish to thank Prof. T. O. Soine of University of Minnesota and Prof. G. Schneider of Walfgang Goethe Universitat for the gift of a sample of S-columbianetin and rutaretin methyl ether, respectively.

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