Phytochemistry, 1980, Vol. 19, pp. 281–284. © Pergamon Press Ltd. Printed in England. 0031-9422/80/0201-0281 $02.00/0

NEW COUMARINS FROM THE UMBELS OF *SESELI SIBIRICUM*

SUNIL K. BANERJEE, BISHAN D. GUPTA, RAMAN KUMAR and C. K. ATAL

Regional Research Laboratory (C.S.I.R.), Jammu-Tawi, India

(*Revised received* 7 *June* 1979)

Key Word Index—*Seseli sibiricum*; Umbelliferae; umbels; coumarins; 2H-1-benzopyran-2-one; seselinal; sesibiricol; sibirinol; isosibiricin; sesibiricin; osthol; coumurrayin; sesebrin; sesebrinol; sibiricin; imperatorin; bergapten; xanthotoxin; isopimpinellin; mexoticin.

Abstract—Three new coumarins, seselinal, sesibiricol and sibirinol, and 12 known coumarins have been isolated from the umbels of *Seseli sibiricum*. The new coumarins have been characterized as 5, 7-dimethoxy-8-(2-methyl-2-formylpropyl)-2H-1-benzopyran-2-one, 5-(3-methylbut-2-enyloxy)-7-methoxy-8-(2-hydroxy-3-methylbut-3-enyl)-2H-1-benzopyran-2-one and 5,7-dimethoxy-8-(2-hydroxy-3-methylbut-3-enyl)-2H-1-benzopyran-2-one, respectively. The known ones were identified as sesibiricin, isosibiricin, osthol, coumurrayin, sesebrin, sesebrinol, sibiricin, imperatorin, bergapten, xanthotoxin, isopimpinellin and mexoticin.

INTRODUCTION

Investigation [1, 2] on *Seseli sibiricum* Benth, has led to the isolation of two coumarins, osthol and sesibiricin, from its roots. Recently we reported [3] the isolation and structures of three new coumarins, sesebrin, sesebrinol and sibiricol, from the roots in addition to the isolation of nine known coumarins, including osthol and sesibiricin. From the umbels, isolation of four coumarins (viz. osthol, imperatorin, bergapten and sibiricin) has been reported [4]. The present communication deals with the isolation of eleven additional coumarins from the umbels.

RESULTS AND DISCUSSION

The umbels of *S. sibiricum* were extracted with hexane. The extract on chromatography yielded osthol, imperatorin, bergapten, sibiricin [4], sesibiricin, coumurrayin, xanthotoxin, isopimpinellin, isosibiricin, sesebrin [3], sesebrinol [3], mexoticin and three new coumarins for which we propose the names seselinal, sesibiricol and sibirinol.

Seselinal (M^+ 290), mp 174–175°, has been assigned the structure 5,7-dimethoxy-8-(2-methyl-2-formylpropyl)-2H-1-benzopyran-2-one (**1**) on the basis of ^1H NMR data (Table 1). The presence of the aldehyde function in **1** was confirmed from its IR spectrum which showed characteristic bands at 2735 and 2842 cm^{-1}. The MS fragmentation pattern of seselinal was in agreement with structure **1**, significant peaks appearing at *m/e* 261, 219 (base peak), 206, 189, 161 and 133. Synthesis of seselinal (**1**) from the epoxide sibiricin (**4**) was achieved by treating **4** with BF_3–etherate followed by water, during which **4** underwent fission–rearrangement to form a mixture of **1** and isosibiricin (**5**) in almost equal amounts which could be separated by PLC. Compound **10** on reflux with 5% aq. H_2SO_4 underwent pinacol–pinacolone rearrangement to form **1** and **5**. Compound **4** on similar treatment also gave **1** and **5** via pinacol (**10**) formation.

Sesibiricol (M^+ 344), mp 110–111°, has been characterized as 5-(3-methylbut-2-enyloxy)-7-methoxy-8-(3-methyl-2-hydroxybut-3-enyl)-2H-1-benzopyran-2-one (**2**). The presence of the secondary hydroxyl in **2** was confirmed by the formation of an acetate (**8**), the ^1H NMR of which showed a triplet at δ 5.41 (-CH_2-CH (OAc)-), a downfield shift of 1.10 from the corresponding proton in the alcohol (**2**). The MS data of sesibiricol were in agreement with structure **2**. Structure **2** for sesibiricol was confirmed by its synthesis from sesebrinol (**6**) which was isolated from the roots of *S. sibiricum* [3]. Sesebrinol (**6**) on treatment with Ac_2O–C_5H_5N formed the monoacetate (**7**) which underwent facile dehydration with $POCl_3$ to form sesibiricol acetate (**8**), the hydrolysis of which afforded sesibiricol (**2**).

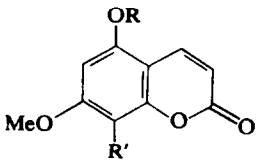
Sibirinol (M^+ 290), mp 121–122°, has been assigned the structure 5,7-dimethoxy-8-(2-hydroxy-3-methylbut-3-enyl)-2H-1-benzopyran-2-one (**3**). It showed a blue fluorescence in UV light. The hydroxyl group in sibirinol is secondary as the α-proton absorbed at δ 4.30 (*t*) (Table 1), shifting to 5.46 in the acetate (**9**). The MS of sibirinol supported structure **3**. Structure **3** for sibirinol was confirmed by its synthesis from mexoticin (**10**), isolated from the umbels during the present investigation. Mexoticin monoacetate (**11**), prepared by treating **10** with Ac_2O–C_5H_5N, was readily dehydrated with $POCl_3$ to give sibirinol acetate (**9**), hydrolysis of which afforded sibirinol (**3**).

Thus *S. sibiricum* has been found to contain a large number of closely related coumarins, viz. coumurrayin (**12**), sesibiricin (**13**), sibiricin (**4**), isosibiricin (**5**), mexoticin (**10**), sesebrin (**14**), sesebrinol (**6**), sesibiricol (**2**), sibirinol (**3**) and seselinal (**1**). Sibiricol (**15**) [3], also occurring in the plant, is presumably the precursor of

Table 1. ^{1}H NMR data of **1–3** (90 MHz, $CDCl_3$)*

Compound	H-3	H-4	H-6	Other groups	
1	6.11 *d* (10)	7.95 *d* (10)	6.29 *s*	OMe's:	3.88 *s*, 3.94 *s*
				Chain at C-8:	1.07 *s* (6*H*, *Me's*), 2.96 *s* (ϕ-C<u>H</u>$_2$-), 9.52 *s* (-CHO)
2	6.15 *d* (10)	8.04 *d* (10)	6.37 *s*	O Prenyl:	1.78 *s* (Me), 1.83 *s* (Me), 4.64 *d* (7), 5.56 *t* (7)
				OMe:	3.92 *s*
				Chain at *C*-8:	1.87 *s*(Me), 2.25 *s* (OH), 3.05 *dd* (7.5, 5.5) (ϕ-CH$_2$-), 4.31 *t* (7.5) (-CH$_2$-C<u>H</u>-), 4.82 *s* and 4.92 *s* (=CH$_2$)
3	6.15 *d* (10)	7.99 *d* (10)	6.35 *s*	OMe:	3.93 *s* (6H)
				Chain at C-8:	1.88*s* (Me, OH), 3.05 *dd* (7.5, 5.5) (ϕ-CH$_2$-), 4.30 *t* (7.5) (-CH$_2$-C<u>H</u>-), 4.82 *s* and 4.91 *s* (=CH$_2$)

*Chemical shifts are δ values; coupling constants (J in parentheses) are given in Hz.



1 R = Me; R′ = —CH$_2$—C(Me)(Me)—CHO

2 R = —CH$_2$—CH=CMe$_2$; R′ = —CH$_2$—CH(OH)—C(=CH$_2$)—Me

3 R = Me; R′ = —CH$_2$—CH(HO)—C(=CH$_2$)—Me

4 R = Me; R′ = —CH$_2$—CH(O)—CMe$_2$

5 R = Me; R′ = —CH$_2$COCHMe$_2$

6 R = —CH$_2$—CH=CMe$_2$; R′ = —CH$_2$—CH(OH)—CMe$_2$(OH)

7 R = —CH$_2$—CH=CMe$_2$; R′ = —CH$_2$—CH(OAc)—CMe$_2$(OH)

8 R = —CH$_2$—CH=CMe$_2$; R′ = —CH$_2$—CH(OAc)—C(=CH$_2$)—Me

9 R = Me; R′ = —CH$_2$—CH(OAc)—C(=CH$_2$)—Me

10 R = Me; R′ = —CH$_2$—CH(OH)—CMe$_2$(OH)

11 R = Me; R′ = —CH$_2$—CH(OAc)—CMe$_2$(OH)

12 R = Me; R′ = —CH$_2$—CH=CMe$_2$

13 R = R′ = —CH$_2$—CH=CMe$_2$

14 R = —CH$_2$—CH=CMe$_2$; R′ = —CH$_2$—CH(O)—CMe$_2$

R = H; R′ = —CH$_2$—CH=CMe$_2$

all these coumarins. Methylation and prenylation of **15** would give coumurrayin (**12**) and sesibiricin (**13**), respectively. The prenyl chain at C-8 can undergo a series of reactions, viz. epoxidation (to form epoxides, sibiricin (**4**) and sesebrin (**14**)), hydration of the epoxides (to form the diols, mexoticin (**10**) and sesebrinol (**6**)), dehydration of the diols (to form sibirinol (**3**) and sesibiricol (**2**)) and pinacol–pinacolone rearrangement of the diols (to form the aldehyde (**1**) or ketone (**5**)).

EXPERIMENTAL

Mps are uncorr. IR spectra were recorded in KBr. ^{1}H NMR spectra were recorded at 90 MHz in $CDCl_3$ unless otherwise stated with TMS as internal standard. TLC was carried out on Si gel G using C_6H_6–Me_2CO (9:1) as solvent. The plant materials (umbels) were collected in a green immature stage from Kashmir (voucher specimen No. 7124 deposited at the Plant Survey Division of R.R.L., Jammu). The identity of the known products was established by comparison of their physical data with those of their authentic samples. These included mps, UV fluorescence, R_f values and ^{1}H NMR. The structures of the new coumarins were elucidated on the basis of spectral data and chemical evidence.

Extraction and isolation. Dried and ground umbels (6 kg) of *S. sibiricum* were extracted with hexane (Soxhlet) for 48 hr. The extract yielded a residue (300 g) on removal of solvent. This was chromatographed over neutral Al_2O_3 (5 kg) deactivated with H_2O (10%). Fractions (107, 11. each) were collected; fractions 1–42 and 43–80 were eluted with hexane and fractions 81–82 and 83–107 with C_6H_6. Fractions 1–42 (185 g) were rechromatographed over Si gel (2.5 kg). Hexane–C_6H_6 (1:1) eluted successively sesibiricin (**13**) (4.2 g), mp 121–122°, R_f 0.76; osthol (14 g), mp 83–84°, R_f 0.68; and coumurrayin (**12**) (200 mg), mp 155–156°, R_f 0.58. Fractions 43–80 (28 g) on concn deposited crystals of sibiricin (**4**) (5 g), mp 152°, R_f 0.44. The mother liquor was chromatographed over Si gel (760 g). C_6H_6 successively eluted imperatorin (1.2 g), mp 102°, R_f 0.60; sesebrin (**14**) (30 mg), mp 111–112°, R_f 0.54; bergapten (1.7 g), mp 188–190°, R_f 0.52; xanthotoxin (0.9 g), mp 145°, R_f 0.51; and isopimpinellin (1.1 g), mp 149°, R_f 0.49. Earlier $CHCl_3$ fractions (3 g) on rechromatography over Si gel afforded a fraction showing two spots on TLC. This on separation by PLC on Si gel using C_6H_6–Me_2CO (9:1) gave two bands. The upper band on extraction with $CHCl_3$ and subsequent removal of the solvent gave seselinal (**1**) (500 mg), mp 174–175°, R_f 0.48. The lower band likewise afforded isosibiricin (**5**) (110 mg), mp 128–129°, R_f 0.46 [5]. The later $CHCl_3$ fractions (6 g) were chromatographed over Si gel (300 g). Earlier $CHCl_3$ eluates gave sesibiricol (**2**) (300 mg), mp 110–111°, R_f 0.38, whilst later fractions on purification by PLC yielded sibirinol (**3**) (430 mg), mp 121–122°, R_f 0.29. Fractions 81–82 (12 g) were chromatographed over Si gel (400 g). Elution with $CHCl_3$–EtOAc (19:1) gave sesebrinol (350 mg), mp 114–116°, R_f 0.07, blue fluorescence in UV light, and $CHCl_3$–EtOAc (9:1) eluted mexoticin (**10**) (400 mg), mp 184–185°, R_f 0.04 [6]. Fractions 83–107 (8 g) on rechromatography over Si gel also gave mexoticin (**10**) (1.2 g), mp 185°.

Seselinal(**1**). Mp 174–175°, needles from Me_2CO–hexane. Blue fluorescence in UV light. R_f 0.48. UV λ_{max} nm: 330, 263, 257 (sh), 240 (sh). IR ν_{max} cm^{-1}: 3070, 2952, 2930, 2842, 2735, 1714, 1620 (sh), 1604, 1250, 840, 810. MS *m/e*: 290 (M^+), 261 (M^+ – CHO), 219 (M^+ – CMe_2·CHO), 206 (M^+ – 3CO), 189 (*m/e* 219 – 2Me), 161 (*m/e* 189 – CO), 133 (*m/e* 161 – CO).

Sesibiricol (**2**). Mp 110–111°. Blue fluorescence in UV light. R_f 0.38. MS *m/e*: 344 (M^+), 329 (M^+ – Me), 276 (M^+ – C_5H_8), 275 (*m/e* 276 – H), 274 [M^+ – CH_2=C(Me)–CH(OH)+H], 260 (*m/e* 275 – Me), 220 (*m/e* 276 – CO – CO), 206 [*m/e* 276 – CH_2=C(Me)–CH(OH)+H]. On treatment with Ac_2O–C_5H_5N, sesibiricol (**2**) gave the acetate (**8**), mp 98–99°; ^{1}H NMR (δ in ppm, 60 MHz): δ 1.82 (9H, *s*, Me's), 1.91 (3H, *s*, OCOMe), 3.07 (2H, *d*, Ar–$\underline{CH_2}$–CH(OAc)–), 4.60 (2H, *d*, Ar–O–$\underline{CH_2}$–CH=), 4.80 (2H, *s*,=CH_2), 5.41 (2H, *t* (overlapping), Ar–O–CH_2–$\underline{CH}$= and Ar–CH_2–$\underline{CH}$(OAc)–), no D_2O exchangeable peak, rest of signal similar to that of **2**.

Sibirinol (**3**). Mp 121–122°. Blue fluorescence on UV light. R_f 0.29. UV λ_{max} nm: 331, 263, 254 (*sh*), 240 (*sh*). IR ν_{max} cm^{-1}: 3478 (OH), 1700, 1605, 1325, 1250, 1105, 895, 812. MS *m/e*: 290 (M^+), 272 (M^+ – H_2O), 220 [M^+ – CH_2=C(Me)–CH(OH)+H], 219 [M^+ – CH_2=C(Me)–CH(OH)–], 204 (*m/e* 219 – Me), 176 (*m/e* 204 – CO). On treatment with Ac_2O–C_5H_5N sibirinol gave the acetate (**9**), mp 137–138°, ^{1}H NMR (δ in ppm, 60 MHz): δ 1.90 (3H, *s*, Me), 1.98 (3H, *s*, OCOMe), 3.14 (2H, *d*, J = 7 Hz, Ar–$\underline{CH_2}$–CH(OAc)–), 3.98 (6H, *s*, OMe's), 4.88 (2H, *s*,=CH_2), 5.46 (1H, *t*, *J* = 7 Hz, -CH_2 – $\underline{CH}$ (OAc) –), 6.13 (1H, *d*, *J* = 9.5 Hz, H-3), 6.66 (1H, *s*, H-6), 7.95 (1H, *d*, *J* = 9.5 Hz, H-4).

Synthesis of seselinal (**1**). A soln of sibiricin (**4**) (100 mg) in dry C_6H_6 (8 ml) was treated at room temp. with BF_3–Et_2O (25 mg), swirled, left to stand for 5 min, and treated with H_2O (5 ml). The organic layer was washed with H_2O, dried (Na_2SO_4) and evapd to a white solid which gave two spots on TLC corresponding to seselinal and isosibiricin. This was resolved by PLC (Si gel, C_6H_6–Me_2CO, 9:1). The less polar product was characterized as seselinal (**1**) (30 mg), mp 175°, on the basis of physical data including mmp with natural product, R_f and ^{1}H NMR. The polar band afforded isosibiricin (**5**) (30 mg), mp 128°, characterized on the basis of mmp, R_f and ^{1}H NMR.

Synthesis of sesibiricol (**2**). Sesebrinol (**6**) (IR ν_{max} cm^{-1}: 3410, 2972, 2953, 1705, 1595, 1315, 1247, 1095, 822 and 802) [3] on treatment with Ac_2O–C_5H_5N gave the monoacetate (**7**), mp 154–155°. ^{1}H NMR of **7** (δ in ppm, 60 MHz): δ 1.30 and 1.34 (3H each, *s*, Me's of side chain at C-8), 1.84 (9H, *s*,=CMe_2 and OCOMe), 2.15 (1H, *s*, OH), 3.07 (2H, *d*, Ar-$\underline{CH_2}$-CH(OAc)-), 3.96 (3H, *s*, OMe), 4.60 (2H, *d*, Ar-O-$\underline{CH_2}$-CH=), 5.08 (1H, *dd*, Ar-CH_2-$\underline{CH}$(OAc)-), 5.54 (1H, *t*, -CH_2-$\underline{CH}$=), 6.13 (1H, *d*, H-3), 6.68 (1H, *s*, H-6), 8.03 (1H, *d*, H-4). To a soln of sesebrinol monoacetate (**7**) (150 mg) in C_5H_5N (2 ml) was added with stirring at 0–5° $POCl_3$ (0.3 ml) and the mixture left at 10° for 1 hr. The mixture was poured in crushed ice, acidified with HCl and taken up in C_6H_6. The C_6H_6 layer was washed with aq. $NaHCO_3$ and H_2O, dried (Na_2SO_4) and evapd to dryness *in vacuo*. The residue on crystallization from Me_2CO–hexane afforded the acetate (**8**) of sesibiricol as needles (110 mg), mp 98–99°. This was found to be identical with the acetate prepared from sesibiricol (mmp, R_f, ^{1}H NMR). This acetate (70 mg) in MeOH (2 ml) was treated with aq. $NaHCO_3$ (0.3 ml, 5%) and the mixture refluxed for 1 hr. MeOH was removed *in vacuo* and the residue extracted with C_6H_6. Evapn of C_6H_6 gave a gum which crystallized from Me_2CO–hexane to yield sesibiricol (**2**) as needles (25 mg), mp 112°, characterized on the basis of fluorescence, mmp, R_f and ^{1}H NMR data.

Synthesis of sibirinol (**3**). Mexoticin (**10**), isolated from the

umbels of *S. sibiricum* on treatment with Ac_2O–C_5H_5N gave mexoticin monoacetate (**11**), mp 153–154°. ^1H NMR of **11** (δ in ppm, 60 MHz): δ 1.33 (*s*) and 1.37 (*s*) (6H, Me's), 1.87 (3H, *s*, OCOMe), 2.30 (1H, *s*, OH), 3.07 (2H, *d*, Ar-$C\underline{H}_2$-CH(OAc)-), 3.98 (6H, *s*, OMe's), 5.10 (1H, *dd*, -CH_2-$\underline{CH}$(OAc)-), 6.14 (1H, *d*, H-3), 6.34 (1H, *s*, H-6), 7.97 (1H, *d*, H-4). To a soln of **11** (100 mg) in C_5H_5N (1 ml) was added with stirring $POCl_3$ (0.2 ml) at 0°. After 1 hr the mixture was worked up as in synthesis of sesibiricol acetate when a product (80 mg) was obtained as needles, mp 138–140°. This was found to be identical with sibirinol acetate (**9**), obtained on acetylation of sibirinol (mmp, co-TLC and ^1H NMR). This acetate (**9**), on refluxing in MeOH with aq. $NaHCO_3$ and work-up similar to the hydrolysis of **8** described previously, afforded needles (35 mg), mp 122–123°. The product was found to be identical with sibirinol on comparison of ^1H NMR, TLC and mmp.

Acknowledgement—The authors wish to thank Dr. M. K. Kaul of the Plant Survey Division of this laboratory for collection of the plant material.

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