Absolute Structures of Two New C_{13}-Norisoprenoids from *Apollonias barbujana*

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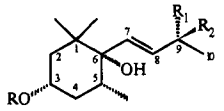
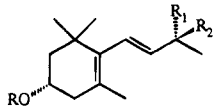
Two new C_{13}-norisoprenoid compounds, (3*S*,5*R*,6*S*,9*R*)-3,6-dihydroxy-5,6-dihydro-β-ionol (**1**) and (3*S*,4*S*,5*S*,6*S*,9*S*)-3,4-dihydroxy-5,6-dihydro-β-ionol (**2**), were isolated from the leaves of *Apollonias barbujana*. The absolute structures were determined by spectroscopic methods and chemical transformations. (3*S*,4*S*,5*S*,6*S*,9*R*)-3,4-Dihydroxy-5,6-dihydro-β-ionol (**3**) was also isolated, the structure of which has been determined by X-ray analysis and whose ^{1}H-NMR, ^{13}C-NMR, and MS data are reported herein.

Apollonias barbujana (Cav.) Bornmueller[1] (Spanish name "barbusano") is an evergreen tree of the family Lauraceae distributed in the Canary and Madeira Islands.[2] Several biological properties of plants in this family have been purported in folk medicine to include diuretic (*Cassytha* spp.),[3] analgesic, antiulcerogenic, cytostatic, cardiotonic (*Cinnamomum* spp.)[4] expectorant, stomachic (*Laurus* spp.),[5] and sedative or carminative (*Lindera* spp.) effects.[6]

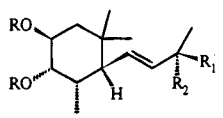
A number of different compounds with a C_{13}-norisoprenoid structure, also known as dihydro-β-ionone derivatives, have been isolated mainly from plants in the Solanaceae (*Nicotiana tabaccum*)[7] and Vitaceae (*Vitis vinifera*).[8] Recently, a glucoside of an ionone-related compound having antiulcerogenic activity[9] has been isolated from *Cinnamomum cassia*. From the leaves of *A. barbujana* we have obtained three new β-ionone compounds (1–**3**), whose structures are reported herein.



1 R=R$_2$=H; R$_1$=OH
1a R=Ac; R$_1$=OAc; R$_2$=H
1e R=Ac; R$_1$=OH; R$_2$=H
1f R=Ac; R$_1$=OBz; R$_2$=H
1g R=H; R$_1$=R$_2$=O



1b R=Ac; R$_1$=OAc; R$_2$=H
1c R=R$_2$=H; R$_1$=OH
1d R=H; R$_1$=R$_2$=O



2 R=H; R$_1$=H; R$_2$=OH
2a R=Ac; R$_1$=H; R$_2$=OAc
3 R=H; R$_1$=OH; R$_2$=H
3a R=Ac; R$_1$=OAc; R$_2$=H
3b R=H; R$_1$=R$_2$=O

Compound **1**, $[\alpha]^{25}_D$, −10.4°, was obtained as a colorless syrup, and its elemental composition was determined to be $C_{13}H_{24}O_3$ by HREIMS. The ^{1}H- and ^{13}C-NMR data in Tables 1 and 2 suggested that **1** has the same structure and relative configuration as the aglucone of dendranthemoside A.[10]

In order to elucidate the absolute configurations at C-3, C-5, and C-6, compound **1** was acetylated with Ac_2O in pyridine to afford the hydroxy-diacetate **1a**, and successive treatment of the resulting diacetate with phosphoryl chloride in pyridine afforded the diene diacetate **1b**. Further hydrolysis of **1b** with KOH in MeOH gave the dienediol **1c**, $[\alpha]^{25}_D$, +104.1°. The ^{1}H- and ^{13}C-NMR data of the derivative **1c** were identical with those of 3-hydroxy-β-ionol[11] ($[\alpha]^{25}_D$, −17.0°), and it was therefore inferred that those compounds were epimers at C-3 or C-9. Subsequent selective oxidation of the diene diol **1c** with manganese dioxide gave (+)-3-hydroxy-β-ionone (**1d**) $[\alpha]^{25}_D$, +75.6°, whose IR, UV, and ^{1}H-NMR data were consistent with those described for (−)-(3*R*)-hydroxy-β-ionone $[\alpha]^{25}_D$, −77.9°.[12] Therefore, derivative **1d** is the enantiomer (+)-(3*S*)-hydroxy-β-ionone, and consequently the chirality at C-3 of product **1** was *S*, the relative configuration (3*S*,5*R*,6*S*)* of which was determined on the basis of the coupling constants observed for the ring protons and NOE experiments (Figure 1). We could thus affirm that the chirality at C-3, C-5, and C-6 are *S*, *R*, and *S*, respectively.

Finally, the absolute configuration of the remaining chiral center, C-9, was determined by the circular dichroism allylic benzoate method. The *p*-bromobenzoate **1f** was obtained from the diacetate **1a** by partial hydrolysis with K_2CO_3 in MeOH to give **1e**, and further benzoylation with *p*-bromobenzoyl chloride in pyridine. The 9*R* chirality of **1f** was deduced from the negative Cotton effect observed at 244.9 nm ($\Delta_\epsilon = -6.9$).[13] The absolute structure assigned to product **1** was consistent with the chirality recently described for the aglucone of dendranthemoside A penta-acetate (3*S*,5*R*,6*S*,9*R*), verified by X-ray analysis.[13]

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Table 1. ^{1}H-NMR Spectral Data of Compounds **1**, **1a**, **1b**, **1c**, **1d**, **1e**, **1f**, and **1g**[a]

H	1	1a	1b	1c	1d	1e	1f	1g
2eq	1.50 ddd (12.4, 4.8, 2.0)	1.45 dd (12.0, 4.79)	1.75 ddd (12.0, 3.7, 1.4)	1.74 ddd (12.0, 3.6, 2.0)	1.80 ddd (12.1, 3.8, 2.0)	1.48 t (12.2)	1.47 t (12.1)	1.55 ddd (12.5, 5.3, 2.9)
2ax	1.62 t (12.4)	1.71 t (12.0)	1.53 t (12.0)	1.44 t (12.1)	1.49 t (12.1)	1.77 t (12.2)	1.74 t (12.1)	1.62 t (12.5)
3	3.85 m	4.92 m	5.03 m	3.99 m	4.05 m	4.95 m		3.89 m
4eq	1.74 br dt (12.1, 4.1)	1.75 br dt (12.3, 4.0)	2.38 dd (6.2, 5.9)	2.34 dd (16.6, 8.0)	2.44 dd (16.5, 8.1)	1.81 m	1.80 m	1.88 br t (12.6)
4ax	1.35 q (12.1)	1.40 t (12.3)	2.05 dd (16.2, 9.8)	1.99 dd (16.5, 10.2)	2.08 dd (16.5, 10.2)	1.42 m	1.53 m	1.34 t (12.6)
5	1.93 m	1.93 m				1.99 m	1.99 m	2.07 m
7	5.57 d (15.6)	5.57 d (16.0)	6,5 d (14.7)	6.05 d (16.3)	7.20 d (16.3)	5.6 d (15, 6)	5.73 d (13.1)	6.75 d (16.0)
8	5.75 dd (15.6, 6.8)	5.67 dd (16.0, 5.5)	5.38 m	5.50 dd (16.0, 6.2)	6.11 d (16.3)	5.77 dd (15.6, 5.5)	5.82 dd (13.1, 5.7)	6.36 d (16)
9	4.36 m	5.34 m	5.38 m	4.37 m		4.40 m	5.60 m	
CH_3-9	1.29 d (6.3)	1.28 d (6.4)	1.34 d (6.2)	1.32 d (6.4)	2.29 s	1.30 d (6.4)	1.46 d (6.3)	2.28 s
CH_3-1	0.97 s	0.98 s	1.06 s	1.03 s	1.10 s	1.02 s	1.02 s	1.03 s
CH_3-1	0.88 s	0.82 s	1.07 s	1.04 s	1.09 s	0.89 s	0.84 s	0.87 s
CH_3-5	0.74 d (6.6)	0.75 d (6.6)	1.65 s	1.77 br s	1.76 br s	0.79 d (6.7)	0.79 d	0.80 d (6.7)
CH_3		2.05 s OAc	2.03 s 2 × OAc			2.02 s OAc	2.2 s OAc	
CH_3		2.03 s OAc					7.58 d (2H, 7.6)	

[a] $CDCl_3$; 200 MHz, J in Hz in parentheses.

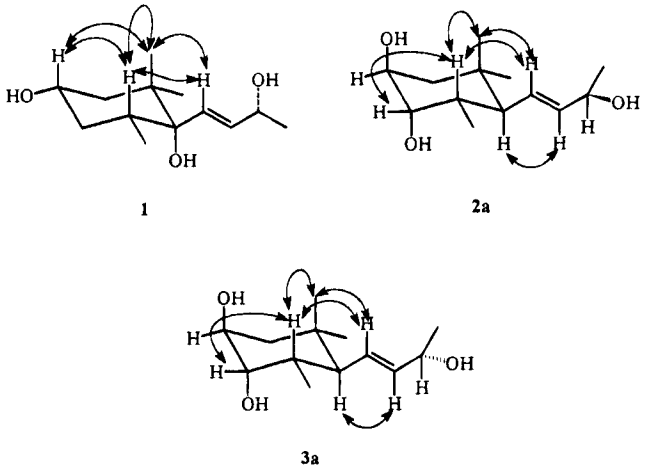

Figure 1. NOE interactions for compounds **1**, **2a** and **3a**.

On the other hand, selective oxidation of compound **1** gave the allylic keto compound **1g**; $[\alpha]^{25}D$, −21.1°; IR, ^{1}H- and ^{13}C-NMR data are identical with those of the natural product boscialin[14] $[\alpha]_D$ −19°, whose absolute structure has not been determined. Therefore, the chirality of boscialin should be established as (3*S*,5*R*,6*S*).

The EIMS showed that compounds **2** and **3** had identical molecular weight and the same fragmentation pattern ($M^+ - H_2O$, calcd for $C_{13}H_{22}O_2$ 210.1598; found 210.1610). Acetylation of **2** gave the triacetate **2a**. The ^{1}H- and ^{13}C-NMR data of **2** (Tables 2 and 3) are practically identical to those of compound **3**. The detailed analysis of the coupling constants of **2** and **3** and homonuclear NOE experiments on their triacetate derivatives **2a** and **3a** (Figure 1) confirmed that these products had identical relative configurations at C-3, C-4, C-5, and C-6, with compound **2** possibly being the C-9 epimer of **3**. This hypothesis was confirmed by the following chemical transformations. Selective oxidation of **3** with MnO_2 in $CHCl_3$ gave the allylic keto diol **3b**; further reduction with $LiAlH_4$ in Et_2O gave (3*S*,4*S*,5*S*,6*S*,9*R*)-3,4-dihydroxy-5,6-dihydro-β-ionol **3** and its C-9 epimer **2**. Therefore, **2** was the 9*S*-epimer of **3**. Finally, the absolute structure of **2** was established as (3*S*,4*S*,5*S*,6*S*,9*S*)-3,4-dihydroxy-5,6-dihydro-β-ionol.

(3*S*,4*S*,5*S*,6*S*,9*R*)-3,4-Dihydroxy-5,6-dihydro-β-ionol (**3**) was isolated as a colorless crystalline solid; mp 162−163 °C; $[\alpha]_D$ −34.0°. Acetylation of **3** gave the triacetate **3a**. The absolute structure of this compound has been determined by X-ray analysis and was published previously.[15] In this paper we report the ^{1}H- and ^{13}C-NMR (Tables 2 and 3, respectively) IR, and MS spectral data (see Experimental Section).

Experimental Section

General Experimental Procedures. Mps were determined with a Kofler block apparatus and are uncorrected. IR spectra were taken on a PE681 spectrophotometer. UV spectra were performed on a Perkin-Elmer Model 320UV. CD spectra were recorded on a Jasco J-500A spectropolarimeter interfaced with a JASCO DP500N data processor. Optical rotations were determined with a Perkin-Elmer model 241 polarimeter. ^{1}H and ^{13}C NMR were recorded on Bruker model WP 200SY (δ scale). LREIMS data were obtained with a Hewlett-Packard 5995. HREIMS data were obtained from a VG Micromass ZAB-2F. The ^{13}C-NMR data were

Table 2. ^{1}H-NMR Spectral Data of Compounds **2**, **2a**, **3**, **3a**, and **3b**[a]

H	2	2a	3	3a	3b
1eq	1.41 dd (14.5, 2.1)	1.70 dd (15.6, 2.6)	1.41 dd (14.5, 2.0)	1.55 dd (15.4, 3.4)	1.50 dd (14.6, 2.7)
1ax	1.67 dd (14.5, 3.1)	1.56 dd (15.6, 3.3)	1.66 dd (14.5, 3.4)	1.69 dd (15.4, 2.8)	1.79 dd (14.6, 3.4)
3	3.58 br s	3.85 dd (6.2, 3.0)	3.81 br s	4.82 br s	3.70 br s
4	3.55 br s	3.90 t (2.6)	3.54 br s	4.90 br s	4.00 br s
5	1.94 m	2.01 m	1.93 m	2.01 m	2.15 m
6	1.87 t (8.3)	1.84 dd (11.7, 8.6)	1.88 t (8.5)	1.83 dd (11.7, 8.5)	2.10 t (9.5)
7	5.34 dd (15.4, 8.3)	5.39 dd (14.0, 8.6)	5.30 dd (15.4, 8.5)	5.37 dd (14.2, 8.5)	6.61 dd (15.8, 9.5)
8	5.45 dd (15.4, 5.7)	5.50 dd (14.0, 6.0)	5.44 dd (15.4, 5.7)	5.48 dd (14.2, 5.8)	6.09 d (15.8)
9	4.21 m	5.33 m	4.20 m	5.31 m	
CH_3-9	1.21 d (6.2)	1.32 d (6.33)	1.20 d (6.1)	1.30 d (6.3)	2.27 s
CH_3-1	1.00 s	0.92 s	1.00 s	0.92 s	1.09 s
CH_3-1	0.80 s	0.84 s	0.82 s	0.83 s	0.86 s
CH_3-5	0.89 d (6.2)	0.79 d (6.7)	0.84 d (7.1)	0.76 d (6.7)	0.90 d (6.5)
3CH_3-3OAc		2.08, 2.05, 2.03, 3 s		2.07, 2.05, 2.03, 3 s	

[a] CD_3OD (**2**, **3**) and $CDCl_3$ (**2a**, **3a**, **3b**); 200 MHz; J in Hz in parentheses.

Table 3. ^{13}C NMR Spectral Data of Compounds **1**, **1a**, **1c**, **1g**, **2**, and **3**[a]

	1	1a	1c	1g	2	3
1	30.45	39.39	36.79	39.93	33.97	33.92
2	45.33	40.62	48.28	45.14	42.28	42.23
3	66.66	69.76	65.08	66.39	75.22	75.18
4	39.45	40.62	42.22	39.01	72.14	72.10
5	34.06	33.83	126.62	33.99	32.69	32.64
6	76.97	76.97	136.80	77.00	50.79	50.73
7	132.92	130.4	125.83	150.31	130.60	130.65
8	134.45	135.60	138.39	130.22	138.67	138.33
9	68.41	70.62	69.76	197.60	68.63	68.65
10	23.85	20.56	23.60	28.17	24.56	24.51
11	25.06	24.79	28.40	25.12	24.56	31.38
12	24.50	24.15	30.05	24.52	24.01	23.96
13	15.80	15.61	21.18	15.84	17.44	17.38
CH_3OCO		170.50				
CH_3OCO		20.15				

[a] $CDCl_3$ (**1**, **1a**, **1c**, **1g**) and $(CD_3)_2CO$ (**2**, **3**); 50 MHz.

studied using DEPT experiments and correlation with the data of closely related ionone derivative substances.

Plant Material. The leaves of *Apollonias barbujana* were collected in San Andrés y Sauces, La Palma, Canary Islands, in September 1990. A voucher specimen is deposited at the Herbarium of the Department of Botany, Faculty of Biology, University of La Laguna, Canary Islands, Spain (FC25324).

Extraction and Isolation. Air-dried leaves (2.2 kg) were ground to a fine powder and extracted in a Soxhlet with MeOH. The extract was concentrated, and the resulting suspension was extracted with EtOAc. The EtOAc extract was evaporated to leave a viscous oil (45 g, 2.25% dry weight), which was chromatographed on silica gel using *n*-hexane with gradually increasing proportions of EtOAc as eluent. The fractions eluted with *n*-hexane-EtOAc (60:40) were combined to obtain **1** (210 mg, 0.0105%), **2** (47 mg, 0.0023%), and **3** (23 mg, 0.0011%).

(3*S*,5*R*,6*S*,9*R*)-3,6-Dihydroxy-5,6-dihydro-β-ionol (1). Isolated as a colorless syrup; $[\alpha]_D$ −10.14° (*c* 1.0, $CHCl_3$); IR, ν_{max} ($CHCl_3$) 3612, 3440, 1360, 1243, 1126, 1034, 983, 932 cm^{-1}; HREIMS *m/z* (calcd for $C_{13}H_{24}O_3$ 228.1724, found 228.1725); EIMS *m/z* 228 $[M]^+$ (3), 210 (5), 195 (3), 167 (4), 142 (36), 128 (13), 124 (100), 111 (23), 98 (15) ^{1}H-NMR data, see Table 1; ^{13}C-NMR data, see Table 3.

Compound **1** (70.2 mg) was acetylated for 12 h with a mixture of $(Ac)_2O$ (0.8 mL) and pyridine (0.8 mL) to afford **1a** (86 mg): colorless oil; $[\alpha]^{25}_D$ +32.5° (*c* 1.2, $CHCl_3$); IR ν_{max} ($CHCl_3$) 3609, 3447, 1727, 1371, 1254, 1147, 1029 cm^{-1}; EIMS *m/z* 252 $[M - AcOH]^+$ (52), 210 (14), 192 (75), 177 (10), 149 (47), 124 (11), 111 (22), 95 (100); ^{1}H-NMR data, see Table 1; ^{13}C-NMR data, see Table 3.

Dehydration of 1a. The diacetate **1a** (41.2 mg) was dissolved in dry pyridine (1 mL) and treated with phosphoryl chloride (0.15 mL) for 10 h at 80°. The mixture was neutralized with $NaHCO_3$ and extracted with EtOAc. The crude product was purified by silica gel CC and *n*-hexane-EtOAc (95:5) as eluent to afford **1b** (31 mg): colorless oil; $[\alpha]^{25}_D$ +158.6° (*c* 0.56, $CHCl_3$); IR ν_{max} ($CHCl_3$) 1729, 1371, 1251, 1144, 1041, 971 cm^{-1}; EIMS *m/z* 234 $[M - AcOH]^+$ (15), 192 (7), 174 (17), 159 (100), 133 (17), 119 (20), 105 (16), 91 (13), 43 (22); ^{1}H-NMR data, see Table 1.

Hydrolysis of 1b. The diene diacetate **1b** (16.8 mg) was treated with K_2CO_3 in MeOH for 2 h at room temperature, worked up in the usual manner, and purified by Si gel CC with *n*-hexane-EtOAc (90:10) as eluent to yield **1c** (12.5 mg): colorless oil; $[\alpha]^{25}_D$ +104.1° (*c* 0.32, $CHCl_3$); IR ν_{max} ($CHCl_3$) 3348, 1456, 1362, 1233, 1138, 1044, 975, 941 cm^{-1}; EIMS *m/z* 210 $[M^+]$ (10), 195 (6), 192 (5), 159 (32), 133 (30), 119 (100), 107 (37), 93 (37); ^{1}H-NMR data, see Table 1; ^{13}C-NMR data, see Table 3.

Oxidation of 1c. A solution of **1c** (9 mg) in $CHCl_3$ (2 mL) was treated with active MnO_2 (45 mg) at room temperature for 4 h with stirring. The reaction mixture was filtered and purified by Si gel CC to yield (+)-(3*S*)-3-hydroxy-β-ionone (**1d**) (6.5 mg): colorless oil; $[\alpha]^{25}_D$, +75.6° (*c* 0.21, $CHCl_3$); IR ν_{max} ($CHCl_3$) 3420, 1670, 1591, 1476, 1360, 1250, 1045, 980 cm^{-1}; UV λ_{max} (EtOH) (ϵ) 220 (6130), 293 (7228) nm; EIMS *m/z* 208 $[M]^+$ (6), 193 (100), 190 (5), 175 (49), 131 (20), 91 (30), 43 (39); ^{1}H-NMR data, see Table 1.

Partial Hydrolysis of Diacetate 1a. K_2CO_3 was added to a solution of diacetate **1a** (10.2 mg) in MeOH (6 mL) at 0 °C. After 40 min, the reaction was quenched with H_2O and extracted with $(C_2H_5)O$ in the usual way. The residue obtained was submitted to chromatography to give **1e** (6.4 mg): colorless oil; ^{1}H-NMR data, see Table 1.

Benzoylation of 1e. To a solution of **1e** (5.6 mg) in dry pyridine (0.5 mL) was added 4-bromobenzoylchloride (10.4 mg). The solution was stirred for 12 h at room temperature, and the excess reagent was destroyed with H_2O and extracted with $(C_2H_5)O$. The reaction mixture was then concentrated *in vacuo* and purified on a microflash Si gel column, *n*-hexane−EtOAc (95:5) to give

1f (8.7 mg): colorless oil; UV (CH_3CN) λ_{max} 242 nm; CD (CH_3CN) λ_{ext} 240.9 nm ($\Delta_\epsilon = -6.9$); ^{1}H-NMR data, see Table 1.

Oxidation of 1. Similar to the oxidation of **1c**, compound **1a** (8 mg) was transformed into the allylic keto **1g** (6 mg), which was chromatographed on a Si gel column; a colorless amorphous solid; $[\alpha]^{25}D$, +21.1° (*c* 0.31, $CHCl_3$); UV λ_{max} (MeOH) (ϵ) 228 nm (14048); IR ν_{max} $CHCl_3$) 3602, 3414, 1693, 1674, 1625, 1456, 1368, 1230, 1142, 1078, 1380 cm^{-1}; EIMS *m/z* 226 $[M]^+$ 226 (2), 208 (6), 170 (25), 126 (33), 111 (100), 98 (26), 83 (22), 71 (16), 55 (33), ^{1}H-NMR data, see Table 1; ^{13}C-NMR data, see Table 3. The ^{1}H-NMR, ^{13}C-NMR, and EIMS data were identical with those of the natural product, boscialin $[\alpha]^{25}D$ −19°.[14]

(3*S*,4*S*,5*S*,6*S*,9*S*)-3,4-Dihydroxy-5,6-dihydro-β-ionol (2). Colorless needles, mp 165−167 °C; $[\alpha]^{25}D$ −15.2° (*c* 0.25, MeOH); EIMS *m/z* 210 $[M - H_2O]^+$ (7), 192 (3), 177 (6), 174 (1), 152 (19), 139 (11), 137 (13), 125 (23), 121 (19). 115 (26), 109 (39), 97 (87), 95 (100), 85 (93), ^{1}H-NMR data, see Table 2; ^{13}C-NMR data, see Table 3.

Acetylation of 2. Compound **2** (5 mg) was acetylated according to the standard procedure for acetylation to give the triacetate **2a**. ^{1}H-NMR data, see Table 2.

(3*S*,4*S*,5*S*,6*S*,9*R*)-3,4-Dihydroxy-5,6-dihydro-β-ionol (3). Colorless solid, mp 162−163 °C; $[\alpha]^{25}D$ −34.0° (*c* 0.52, MeOH); EIMS *m/z* 210 $[M-H_2O]^+$ (10), 192 (4), 177 (7), 174 (1), 152 (24), 139 (10), 137 (11), 125 (18), 121 (17), 115 (28), 109 (28), 97 (88), 95 (100), 85 (90), ^{1}H-NMR data, see Table 2; ^{13}C-NMR data, see Table 3.

Acetylation of 3. Compound **3** (4.5 mg) was acetylated according to the standard procedures for acetylation to give **3a**. ^{1}H-NMR data, see Table 2.

Oxidation of 3. Similarly to **1c**, compound **3** (12 mg) was treated with MnO_2 in $CHCl_3$, to give the allylic keto **3b** (9.5 mg). ^{1}H-NMR data, see Table 2.

Reduction of 3b. Reduction of **3b** with $LiAlH_4$ leading to the mixture of **2** and **3** (1:1). To a solution of **3b** (7 mg) in ether (5 mL) was added $LiAlH_4$ (9.7 mg), and this was stirred at 40 °C for 2 h, poured into cold saturated aqueous NaCl (12 mL), and worked up in the usual manner to give a mixture of **2** and **3** (1:1).

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