

Novel 1,3-Dioxanes from Apple Juice and Cider

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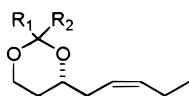
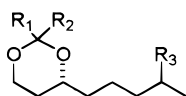
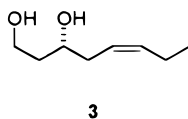
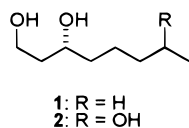
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Extracts obtained by XAD solid-phase extraction of apple juice and cider were separated by liquid chromatography on silica gel. Several new 1,3-dioxanes including the known 2-methyl-4-pentyl-1,3-dioxane and 2-methyl-4-[2'-(*Z*)-pentenyl]-1,3-dioxane, were identified in the nonpolar fractions by GC/MS analysis and confirmed by chemical synthesis. The enantioselective synthesis of the stereoisomers of the 1,3-dioxanes was performed using (*R*)- and (*R,S*)-octane-1,3-diol and (*R*)- and (*R,S*)-5(*Z*)-octene-1,3-diol as starting material. Comparison with the isolated products indicated that the natural products consisted of a mixture of (2*S*,4*R*) and (2*R*,4*R*) stereoisomers in the ratio of approximately 10:1, except for 1,3-dioxanes generated from acetone and 2-butanone. It is assumed that the 1,3-dioxanes are chemically formed in the apples and cider from the natural apple ingredients (*R*)-octane-1,3-diol, (*R*)-5(*Z*)-octene-1,3-diol, (3*R*,7*R*)- and (3*R*,7*S*)-octane-1,3,7-triol, and the appropriate aldehydes and ketones, which are produced either by the apples or by yeast during fermentation of the apple juice.

Keywords: Apple; cider; 1,3-dioxane; acetal; stereoisomers

INTRODUCTION

Recently, the natural occurrence of (2*S*,4*R*)- and (2*R*,4*R*)-2-methyl-4-pentyl-1,3-dioxane **4** as well as (2*S*,4*R*)- and (2*R*,4*R*)-2-methyl-4-[2'-(*Z*)-pentenyl]-1,3-dioxane **14** in cider has been reported (Dietrich et al., 1997). It was assumed that the 1,3-dioxanes were formed in cider by chemical reactions between acetaldehyde and (*R*)-octane-1,3-diol (**1**) and (*R*)-5(*Z*)-octene-1,3-diol (**3**), respectively. Compounds **1** and **3** have been



- | | |
|---|---|
| 4: R ₁ = CH ₃ , R ₂ = H, R ₃ = H | 14: R ₁ = CH ₃ , R ₂ = H |
| 5: R ₁ = C ₂ H ₅ , R ₂ = H, R ₃ = H | 15: R ₁ = C ₂ H ₅ , R ₂ = H |
| 6: R ₁ = C ₃ H ₇ , R ₂ = H, R ₃ = H | 16: R ₁ = C ₃ H ₇ , R ₂ = H |
| 7: R ₁ = CH(CH ₃) ₂ , R ₂ = H, R ₃ = H | 17: R ₁ = CH(CH ₃) ₂ , R ₂ = H |
| 8: R ₁ = C ₅ H ₁₁ , R ₂ = H, R ₃ = H | 18: R ₁ = C ₅ H ₁₁ , R ₂ = H |
| 9: R ₁ = CH ₂ CH(CH ₃) ₂ , R ₂ = H, R ₃ = H | 19: R ₁ = CH ₂ CH(CH ₃) ₂ , R ₂ = H |
| 10: R ₁ = CH(CH ₃)C ₂ H ₅ , R ₂ = H, R ₃ = H | 20: R ₁ = CH(CH ₃)C ₂ H ₅ , R ₂ = H |
| 11: R ₁ = CH ₃ , R ₂ = CH ₃ , R ₃ = H | 21: R ₁ = CH ₃ , R ₂ = CH ₃ |
| 12: R ₁ = CH ₃ , R ₂ = C ₂ H ₅ , R ₃ = H | 22: R ₁ = CH ₃ , R ₂ = C ₂ H ₅ |
| 13: R ₁ = CH ₃ , R ₂ = H, R ₃ = OH | |

identified in juice from a number of apple (Beuerle et al., 1996; Berger et al., 1988) and pear (Beuerle and Schwab, 1997) cultivars and in the mountain papaya fruit (*Carica pubescens*) (Krajewski et al., 1997). Acetaldehyde is one of the major products formed by yeast during fermentation of apple juice (Dietrich, 1987).

French apple varieties (Beuerle et al., 1996) used for cider production contain large amounts of **1** and **3**, and **2** was recently identified in the variety Peau de Chien (Beuerle et al., 1999). Because yeast (Dietrich, 1987) and apples (Paillard, 1990) produce a number of aldehydes such as propanal, butanal, 2-methylpropanal, hexanal, 3-methylbutanal, and 2-methylbutanal, as well as the ketones acetone and 2-butanone, we expected the occurrence of 1,3-dioxanes derived from 1,3-diols and these carbonyl compounds in apples and cider. This paper describes the chemical synthesis of **4**–**22**, the determination of their absolute configuration and conformation, and the identification of 1,3-dioxanes in apples and cider.

EXPERIMENTAL PROCEDURES

General Procedures. ¹H and ¹³C NMR spectra were recorded on a 250 MHz/63 MHz or 400 MHz/100 MHz spectrometer (Bruker). All NMR data are reported in parts per million (δ) downfield from the internal standard TMS or solvent signals (CDCl₃, δ_{H/C} 7.27/77.0). Silica gel 60 (0.063–0.2 mm) was used for flash chromatography. Solvents were redistilled before use. The purities of the compounds were shown to be ≥90% by ¹H NMR, TLC, and/or GC/MS. An HP 5890-2 gas chromatograph with FID was used for the GC analyses. Split injection (1:20) was employed. The GC was equipped either with a J&W fused silica DB-Wax capillary column (30 m × 0.25 mm, d_f = 0.25 μm), with a DB-5 capillary column (30 m × 0.25 mm, d_f = 0.25 μm), or with a 30% 2,3-*O*-diethyl-6-*O*-*tert*-butyldimethylsilyl-β-CD/PS086 column (25 m × 0.25 mm, d_f = 0.15 μm) for the separation of the enantiomers. The temperature program for the DB-Wax capillary column was as follows: 3 min isothermal at 50 °C, increased from 50 to 240 °C at 4 °C/min. The temperature program for the DB-5 capillary column was from 60 to 300 °C at 5 °C/min and then held for 10 min at this temperature. Helium was used as carrier gas (2.0 mL/min). Calculation of retention indices for the DB-Wax column (R_i) was conducted on the basis of *n*-hydrocarbons with the aid of an additional BASIC program (Baugh, 1993). The temperature program for the 2,3-*O*-diethyl-6-*O*-*tert*-butyldimethylsilyl-β-CD/PS086 column was 1 min isothermal at

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Table 1. R_f Values and EIMS Data of 1,3-Dioxanes 5–13

| | R_1 | $2S,4R$ | | R_1 | $2R,4R$ |
|-----------|-------|--|--|-------|---|
| 5 | 1477 | 69 (100), 57 (42), 55 (41), 111 (26), 86 (22), 58 (15), 157 (13), 115 (6), 185 (3) | | 1560 | 69 (100), 55 (40), 57 (26), 111 (21), 115 (21), 73 (18), 157 (13), 59 (11), 43 (11), 67 (5), 83 (4), 185 (3) |
| 6 | 1568 | 69 (100), 111 (53), 55 (47), 157 (29), 71 (27), 100 (22), 43 (19), 57 (18), 72 (10), 83 (8), 129 (7), 199 (6) | | 1649 | 69 (100), 55 (48), 111 (40), 157 (23), 129 (20), 57 (18), 43 (15), 73 (10), 87 (7), 83 (6), 199 (2) |
| 7 | 1471 | 69 (100), 55 (55), 111 (43), 71 (26), 157 (20), 57 (18), 100 (15), 83 (12), 72 (11), 112 (6), 129 (5), 199 (3) | | 1565 | 69 (100), 55 (55), 111 (38), 157 (20), 57 (19), 129 (15), 83 (11), 73 (10), 70 (8), 67 (8), 112 (4), 158 (3), 199 (2) |
| 8 | 1765 | 69 (100), 111 (67), 157 (48), 55 (53), 99 (25), 57 (16), 83 (15), 71 (10), 128 (8), 158 (6), 85 (5), 227 (5) | | 1847 | 69 (100), 157 (70), 111 (65), 55 (47), 57 (14), 83 (12), 70 (8), 158 (7), 85 (6), 99 (5), 227 (3) |
| 9 | 1606 | 69 (100), 111 (48), 55 (35), 157 (27), 85 (24), 57 (20), 71 (11), 83 (9), 114 (8), 112 (6), 99 (5), 158 (5), 213 (4), 143 (4), 127 (2) | | 1678 | 69 (100), 111 (36), 55 (30), 157 (20), 57 (15), 143 (10), 71 (9), 67 (7), 83 (5), 87 (4), 85 (4), 158 (3), 213 (1), 127 (1) |
| 10 | 1575 | 69 (100), 111 (43), 55 (35), 57 (24), 157 (23), 85 (15), 58 (12), 83 (7), 67 (7), 114 (5), 213 (3), 143 (3), 158 (3), 127 (1) | | 1660 | 69 (100), 111 (40), 55 (35), 157 (18), 57 (17), 85 (12), 67 (8), 70 (7), 83 (6), 143 (5), 114 (4), 213 (2), 158 (3), 127 (1) |
| 11 | 1429 | 69 (100), 171 (33), 111 (32), 59 (31), 55 (30), 58 (14), 57 (13), 115 (12), 86 (10), 70 (8), 73 (7), 67 (7), 172 (5), 110 (4), 83 (4), 82 (4), 81 (4), 129 (2) | | | |
| 12 | 1485 | 69 (100), 55 (36), 57 (30), 73 (27), 111 (25), 185 (14), 72 (11), 129 (7), 67 (7), 171 (6), 100 (5), 83 (4), 81 (3) | | 1516 | 69 (100), 55 (37), 111 (27), 73 (20), 171 (20), 57 (15), 67 (8), 129 (6), 100 (5), 83 (5), 172 (4), 81 (4) |
| 13 | 2067 | 43 (100), 45 (88), 67 (65), 57 (58), 55 (53), 72 (50), 101 (42), 109 (30), 71 (29), 59 (24), 81 (27), 54 (23), 69 (16), 83 (15), 99 (12), 127 (10), 97 (10), 85 (9), 98 (8), 93 (7), 111 (5), 79 (4), 173 (4), 126 (4), 155 (2), 187 (1) | | 2157 | 43 (100), 67 (72), 55 (66), 72 (60), 57 (56), 45 (50), 101 (40), 59 (39), 71 (38), 81 (36), 127 (20), 69 (18), 54 (16), 70 (15), 109 (14), 68 (14), 83 (11), 85 (10), 79 (8), 97 (7), 98 (7), 116 (4), 102 (4), 99 (4), 173 (3), 143 (3), 187 (1) |

Table 2. R_f Values and EIMS Data of 1,3-Dioxanes 15–22

| | R_1 | 2 <i>S</i> ,4 <i>R</i> | | R_1 | 2 <i>R</i> ,4 <i>R</i> |
|-----------|-------|---|-------------|---|------------------------|
| 15 | 1537 | 115 (100), 73 (100), 67 (85), 57 (85), 59 (67), 109 (62), 55 (50), 69 (27), 81 (26), 79 (15), 93 (14), 53 (14), 97 (10), 85 (8), 77 (7), 82 (7), 116 (6), 110 (5), 183 (4), 184 (3), 144 (3), 126 (3), 124 (3) | 1616 | 115 (100), 73 (77), 57 (60), 59 (58), 67 (55), 109 (25), 55 (25), 81 (15), 69 (13), 79 (8), 54 (7), 52 (7), 116 (5), 155 (5), 183 (1) | |
| 16 | 1631 | 55 (100), 67 (93), 109 (78), 57 (76), 129 (73), 87 (47), 81 (29), 71 (29), 93 (17), 79 (17), 53 (13), 69 (12), 68 (10), 155 (9), 83 (8), 110 (6), 77 (6), 97 (5), 197 (5), 126 (4), 198 (4) | 1708 | 55 (100), 129 (86), 67 (78), 57 (76), 73 (56), 87 (45), 109 (42), 81 (20), 71 (15), 79 (12), 53 (12), 155 (10), 69 (8), 83 (8), 77 (6), 93 (5), 130 (5), 197 (1) | |
| 17 | 1522 | 67 (100), 109 (84), 55 (78), 58 (57), 129 (46), 73 (46), 83 (28), 81 (26), 85 (14), 71 (14), 79 (13), 93 (11), 69 (10), 53 (10), 155 (8), 87 (7), 110 (6), 198 (5), 197 (5), 111 (5), 130 (4), 169 (1) | 1600 | 67 (100), 55 (94), 129 (73), 57 (70), 109 (46), 73 (46), 83 (23), 53 (23), 71 (22), 155 (20), 85 (17), 45 (8), 87 (7), 69 (7), 77 (6), 67 (6), 111 (6), 65 (5), 130 (3), 107 (3), 197 (1) | |
| 18 | 1834 | 109 (100), 55 (100), 67 (94), 57 (61), 57 (61), 83 (55), 157 (52), 85 (43), 73 (32), 81 (28), 69 (26), 93 (18), 79 (15), 71 (15), 155 (15), 87 (12), 53 (11), 115 (9), 99 (9), 97 (8), 95 (8), 158 (5), 225 (4), 126 (4), 124 (3), 101 (3), 226 (2) | 1909 | 55 (100), 67 (79), 157 (63), 109 (60), 57 (57), 83 (48), 85 (42), 73 (33), 81 (20), 69 (20), 155 (15), 87 (12), 99 (7), 95 (6), 93 (6), 97 (5), 158 (4), 110 (4), 139 (3), 225 (1) | |
| 19 | 1663 | 67 (100), 69 (84), 109 (77), 71 (50), 143 (48), 57 (46), 55 (39), 87 (27), 81 (26), 101 (16), 79 (16), 93 (15), 108 (13), 83 (12), 54 (12), 155 (11), 85 (10), 97 (6), 144 (5), 212 (4), 211 (3), 126 (3), 125 (3) | 1743 | 69 (100), 67 (95), 143 (68), 109 (65), 71 (55), 57 (54), 55 (39), 87 (36), 81 (21), 101 (17), 79 (16), 155 (15), 85 (9), 83 (7), 77 (7), 144 (6), 93 (5), 97 (4), 125 (3), 95 (3), 212 (3), 211 (3) | |
| 20 | 1636 | 67 (100), 109 (72), 69 (53), 57 (30), 55 (29), 81 (26), 45 (21), 143 (19), 71 (16), 79 (15), 73 (15), 155 (13), 93 (9), 108 (9), 110 (7), 97 (6), 99 (5), 212 (4), 125 (3), 101 (3), 126 (2) | 1723 | 67 (100), 69 (93), 109 (69), 143 (55), 57 (50), 55 (42), 73 (27), 71 (27), 81 (23), 79 (17), 155 (15), 53 (14), 54 (14), 87 (13), 75 (10), 85 (8), 77 (7), 97 (6), 144 (6), 125 (5), 99 (5), 101 (4), 212 (1), 211 (1) | |
| 21 | 1487 | 115 (100), 67 (92), 59 (78), 73 (45), 57 (40), 109 (38), 55 (27), 81 (23), 169 (20), 58 (12), 54 (12), 108 (11), 97 (10), 69 (9), 68 (9), 116 (8), 93 (7), 110 (5), 170 (3), 126 (3), 91 (3) | | | |
| 22 | 1550 | 67 (100), 73 (60), 109 (46), 57 (45), 129 (40), 55 (38), 81 (21), 183 (13), 79 (10), 169 (8), 68 (8), 54 (8), 110 (6), 108 (6), 93 (6), 77 (6), 130 (4), 97 (4), 91 (4) | 1570 | 67 (100), 109 (46), 73 (47), 55 (40), 169 (23), 129 (22), 81 (18), 57 (18), 79 (10), 68 (7), 54 (7), 69 (5), 77 (4), 110 (4), 93 (4), 91 (3) | |

80 °C, increased from 80 to 190 °C at 1.5 °C/min. Helium was used as carrier gas (65 kPa). GC/MS was performed with a Fisons 8000 gas chromatograph with a split injector (1:30) coupled to the Fisons MD mass spectrometer and MassLab data system. The temperature program was as follows: 3 min isothermal at 50 °C, increased from 50 to 240 °C at 4 °C/min. Conditions of the mass spectrometer: temperature of the ion source, 230 °C; temperature of all connection parts, 200 °C; electron energy, 70 eV; cathodic current, 4 mA; mass range, 40–250 or 40–499 Da.

Plant Material. Apple fruits, cv. Peau de Chien, and French cider were kindly provided by Pernod Ricard, France.

Extraction and Isolation. Apple juice (2.5 kg) or cider (8 L) was subjected to solid-phase extraction on Amberlite XAD-2

resin (Beuerle et al., 1997). The resin was eluted with Et₂O and the extract further fractionated by flash chromatography on silica gel using pentane/Et₂O mixtures of increasing polarity. Fractions were monitored by GC, GC/MS and TLC on silica gel. The TLC was developed in pentane/Et₂O (9:1) and visualized by spraying with 1% vanillin in H₂SO₄ (concentrated).

(*R,S*)-Octane-1,3-diol (rac-1). The preparation was performed in the same manner as reported (Beuerle et al., 1996). Spectral data were in accordance with previously published values (Berger et al., 1988; Schwab et al., 1989).

3(*Z*)-Hexenyl Chloride. Thionyl chloride (31.65 g, 0.266 mol) was added to a solution of 3(*Z*)-hexenoic acid (15.16 g, 0.133 mol) in benzene (50 mL), and the mixture was stirred for 4 h at room temperature (Smith et al., 1984). Excess of

Table 3. ^{13}C NMR Data of Dioxanes 5–13 and 15–22^a

| carbon | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 15 | 16 | 17 | 18 | 20 | 19 | 21 | 22 |
|--------|-------|-------|-------|-------|-------|-------|--------|------|------|-------|-------|-------|-------|-------|-------|--------|-------|
| C2 | 103.2 | 102.0 | 105.9 | 102.3 | 101.2 | 105.2 | 98.2 | 99.0 | 98.9 | 103.0 | 102.0 | 105.7 | 102.3 | 104.9 | 101.2 | 98.2 | 99.5 |
| | | | | | | 105.4 | | 99.4 | | | | | | | | | 100.4 |
| C4 | 76.8 | 76.7 | 76.7 | 76.8 | 76.7 | 77.0 | 68.9 | 68.3 | 76.5 | 76.4 | 76.4 | 76.4 | 76.5 | 76.4 | 76.5 | 68.9 | 68.4 |
| | | | | | | | | 68.6 | | | | | | | | | 68.6 |
| C5 | 36.1 | 36.1 | 36.1 | 36.1 | 36.0 | 36.4 | 36.5 | 36.5 | 35.8 | 33.8 | 33.8 | 33.9 | 33.9 | 33.9 | 33.8 | 34.3 | 34.4 |
| | | | | | | | | 36.6 | | | | | | | | | 35.6 |
| C6 | 66.7 | 66.7 | 66.7 | 66.7 | 66.6 | 67.0 | 60.0 | 59.5 | 66.4 | 66.5 | 66.6 | 66.6 | 66.6 | 60.6 | 66.6 | 60.0 | 59.5 |
| | | | | | | | | 59.9 | | | | | | | | | 59.8 |
| C7 | 31.8 | 31.8 | 31.7 | 31.8 | 31.7 | 32.1 | 31.8 | 31.6 | 31.0 | 31.1 | 31.1 | 31.2 | 31.1 | 31.2 | 31.1 | 30.9 | 30.7 |
| | | | | | | | | 31.8 | | | | | | | | | 31.1 |
| C8 | 24.7 | 24.7 | 24.7 | 24.7 | 24.6 | 24.6 | 24.6 | 24.6 | 23.4 | 123.7 | 123.7 | 123.9 | 123.8 | 124.0 | 123.8 | 123.8 | 123.9 |
| | | | | | | 24.7 | | 24.7 | | | | | | | | | |
| C9 | 31.6 | 31.6 | 31.6 | 31.6 | 31.6 | 32.0 | 31.4 | 31.2 | 39.1 | 133.9 | 133.9 | 133.8 | 134.0 | 133.8 | 133.9 | 133.9 | 133.8 |
| | | | | | | | | | | | | | | | | | 133.9 |
| C10 | 22.6 | 22.6 | 22.6 | 22.6 | 22.5 | 22.9 | 22.6 | 22.6 | 67.8 | 20.6 | 20.7 | 20.7 | 20.7 | 20.7 | 20.6 | 20.7 | 20.7 |
| | | | | | | | | 22.5 | | | | | | | | | |
| C11 | 14.0 | 14.0 | 13.9 | 13.9 | 13.9 | 14.3 | 14.0 | 13.9 | 21.2 | 14.0 | 14.1 | 14.1 | 14.1 | 14.1 | 14.1 | 14.1 | 14.0 |
| | | | | | | | | | | | | | | | | | 14.1 |
| C12 | 28.3 | 37.3 | 32.9 | 35.2 | 43.9 | 39.7 | a 30.0 | 35.7 | 21.1 | 28.2 | 37.2 | 32.9 | 35.2 | 39.5 | 43.9 | a 30.0 | 34.1 |
| | | | | | | 39.8 | e 19.3 | 36.1 | | | | | | | | e 19.2 | 34.3 |
| C13 | 8.4 | 17.5 | 17.1 | 23.8 | 23.9 | 25.0 | | 17.2 | | 8.4 | 17.3 | 17.1 | 23.8 | 24.2 | 23.9 | | 17.3 |
| | | | | | | | | 21.2 | | | | | | 24.3 | | | 21.3 |
| C14 | | 13.9 | 17.1 | 31.7 | 22.8 | 11.6 | | 23.9 | | | 13.9 | 17.1 | 31.7 | 11.4 | 22.9 | | 23.8 |
| | | | | | | 11.7 | | 26.1 | | | | | | | | | 26.3 |
| C15 | | | | 22.6 | 22.8 | 14.0 | | | | | | | 22.5 | 13.6 | 22.7 | | |
| | | | | | | 14.1 | | | | | | | | | | | |
| C16 | | | | 14.0 | | | | | | | | | 13.9 | | | | |

^a a, axial; e, equatorial.

thionyl chloride and benzene was removed (100 mbar, 40 °C), and the product was distilled (3 mbar, 45–47 °C): 12.0 g (0.091 mol, 68%), IR(KBr) ν_{max} 3010 (C=C), 2950 (CH₃), 2880 (CH₃), 2910 (CH₂), 2850 (CH₂), 1785 (C=O), 735 [C=C–H of (Z)-double bond].

Malonic Acid Monoethyl Ester. Potassium ethyl malonate (25 g, 0.147 mol) was dissolved in H₂O (16 mL) and cooled (5 °C). Concentrated HCl (12.5 mL) was carefully added to the aqueous mixture while the temperature was maintained below 10 °C (Strube, 1993). The resulting precipitate was removed by filtration and washed with Et₂O (75 mL). The aqueous solution was extracted (three times) with Et₂O. The organic extracts were combined and dried (Na₂SO₄), and the solvent was removed in vacuo to yield the ester: 19.1 g (0.145 mol, 99%); IR(KBr) ν_{max} 3500–2600 (OH), 2960 (CH₃), 2925 (CH₂), 1710 (C=O), 1730 (C=O), 1360, 1145, 950.

Ethyl 3-Oxo-5(Z)-octenoate. Monoethyl ester (19.1 g, 0.145 mol) and 2,2'-bipyridine (5 mg) were dissolved in THF (250 mL) under argon and cooled to –65 °C. *N*-Butyllithium (~0.3 mol) dissolved in hexane was carefully added until the indicator remained pink and the temperature increased to –5 °C. The solution was cooled to –65 °C, and 3(Z)-hexenoic chloride (10.43 g, 0.079 mol) was added dropwise (Wierenga and Skulnick, 1979). After 15 min of stirring at –65 °C, the mixture was poured in a mixture of Et₂O (400 mL) and 1 N HCl (200 mL). The organic layer was washed twice with saturated NaHCO₃ solution (100 mL) and H₂O (100 mL). The extract was dried (Na₂SO₄), and ethyl 3-oxo-5(Z)-octenoate was distilled in vacuo to yield the octenoate: 12.2 g (0.066 mol, 84%); spectral data were identical with previously published data (Beuerle et al., 1996; Berger et al., 1988).

(R,S)-5(Z)-Octene-1,3-diol (rac-3). Ethyl 3-oxo-5(Z)-octenoate (5.2 g, 0.029 mol) was reduced by LiAlH₄ in absolute Et₂O. 2.9 g (0.02 mol, 69%). Spectral data were in accordance with previously published data (Beuerle et al., 1996; Berger et al., 1988).

(R)-Octane-1,3-diol (R-1). Compound **R-1** was synthesized according to the method of Dietrich et al. (1997). EIMS, *R*_f and ¹H and ¹³C NMR were identical with previously published data (Beuerle et al., 1996).

1-Tosyl-2-pentyne. 2-Pentyne-1-ol was tosylated according to a published procedure (Ishchenko et al., 1987): *R*_f 0.78 (Et₂O); *R*_f 1900; ¹H NMR (CDCl₃, 400 MHz) δ 1.01 (H₃CCH₂, t, 7.36 Hz), 2.04–2.12 (CH₃CH₂C \equiv , m), 2.45 (CH₃Ph, s), 4.69

(–CH₂OSO₂–, t, 2.21 Hz), 7.34 and 7.81 (PhH, d, 8.2 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 12.3 (H₃CCH₂C \equiv), 13.1 (H₃CCH₂–), 21.5 (CH₃Ph), 58.7 (–CH₂OSO₂–), 71.2 (CH₂C \equiv C), 128.1, 129.7, 144.8 (C₆H₄); EIMS *m/z* 91 (100), 139 (75), 65 (60), 92 (43), 66 (40), 83 (20), 67 (15), 117 (12), 155 (10).

1-Bromo-2-pentyne. Nucleophilic substitution of 1-tosyl-2-pentyne with NaBr yielded 1-bromo-2-pentyne (Ishchenko et al., 1987): yield, 50% for both steps; *R*_f 0.57 [*n*-hexane/EtOAc (95:5)]; *R*_f 1301; IR(KBr) ν_{max} 3010 (C=CH), 2950 (CH), 2910 (CH), 2850 (CH), 2210 (C=C), 600 (CBr); ¹H NMR (CDCl₃, 400 MHz) δ 1.14 (H₃C–, t, 7.35 Hz), 2.25 (CH₃CH₂C \equiv , m), 3.93 (≡CCH₂Br, t, 2.39 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 12.6 (H₃CCH₂C \equiv), 13.4 (H₃CCH₂–), 15.5 (≡CCH₂Br), 74.7 (–CH₂C \equiv), 89.4 (C \equiv CH₂Br); EIMS *m/z* 67 (100), 65 (14), 148 [M]⁺ (13), 68 (12), 146 (12).

2,5-Octadiinol. 1-Bromo-2-pentyne and 2-(propargyloxy)-tetrahydropyran were coupled according to the procedure of Kobayashi et al. (1989), Mori and Ebata (1986), and Cossey and Acilnou (1990): yield, 73%; *R*_f 2113; EIMS, *m/z* 77 (100), 91 (60), 104 (55), 79 (45), 65 (40), 103 (30), 51 (30), 53 (25), 63 (23), 107 (15), 93 (12); ¹H and ¹³C NMR were in accordance with previously published data (Kobayashi et al., 1989; Mori and Ebata, 1986; Cossey and Acilnou, 1990; Nigam and Weedon, 1956).

2(Z),5(Z)-Octadienol. Reduction of 2,5-octadiinol according to Lindlar's method was performed in the same manner as reported (Kobayashi et al., 1989; Mori and Ebata, 1986; Cossey and Acilnou, 1990; Nigam and Weedon, 1956; Lindlar and Dubius, 1966). The product was purified by flash chromatography on silica gel with pentane/Et₂O (7:3): yield, 86%; *R*_f 0.29 [Et₂O/pentane (3:7)]; *R*_f 1681; EIMS, *m/z* 79 (100), 55 (45), 67 (39), 77 (25), 93 (25), 70 (21), 53 (18), 80 (15), 91 (15), 108 [M – H₂O]⁺ (15).

(2S,3R)-Epoxy-5(Z)-octenol. Epoxidation of 2(Z),5(Z)-octadienol was conducted according to the method of Katsuki and Sharpless (1980) as described by Beuerle et al. (1996): yield, 97%; *R*_f 0.75 (Et₂O); *R*_f 1998; EIMS, *m/z* 67 (100), 55 (90), 111 (70), 81 (65), 69 (47), 53 (43), 79 (43), 57 (40), 93 (38), 83 (34), 77 (25), 65 (21), 91 (18).

(R)-5(Z)-Octene-1,3-diol (R-3). Red-Al-solution [65% in toluene (12 mL, 39 mmol)] (Sugiyama et al., 1990) was added dropwise to a cooled (0 °C) solution of (2S,3R)-epoxy-5(Z)-octen-1-ol (2.6 g, 0.019 mol) in THF (100 mL) until no more formation of gas was detectable. The mixture was stirred for 8 h at 0 °C,

and the reaction was stopped with 10% HCl (100 mL). The aqueous phase was extracted (three times) with Et₂O (50 mL). The organic layers were combined, dried (Na₂SO₄), and concentrated. The product was purified by flash chromatography on silica gel with Et₂O/pentane (7:3) and Et₂O. The ratio 1,3-diol/1,2-diol was 95:5: 1.95 g (0.014 mol, 76%); IR, ¹H and ¹³C NMR, R_f, and EIMS were in accordance with previously published data (Beuerle et al., 1996).

General Preparation of 1,3-Dioxanes. Diol (2 mmol), aldehyde or ketone (2 mmol), *p*-toluenesulfonic acid (6 mg), and Na₂SO₄ (40 mg) were suspended in Et₂O, and the mixture was stirred overnight until the diol completely disappeared. 1,3-Dioxanes were purified by flash chromatography with pentane/Et₂O (9:1) on silica gel (Dietrich et al., 1997): yields, 0.25–0.35 g (1.4–1.9 mmol, 70–95%); R_f and EIMS (cf. Tables 1–2); ¹H and ¹³C NMR (cf. Tables 3–5).

RESULTS AND DISCUSSION

During our investigation on the biogenesis of (*R*)-octane-1,3-diol [(*R*)-**1**] and (*R*)-5(*Z*)-octene-1,3-diol [(*R*)-**3**] in apples and pears we identified (2*S*,4*R*)- and (2*R*,4*R*)-2-methyl-4-pentyl-1,3-dioxane **4** as well as (2*S*,4*R*)- and (2*R*,4*R*)-2-methyl-4-[2'(*Z*)-pentenyl]-1,3-dioxane **14** for the first time in apple products such as cider (Dietrich et al., 1997). However, we expected the occurrence of further 1,3-dioxanes formed from 1,3-diols and carbonyl compounds because yeast and apples produce a number of aldehydes and ketones. Therefore, reference compounds were prepared to identify the anticipated 1,3-dioxanes.

(*R,S*)-Octane-1,3-diol [(*R,S*)-**1**] and (*R,S*)-5(*Z*)-octene-1,3-diol [(*R,S*)-**3**] were synthesized by LiAlH₄ reduction of their respective 3-oxo ethyl esters, whereas (*R*)-octane-1,3-diol [(*R*)-**1**] and (*R*)-5(*Z*)-octane-1,3-diol [(*R*)-**3**] were obtained by Sharpless epoxidation of their allylic alcohols using (+)-diethyl tartrate as the chiral ligand (Dietrich et al., 1997). The synthesis of (3*R*,7*R*)- and (3*R,S*,7*R,S*)-octan-1,3,7-triol denoted, respectively, as [(3*R*,7*R*)- and (3*R,S*,7*R,S*)-**2**] has been reported recently (Beuerle et al., 1999). The (4*R,S*,2*R,S*) stereoisomers of **4**–**10**, **12**–**20**, and **22** were obtained by the reaction of racemic 1,3-diols with the aldehydes or ketones, and (4*R*,2*R,S*) diastereomers were formed from (3*R*)-diols and the aldehydes or ketones. Tables 1–5 show the mass spectra and ¹³C and ¹H NMR data. Separation of the diastereomers by flash chromatography on silica gel afforded pure (4*R*,2*R*)- and (4*R*,2*S*)-1,3-dioxanes in a ratio of approximately 1:10, except for **11** and **21** as they did not appear as diastereomers. However, separation of stereoisomers of **12** and **22** was not achieved by flash chromatography on silica gel. GC analysis revealed a ratio of 2:3 for (4*R*,2*R*)-**12**/(4*R*,2*S*)-**12** and (4*R*,2*R*)-**22**/(4*R*,2*S*)-**22**. ¹H NMR homonuclear decoupling experiments of (4*R*,2*S*)-**4** and (4*R*,2*S*)-**14** showed vicinal coupling between 4-H and 5-H *axial* (*J* = 12 Hz) and 5-H *equatorial*, respectively (*J* = 1 Hz). These are typical coupling constants for axial protons, and they are inconsistent with the presence of equatorial protons at position 4 (Dietrich et al., 1997; Eliel and Knoeber, 1968). The configuration at carbon 2, originating from the carbonyl carbon of the aldehydes, is determined by the disposition of the 2-alkyl group, which prefers the equatorial position (Eliel and Knoeber, 1968). NOE experiments of (4*R*,2*S*)-1,3-dioxanes showed positive enhancement of H-6 *axial* and H-4 after irradiating H-2 and vice versa. Consequently, protons at positions 2, 4, and 6 *axial* are all axial, confirming the chair conformation of the 1,3-dioxanes and the (*S*)-configuration at

Table 4. ¹H NMR Data of Dioxanes 5–13^a

| proton | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
|--------|---|---|---|---|---|---|-------------------------------------|--------------------------------------|---|
| H2 | 4.42 (t, <i>J</i> = 5.1, 1H) | 4.50 (t, <i>J</i> = 5.5, 1H) | 4.17 (d, <i>J</i> = 5.1, 1H) | 4.49 (t, <i>J</i> = 5.5, 1H) | 4.54 (t, <i>J</i> = 5.0, 1H) | 4.26 (d, <i>J</i> = 5.0, 1H) | | | 4.64 (q, <i>J</i> = 5.1, 1H) |
| H6e | 4.09 (ddd, <i>J</i> = 11.0, 5.0, 1.3, 1H) | 4.10 (ddd, <i>J</i> = 11.4, 5.0, 1.3, 1H) | 4.09 (ddd, <i>J</i> = 11.0, 4.5, 1.1, 1H) | 4.09 (ddd, <i>J</i> = 11.4, 5.0, 1.1, 1H) | 4.08 (ddd, <i>J</i> = 11.0, 5.0, 1.1, 1H) | 4.09 (ddd, <i>J</i> = 11.0, 5.0, 1.3, 1H) | 3.75–3.87 (m, 2H) | 3.75–3.87 (m, 2H) | 4.04 (ddd, <i>J</i> = 11.2, 5.0, 1.0, 1H) |
| H6a | 3.71 (dt, <i>J</i> = 12.0, 2.5, 1H) | 3.72 (dt, <i>J</i> = 12.0, 2.5, 1H) | 3.69 (dt, <i>J</i> = 12.0, 2.5, 1H) | 3.72 (dt, <i>J</i> = 12.0, 2.5, 1H) | 3.72 (dt, <i>J</i> = 12.0, 2.5, 1H) | 3.70 (dt, <i>J</i> = 12.0, 2.5, 1H) | 3.96 (dq, <i>J</i> = 12.0, 3.0, 1H) | 3.94 (dq, <i>J</i> = 12.0, 3.0, 1H) | 3.69 (dt, <i>J</i> = 12.0, 2.2, 1H) |
| H4a | 3.54 (m, 1H) | 3.56 (m, 1H) | 3.53 (m, 1H) | 3.55 (m, 1H) | 3.55 (m, 1H) | 3.52 (m, 1H) | see H6e | see H6e | 3.56 (m, 1H) |
| H5 | 1.2–1.63 (m, 12H) | 1.2–1.63 (m, 14H) | 1.2–1.65 (m, 10H) | 1.2–1.65 (m, 18H) | 1.2–1.65 (m, 12H) | 1.2–1.65 (m, 13H) | 1.2–1.6 (m, 10H) | 1.25–1.65 (m, 10H) | 1.30–1.65 (m, 8H) |
| H7–9 | see H5 | see H5 | see H5 | see H5 | see H5 | see H5 | see H5 | see H5 | see H5 |
| H10 | see H5 | see H5 | see H5 | see H5 | see H5 | see H5 | see H5 | see H5 | 3.75 (m, 1H) |
| H11 | 0.89 (t, <i>J</i> = 7.0, 3H) | 0.88 (t, <i>J</i> = 7.0, 3H) | 0.88 (t, <i>J</i> = 7.0, 3H) | 0.88 (t, <i>J</i> = 7.0, 6H) | 0.88 (t, <i>J</i> = 7.0, 9H) | 0.87 (t, <i>J</i> = 7.0, 9H) | 0.88 (t, <i>J</i> = 7.0, 3H) | 0.87 (m, 6H) | 1.14 (d, <i>J</i> = 6.2, 3H) |
| H12 | see H5 | see H5 | 1.78 (m, 1H) | see H5 | see H5 | see H5 | e 1.38 (s, 3H) a 1.45 (s, 3H) | e 1.75 (m, 1.2H) a 1.98 (m, 0.8H) | 1.27 (d, <i>J</i> = 5.1, 3H) |
| H13 | 0.94 (t, <i>J</i> = 7.5, 3H) | see H5 | 0.92 (d, <i>J</i> = 6.8, 6H) | see H5 | 1.8 (m, 1H) | see H5 | | see H11 | |
| H14 | | 0.94 (t, <i>J</i> = 7.5, 3H) | | see H5 | see H11 | see H11 | | e 1.29 (s, 1.8H) a 1.37 (s, 1.2H) | |
| H15 | | | | see H5 | see H11 | see H11 | | | |
| H16 | | | | see H11 | see H11 | see H11 | | | |

^a a, axial; e, equatorial.

Table 5. ¹H NMR Data of Dioxanes 15–22^a

| proton | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 |
|--------|------------------------------------|------------------------------------|------------------------------------|------------------------------------|------------------------------------|------------------------------------|------------------------------|------------------------------|
| H2 | 4.45 (t, J = 5.2, 1H) | 4.52 (t, J = 5.5, 1H) | 4.20 (d, J = 5.1, 1H) | 4.49 (t, J = 5.5, 1H) | 4.55 (t, J = 5.0, 1H) | 4.29 (d, J = 5.0, 1H) | | |
| H6e | 4.10 (ddd, J = 11.0, 5.0, 1.3, 1H) | 4.10 (ddd, J = 11.4, 5.0, 1.1, 1H) | 4.10 (ddd, J = 11.0, 4.5, 1.1, 1H) | 4.10 (ddd, J = 11.4, 5.0, 1.1, 1H) | 4.08 (ddd, J = 11.0, 5.0, 1.3, 1H) | 4.09 (ddd, J = 11.0, 5.0, 1.3, 1H) | 3.75–3.87 (m, 2H) | 3.75–3.87 (m, 2H) |
| H6a | 3.71 (dt, J = 11.9, 2.5, 1H) | 3.72 (dt, J = 12.0, 2.5, 1H) | 3.69 (dt, J = 11.9, 2.5, 1H) | 3.71 (dt, J = 12.0, 2.5, 1H) | 3.70 (dt, J = 12.0, 2.5, 1H) | 3.69 (dt, J = 12.0, 2.5, 1H) | 3.94 (dq, J = 12.0, 3.0, 1H) | 3.94 (dq, J = 12.0, 3.0, 1H) |
| H4a | 3.59 (m, 1H) | 3.59 (m, 1H) | 3.57 (m, 1H) | 3.58 (m, 1H) | 3.58 (m, 1H) | 3.57 (m, 1H) | see H6e | see H6e |
| H5 | 1.4–1.65 (m, 4H) | 1.4–1.7 (m, 6H) | e 1.43 (m, 1H) | 1.2–1.65 (m, 10H) | 1.3–1.65 (m, 4H) | 1.3–1.65 (m, 5H) | 1.4–1.6 (m, 2H) | 1.45–1.65 (m, 2H) |
| H7 | a 2.24 (m, 1H) | a 2.23 (m, 1H) | a 2.23 (m, 1H) | a 2.23 (m, 1H) | a 2.23 (m, 1H) | a 2.24 (m, 1H) | a 2.24 (m, 1H) | a 2.24 (m, 1H) |
| H8 | b 2.34 (m, 1H) | b 2.32 (m, 1H) | b 2.32 (m, 1H) | b 2.32 (m, 1H) | b 2.32 (m, 1H) | b 2.34 (m, 1H) | b 2.34 (m, 1H) | b 2.34 (m, 1H) |
| H9 | 5.36 (m, 1H) | 5.36 (m, 1H) | 5.36 (m, 1H) | 5.36 (m, 1H) | 5.34 (m, 1H) | 5.34 (m, 1H) | 5.33 (m, 1H) | 5.35 (m, 1H) |
| H10 | 5.49 (m, 1H) | 5.49 (m, 1H) | 5.49 (m, 1H) | 5.49 (m, 1H) | 5.47 (m, 1H) | 5.46 (m, 1H) | 5.46 (m, 1H) | 5.47 (m, 1H) |
| H11 | 2.06 (m, 2H) | 2.06 (m, 2H) | 2.06 (m, 2H) | 2.06 (m, 2H) | 2.06 (m, 2H) | 2.06 (m, 2H) | 2.06 (m, 2H) | 2.06 (m, 2H) |
| H12 | 0.96 (t, J = 7.4, 3H) | 0.95 (t, J = 7.7, 3H) | 0.96 (t, J = 7.7, 3H) | 0.88 (t, J = 7.4, 9H) | 0.94 (t, J = 7.0, 3H) | 0.96 (t, J = 7.0, 3H) | 0.95 (t, J = 7.0, 3H) | 0.91 (m, 6H) |
| H13 | see H5 | see H5 | 1.78 (m, 1H) | see H5 | see H5a | see H5 | e 1.39 (s, 3H) | e 1.79 (m, 1.2H) |
| H14 | 0.94 (t, J = 7.5, 3H) | see H5 | 0.92 (d, J = 6.8, 6H) | see H5 | 1.79 (m, 1H) | see H5 | a 1.95 (m, 0.8H) | a 1.95 (m, 0.8H) |
| H15 | | | | see H5 | 0.9 (m, 6H) | 0.9 (m, 6H) | a 1.45 (s, 3H) | e 1.31 (s, 1.8H) |
| H16 | | | | 0.88 (t, J = 7.0, 3H) | see H14 | see H14 | | a 1.38 (s, 1.2H) |

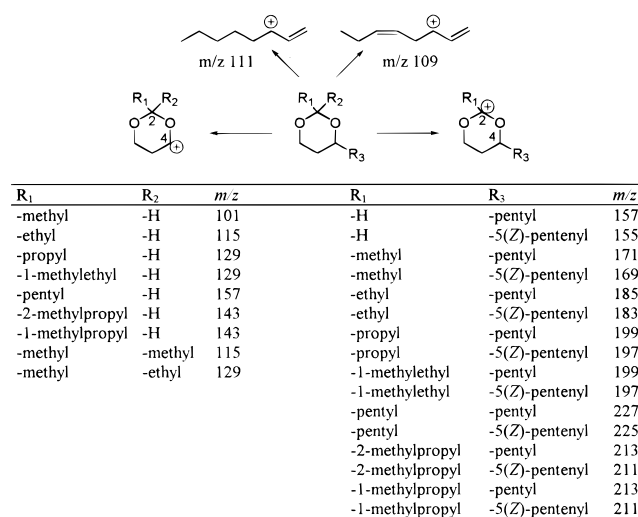
^a a, axial; e, equatorial.

Figure 1. Fragmentation pattern of 1,3-dioxanes.

Table 6. 1,3-Dioxanes in Apples and Cider

| 1,3-dioxane | apple | cider | 1,3-dioxane | apple | cider |
|-------------|-------|-------|-------------|-------|-------|
| 4 | ++ | +++ | 14 | + | ++ |
| 5 | + | ++ | 15 | nd | + |
| 6 | + | + | 16 | nd | + |
| 7 | nd | + | 17 | nd | + |
| 8 | + | + | 18 | + | + |
| 9 | nd | ++ | 19 | nd | + |
| 10 | nd | + | 20 | nd | + |
| 11 | nd | + | 21 | nd | + |
| 12 | nd | ++ | 22 | nd | + |
| 13 | nd | + | | | |

^a nd, not detected; +, 0.001–0.1 mg/L; ++, 0.1–1 mg/L; +++, > 1 mg/L.

position 2 as expected for the major products (Dietrich et al., 1997). The minor compounds were assigned as (4*R*,2*R*)-1,3-dioxanes on the basis of their chromatographic behavior and mass spectra.

The mass spectra of the 1,3-dioxanes showed characteristic fragmentation patterns (Figure 1). Cleavage between C₂/R₁ and C₂/R₂ as well as C₄/R₃ was preferred. Acetals displayed the [M – H]⁺ ion, which was not detected for the ketals. Aldehydic characteristic *m/z* fragments based on the R₁ substituent were obtained. The pentyl- and 2(*Z*)-pentenyl moieties were indicated by the fragment ions *m/z* 111 and 109, which served to distinguish 1,3-dioxanes from **1** and **3**, respectively (Figure 1).

Compounds **4**–**22**, ranging in concentration from 10^{–3} to 10 ppm, were detected by GC/MS analysis in extracts of apples and cider aged for one year (Table 6). The configuration at carbon 4' in naturally occurring **13** was deduced by multidimensional gas chromatographic (MDGC) analysis by comparison with the synthesized reference compounds. A ratio of 4'*R*/4'*S* in **13** of 3:2 corresponding to the enantiomeric ratio in naturally occurring **2** at position 7 was found (Beuerle et al., 1999).

Therefore, we believe that the 1,3-dioxanes are chemically formed from the natural apple ingredients (*R*)-octane-1,3-diol, (*R*)-5(*Z*)-octene-1,3-diol, (3*R*,7*R*)- and (3*R*,7*S*)-octane-1,3,7-triol and the respective aldehydes and ketones, which are produced either by the apples (Paillard 1990) or by the yeast fermentation of the apple juice. The dioxanes exhibit a weak “green note” flavor so they might contribute to the overall flavor of cider by decreasing the concentration of undesirable alde-

hydes and ketones by converting them into compounds with pleasant aroma.

ABBREVIATIONS USED

FID, flame ionization detector; GC, capillary gas chromatography; GC/MS, capillary gas chromatography/mass spectrometry; HPLC, high-performance liquid chromatography; TLC, thin-layer chromatography; XAD, polystyrene resin.

ACKNOWLEDGMENT

The support of Dr. P. Brunerie, Pernod Ricard, Centre de Recherche, Créteil, France, who kindly provided apples, is gratefully acknowledged.

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Received for review June 29, 1999. Revised manuscript received September 30, 1999. Accepted October 7, 1999. This work was supported by the Deutsche Forschungsgemeinschaft, Bonn (Schw 634/1-1 and Schw 634/1-2).

JF990714X