# 25. The Synthesis of Natural Acetylenic Compounds from *Eutypa lata* (Pers: F.) TUL.

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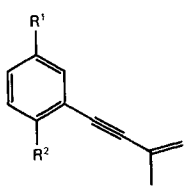
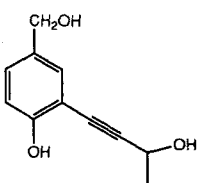
The synthesis of a series of novel acetylenic compounds **1–7**, isolated recently from the fungus *Eutypa lata*, is described. The crucial step is the coupling reaction between a protected aryl halogenide and the acetylenic chain as a cuprous acetylide (*Scheme 1*). A more efficient method using bis(triphenylphosphine)palladium dichloride ($[Pd(PPh_3)_2Cl_2]$) as catalyst was also carried out with success.

**Introduction.** – The fungus *Eutypa lata* also named *Eutypa armeniacae* is responsible for the dieback of vineyards (eutypiosis) observed during the last years in Switzerland, France, and many other countries [1]. In the course of our search for secondary metabolites with a phytotoxic activity in the culture medium of *Eutypa lata*, a series of new acetylenic compounds **1–7** were isolated [2] [3]. Compound **1** ( = 4-hydroxy-3-(3-methylbut-3-en-1-ynyl)benzaldehyde), named eutypine, was found to be the most phytotoxic compound isolated [2] [3].




**7**

**1** $R^1 = CHO$, $R^2 = OH$

**2** $R^1 = CHO$, $R^2 = MeO$

**3** $R^1 = COOH$, $R^2 = OH$

**4** $R^1 = OH$, $R^2 = OH$

**5** $R^1 = CH_2OH$, $R^2 = OH$

**6** $R^1 = CH_2OH$, $R^2 = MeO$

To study the role played by eutypine **1** and the related compounds **2–7** in the pathogenesis of eutypiosis, more specific tests (by protoplast bioassay) are necessary. Thus, to acquire bigger quantities of material for the bioassay, compounds **1–7** were synthesized from the commercially available 4-hydroxybenzaldehyde.

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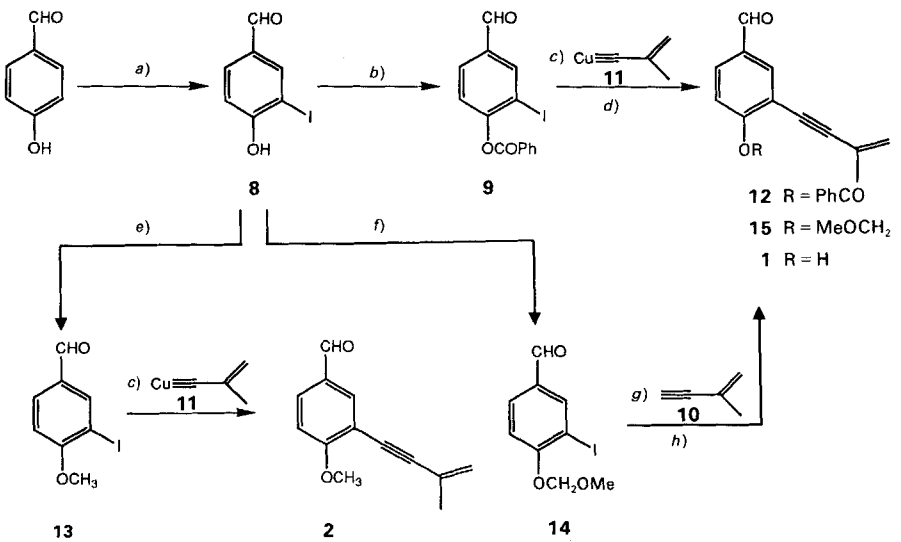
**Results and Discussion.** – The series of new acetylenic compounds is structurally similar to the previously reported frustulosin [4] and contains the same acetylenic chain, except for **7**. Retrosynthetic analysis suggested that **1** could be prepared by coupling the alkyne chain (as a cuprous acetylide) with an aryl halogenide [5]. Thus the iodo compound **8**, which was more reactive than the bromo or the chloro analogue, was prepared by iodination of 4-hydroxybenzaldehyde [6] (*Scheme 1*). However, direct coupling of **8** prior to protection of the phenol function produced cyclisation of the *ortho*-hydroxyacetylide leading to a benzofuran derivative[3]). Since eutypine (**1**) was relatively stable under basic conditions, we decided to protect the phenol as an ester (benzoate **9**) which was stable under the coupling conditions. Other protecting groups such as $MeOCH_2$, tetrahydro-2*H*-pyran-2-yl, $Me_3Si$, or (*t*-Bu)$Me_2Si$ were unsuitable and led to the benzofuran derivative. The acetylenic chain 2-methylbut-1-en-3-yne (**10**) was prepared by

*Scheme 1*




*a*) $I_2$, KI, $Me_2NH$. *b*) PhCOCl, $Et_3N$, $Et_2O$. *c*) DMF, 120°. *d*) EtOH, 3% aq. NaOH soln. *e*) $Me_2SO_4$, $K_2CO_3$, acetone. *f*) $CH_2(OMe)_2$, $P_2O_5$, $CH_2Cl_2$. *g*) $Et_2NH$, $[Pd(PPh_3)_2Cl_2]$, CuI. *h*) AcOH/HCl.

dehydration of the commercially available 2-methylbut-3-yn-2-ol in $Ac_2O$/concentrated $H_2SO_4$ solution [7] and transformed to the cuprous acetylide **11** by using CuI in $NH_4OH$ following *Atkinson*'s method [8]. Coupling of **9** and **11** was then accomplished in DMF for 3 h, affording compound **12**. The coupling temperature was crucial, the phenol protection (benzoate) being cleaved above 120° to give as the major product again the benzofuran derivative. Intermediate **12** was directly saponified without further purification to afford **1**. The overall yield was 20%, and large-scale synthesis was possible. Compound **2** was prepared in the same manner by coupling the iodo compound **13** with the cuprous acetylide **11**. The MeO group present in **2** could not serve as protecting group

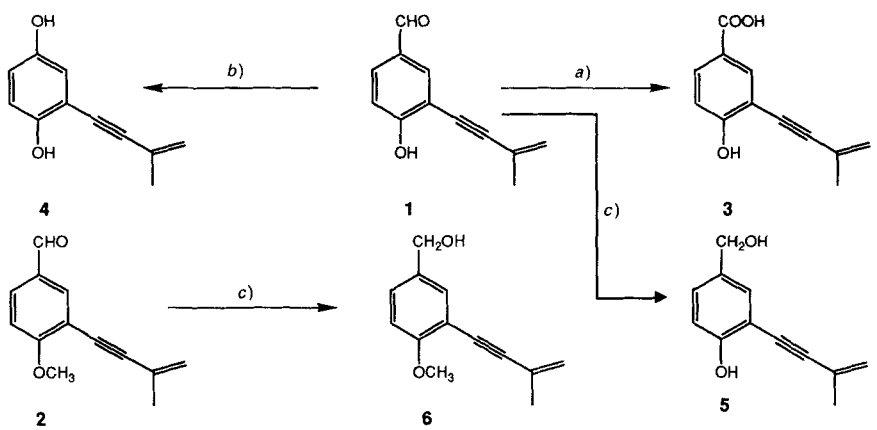
[3]) This type of benzofuran derivatives was also found in the culture media of *Eutypa lata*.

of the phenolic function in the synthesis of **1**, since **1** was unstable under the deprotection conditions. Compound **2** was also prepared from **1** by direct methylation with MeI.

A more efficient method of synthesizing **1** consisted in coupling the acetylenic chain **10** with an aryl halogenide in the presence of a catalyst, bis(triphenylphosphine)-palladium dichloride ($[Pd(PPh_3)_2Cl_2]$), in basic media [9]. In this case, the PhCO protecting group could not be used; it was replaced by the $MeOCH_2$ group which was easily introduced using dimethoxymethane in acidic media (**8** → **14**; *Scheme 1*). Subsequent coupling with **10** in the presence of $[Pd(PPh_3)_2Cl_2]$ in $Et_2NH$ afforded, in good yield, **15** as a precursor of **1**. In acidic media, **15** was relatively unstable. Thus, hydrolysis of the $MeOCH_2$ group had to be performed under particularly mild conditions, *i.e.* in AcOH/concentrated HCl solution, leading to **1** in 55% overall yield.

Carboxylic acid **3** was obtained in good yield as white needles by oxidation of **1** using $NaClO_2$ in $H_2O$/dioxane solution [11] (*Scheme 2*). Under these conditions, $Cl_2$ was liberated. Thus, sulfamic acid was added to avoid chlorination of the product. However, some chlorohydrine derivative produced by chlorination of the double bond was also

*Scheme 2*

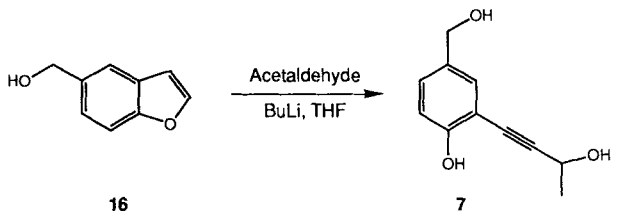



*a*) $NH_2SO_3H$, $NaClO_2$, dioxane/$H_2O$. *b*) $H_2O_2$, aq. KOH soln. *c*) $NaBH_4$, 1% aq. NaOH soln.

formed in low yield ( < 5%). For the synthesis of hydroxyquinone **4**, **1** was treated with 3-chloroperbenzoic acid (*Baeyer-Villiger* reaction [12]) which resulted to the total degradation of **1**. However, using $H_2O_2$ in basic medium (*Dakin*'s reaction [13]), we obtained **4** in good yield. Compound **4** was identical to siccayne (described by *Pinault et al.* [14]) by spectroscopic means (NMR, MS). Diol **5** was obtained in quantitative yield by reduction of **1** using $NaBH_4$. The same procedure was applied to the reduction of **2** to afford **6**.

Triol **7** could not be prepared by coupling iodo compound **9** with the corresponding acetylenic chain (but-3-yn-2-ol), because the cuprous acetylide was unstable. By protecting the alcohol group of but-3-yn-2-ol with a tetrahydro-2*H*-pyran-2-yl group, the cuprous acetylide became more stable, but it was not reactive enough for coupling. Because of the high coupling temperature required, we only observed cyclisation to a benzofuran derivative (see above). However, the reversed reaction (opening of the benzo-

*Scheme 3*




**16** **7**

furan ring) was possible [15] and studied in our laboratory [16]. Thus, alkylation of benzofuran **16**[4]) by acetaldehyde followed by ring-opening in the presence of the strong base BuLi yielded 53% of **7** (*Scheme 3*).

NMR and GC/MS comparison of the synthetic compounds **1–7** with the corresponding natural products confirmed their established structures. These compounds could be synthesized in large scale and are presently being tested for their phytotoxicity.

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## Experimental Part

*General.* All commercially available chemical reagents were used without further purification. All reactions were followed by TLC: aluminium sheets silica gel *60 $F_{254}$* (*Merck*). Prep. column chromatography (CC): silica gel (*Merck 60*, 0.063–0.200 mm). M.p.: *Gallenkamp MFB-595-010M*. FT-IR [$cm^{-1}$]: *Perkin-Elmer 1720X*; KBr disks, unless otherwise indicated. $^1$H-NMR: *Bruker AMX 400*; $\delta$ in ppm using TMS as internal standard, $J$ in Hz. EI-MS: positive mode; *Nermag-R-3010* spectrometer. The microanalyses were done at the Laboratory for Organic Chemistry of ETH, Zurich.

*4-Hydroxy-3-iodobenzaldehyde* (**8**). To a soln. of commercial 4-hydroxybenzaldehyde (24.4 g, 0.2 mol) in 30% aq. $Me_2NH$, an aq. soln. of $I_2$ (40.6 g, 0.16 mol) and KI (50 g, 0.3 mol) was added dropwise at r.t. The mixture was stirred for 3 h, then cooled to 0°, acidified with 10% aq. HCl soln., and extracted with $Et_2O$. The org. layer was washed with 1% aq. $NaHSO_3$ soln., then with 5% aq. $NaHCO_3$ soln., dried ($MgSO_4$), and evaporated, and the residue purified by CC ($CH_2Cl_2$): **8** (28.8 g, 58%). M.p. 116–117°. FT-IR: 3300–3100 (OH), 1667, 1593, 1567, 1506, 1494, 1408, 1294, 1217, 1190, 1152, 1138, 890, 825. $^1$H-NMR (400 MHz, $CDCl_3$): 9.80 (*s*, CHO); 8.23 (*d*, $J$ = 1.9, H–C(2)); 7.79 (*dd*, $J$ = H–C(6)); 7.11 (*d*, $J$ = 8.3, H–C(5)); 6.50 (br. *s*, OH). EI-MS: 248 (100, $M^+$), 247 (95, $[M-H]^+$), 219 (18), 92 (32), 63 (30).

*4-(Benzoyloxy)-3-iodobenzaldehyde* (**9**). To a soln. of **8** (6 g, 24 mmol) and $Et_3N$ (3.7 g, 37 mmol) in dry $Et_2O$, an $Et_2O$ soln. of benzoyl chloride (3.7 g, 26.5 mmol) was added dropwise at r.t. After 30 min, the soln. was filtered, washed with 0.5% aq. HCl soln., twice with 2% aq. $NaHCO_3$ soln., dried ($MgSO_4$), and evaporated, and the residue recrystallised in $CH_2Cl_2$/ligroine: **9** (7.3 g, 83%). M.p. 96°. FT-IR: 3060, 2855, 1745, 1700, 1590, 1565, 1475, 1450, 1375, 1270, 1245, 1215, 1185, 1170, 1060, 1020, 890, 815. $^1$H-NMR (400 MHz, $CDCl_3$): 9.97 (*s*, CHO); 8.41 (*d*, $J$ = 1, H–C(2)); 8.28 (*m*, H–C(2′), H–C(6′)); 7.95 (*dd*, H–C(6)); 7.60–7.80 (*m*, H–C(3′), H–C(4′), H–C(5′)); 7.50 (*d*, $J$ = 8, H–C(5)). EI-MS: 352 (1, $M^+$), 105 (100, $C_6H_5CO^+$), 77 (40, $C_6H_5^+$).

*3-Iodo-4-methoxybenzaldehyde* (**13**). To a soln. of **8** (5 g, 20 mmol) in dry acetone (100 $cm^3$) was added anh. $K_2CO_3$ (10 g, 72 mmol) and $Me_2SO_4$ (1.9 g, 15 mmol). The mixture was stirred for 3 h at r.t., then diluted with $H_2O$, and concentrated under vacuum. The aq. layer was extracted with $Et_2O$, the org. layer washed successively with 1% aq. NaOH soln. and sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue purified by CC ($CH_2Cl_2$): **13** (4.2 g, 80%). M.p. 103°. FT-IR: 3010, 2970, 2935, 2830, 1675, 1650, 1590, 1565, 1490, 1440, 1310, 1275, 1255, 1180, 1155, 1045, 1015, 885, 825. $^1$H-NMR (400 MHz, $CDCl_3$): 9.82 (*s*, CHO); 8.30 (*d*, $J$ = 2, H–C(2)); 7.85 (*dd*, H–C(6)); 6.92 (*d*, $J$ = 9, H–C(5)); 3.97 (*s*, MeO). EI-MS: 262 (100, $M^+$), 261 (74, $[M-H]^+$), 119, 77.

[4]) Compound **16** was prepared in our laboratory in five steps from salicylaldehyde in 12% overall yield [16].

*3-Iodo-4-(methoxymethoxy)benzaldehyde* (**14**). To a soln. of **8** (10 g, 0.04 mol) and $CH_2(OMe)_2$ (20 equiv., 72 ml) in dry $CH_2Cl_2$ (100 ml) was added $P_2O_5$ (35 g) portionwise. After 2 h, more $P_2O_5$ (20 g) was added. The mixture was stirred for 5 h (complete disappearance of **8**). The mixture was then diluted with $CH_2Cl_2$, washed with 1N aq. NaOH and sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated. The yellow residue was used in the next step without purification. CC ($CH_2Cl_2$) yielded pure **14** (9.3 g, 80%). M.p. 66–67°. FT-IR: 3050, 2960, 2900, 2840, 1682, 1589, 1489, 1455, 1440, 1417, 1371, 1310, 1249, 1199, 1161, 1140, 1082, 1038, 1013, 973, 925. $^1$H-NMR (400 MHz, $CDCl_3$): 9.84 (*s*, CHO); 8.31 (*d*, *J* = 1.8, H–C(2)); 7.82 (*dd*, H–C(6)); 7.17 (*d*, *J* = 8.3, H–C(5)); 5.34 (*s*, $CH_2$); 3.52 (*s*, Me). EI-MS: 292 (10, $M^+$), 231 (5), 219 (5), 45 (100).

*2-Methylbut-1-en-3-yne* (**10**). A soln. of $Ac_2O$ (50 g, 0.49 mol) and conc. $H_2SO_4$ (2 g) was added dropwise to 2-methylbut-3-yn-2-ol at 50°. Compound **10** was purified by distillation (11.4 g, 72%). B.p. 32–33°. $n_D^{20}$ = 1.411 ([7]: 1.4099). $^1$H-NMR (400 MHz, $CDCl_3$): 5.39–5.29 (2*t*, C=$CH_2$); 2.87 (*s*, CH≡C); 1.90 (*t*, Me). EI-MS: (100, $M^+$), 65 (50, [$M - H^+$]), 63, 51, 50, 40, 39.

*Copper(I) 3-Methylbut-3-en-1-yn-1-ide* (**11**). To a soln. of CuI (8 g, 42 mmol) in 25% aq. $NH_4OH$ soln. (100 ml), $NH_2OH \cdot HCl$ (200 mg) was added until the soln. was light blue. Then **10** (2.3 g, 34 mmol) in EtOH (10 ml) was added and the mixture stirred vigorously for 15 min and poured into $H_2O$ (600 ml; → yellow precipitate). After 10–15 min, the mixture was filtered and the precipitate washed with $H_2O$ and then EtOH and dried: **11** (2.2 g, 50%).

*4-(Benzoyloxy)-3-(3-methylbut-3-en-1-ynyl)benzaldehyde* (**12**). Under $N_2$, **9** (2.0 g, 5.7 mmol) and **11** (1.45 g, 11.4 mmol) in dry DMF (50 ml) were heated at 110–120° for 3 h. The soln. was then concentrated by distillation under vacuum and AcOEt added. The insoluble $Cu^I$-salt was filtered off and the org. layer washed twice with sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated to give a brown oil which was used without further purification for the next reaction. CC ($CH_2Cl_2$/hexane) gave pure **12** (0.64 g, 39%). EI-MS: 290 (5, $M^+$), 105 (100, $C_6H_5CO^+$), 77 (40, $C_6H_5^+$).

*4-Hydroxy-3-(3-methylbut-3-en-1-ynyl)benzaldehyde* ( = *Eutypine*; **1**). *a*) To an EtOH soln. (40 ml) of **12** (0.6 g) was added 3% aq. NaOH soln. (20 ml). After stirring for 2 h, the soln. was diluted with $H_2O$, concentrated under vacuum, and washed with $Et_2O$. The aq. layer was then acidified with 5% aq. HCl soln. and extracted with AcOEt. The org. layer was washed with 2% aq. $NaHCO_3$ soln., dried ($MgSO_4$), and evaporated. The residual oil was purified by CC ($CH_2Cl_2$) to give **1** (120 mg, 62%). White needles. M.p. 76–77°. FT-IR: 3500–3100 (OH), 2959, 2922, 2852, 1670, 1600, 1567, 1496, 1435, 1375, 1321, 1295, 1265, 1251, 1143, 920, 831. $^1$H-NMR (400 MHz, $CDCl_3$): 9.85 (*s*, CHO); 7.89 (*d*, *J* = 1.8, H–C(2)); 7.79 (*dd*, H–C(6)); 7.08 (*d*, *J* = 8.5, H–C(5)); 6.39 (br. *s*, OH); 5.49–5.42 (2*s*, C=$CH_2$); 2.03 (*s*, Me). EI-MS: 186 (100, $M^+$), 185 (80, [$M - H$]$^+$), 157 (50, [$M$ – CHO]$^+$), 128, 77. Anal. calc. for $C_{12}H_{10}O_2$ (186.21): C 77.40, H 5.41; found: C 77.10, H 5.26.

*b*) To a soln. of **15** (see below; 2.4 g, 0.01 mol) in AcOH (60 ml) were added five drops of 12N HCl. The soln. was stirred at r.t. under $N_2$ for 8 h and then poured slowly to sat. aq. $NaHCO_3$ soln. and extracted with $Et_2O$. The org. layer was washed several times with sat. aq. $NaHCO_3$ soln. and extracted again with 1N aq. NaOH soln. The aq. layer which contained **1** was then acidified with 5% aq. HCl soln. and extracted with $Et_2O$. The org. layer was washed with sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated. The residual oil was purified by CC ($CH_2Cl_2$): **1** (1.52 g, 78%). White needles.

*4-(Methoxymethoxy)-3-(3-methylbut-3-en-1-ynyl)benzaldehyde* (**15**). A mixture of **14** (1.6 g, 0.006 mol), 2-methylbut-1-en-3-yne (**10**; 3 equiv., 1.1 g), [Pd($PPh_3$)$_2Cl_2$] (0.01 equiv., 40 mg), and CuI (0.01 equiv., 11 mg) in $Et_2NH$ (40 ml) was stirred overnight under $N_2$ at r.t. The mixture was then diluted with $Et_2O$, washed twice with 5% aq. HCl, twice with sat. aq. NaCl, dried ($MgSO_4$), and evaporated. The residual yellow oil was submitted to CC (silica gel): **15** (1.07 g, 85%). Pale-yellow oil. FT-IR (NaCl, film): 2958, 2922, 2829, 1697, 1595, 1573, 1496, 1444, 1430, 1371, 1311, 1246, 1154, 1124, 1114, 1083, 977, 818. $^1$H-NMR (400 MHz, $CDCl_3$): 9.87 (*s*, CHO); 7.94 (*d*, *J* = 2.1, H–C(2)); 7.78 (*dd*, H–C(6)); 7.23 (*d*, *J* = 8.6, H–C(5)); 5.45–5.35 (2*s*, C=$CH_2$); 5.33 (*s*, $CH_2O$); 3.53 (*s*, MeO); 2.01 (*s*, Me). EI-MS: 230 (20, $M^+$), 215 (15, [$M$ – Me]$^+$), 199 (20), 128 (40), 45 (100).

*4-Methoxy-3-(3-methylbut-3-en-1-ynyl)benzaldehyde* (**2**) was prepared by the same route as **1** by coupling **13** with **11**. Yield 50%. M.p. 49–50°. FT-IR: 3095, 2950, 2840, 1695, 1595, 1575, 1500, 1460, 1440, 1300, 1260, 1130, 1120, 1020, 905, 815. $^1$H-NMR (400 MHz, $CDCl_3$): 9.86 (*s*, CHO); 7.94 (*d*, *J* = 1.8, H–C(2)); 7.82 (*dd*, H–C(6)); 6.99 (*d*, *J* = 8.5, H–C(5)); 5.45–5.35 (2*m*, C=$CH_2$); 3.97 (*s*, MeO); 2.02 (*s*, Me). EI-MS: 200 (100, $M^+$), 159 (40, [$M - C_3H_5$]$^+$), 128 (50, [$M - C_3H_4O_2$]$^+$), 43 (45, $C_3H_7^+$).

*4-Hydroxy-3-(3-methylbut-3-en-1-ynyl)benzoic Acid* (**3**). To **1** (0.2 g, 1.07 mmol) in dioxane/$H_2O$ 3:2 (50 ml) was added sulfamic acid (0.6 g, 6.2 mmol) and $NaClO_2$ (0.96 g, 0.85 mmol). After 1 h stirring at r.t., $NaHCO_3$ (2 g) was added and the soln. concentrated and washed with AcOEt, acidified with 5% aq. HCl soln., and extracted with AcOEt. The org. layer was dried ($MgSO_4$) and evaporated. CC ($CH_2Cl_2$/AcOEt/AcOH 7:3:1): **3** (170 mg, 79%). White needles. M.p. 112°. FT-IR: 3470, 3410, 2925, 2855, 1685, 1610, 1580, 1495, 1420, 1320, 1280, 1220, 1170,

1120, 1100, 910, 840. $^1$H-NMR (400 MHz, $CDCl_3$): 10.90 (br. *s*, COOH); 8.15 (*d*, $J = 0.9$, H–C(2)); 8.01 (*dd*, H–C(6)); 7.02 (*d*, $J = 8.5$, H–C(5)); 5.49–5.41 (2*m*, C=$CH_2$); 2.03 (*s*, Me). EI-MS: (100, $M^+$), 185 (30, $[M - OH]^+$), 157 (20, $[M - COOH]^+$), 128 (10), 51 (10).

*2-(3-Methylbut-3-en-1-ynyl)benzene-1,4-diol* ( = *Siccayne*; **4**). To a soln. of **1** (0.28 g, 5 mmol) in aq. KOH soln. (20 ml), 3% aq. $H_2O_2$ soln. (5 ml) was added at r.t. under vigorous stirring. After 18 h, the aq. soln. was washed with $Et_2O$, acidified with 5% aq. HCl soln., and extracted with AcOEt. The org. layer was washed with 0.2% aq. $NaHCO_3$ soln., dried ($MgSO_4$), and evaporated. CC ($CH_2Cl_2$) gave pure **4** (150 mg, 86%). M.p. 115° ([14]: 114–116°). FT-IR: 3500–3100 (OH), 2920, 1615, 1450, 1375, 1235, 1210, 1190, 1160, 1110, 990, 925, 890. $^1$H-NMR (400 MHz, $CDCl_3$): 6.79 (*m*, H–C(3), H–C(5), H–C(6)); 5.45–5.35 (2*m*, $J = 0.5$, C=$CH_2$); 4.91 (br. *s*, OH); 2.00 (*m*, $J = 0.5$, Me). EI-MS: 174 (100, $M^+$), 173 (30, $[M - H]^+$), 159 (30, $[M - Me]^+$), 147 (20), 131 (20), 115 (15), 103 (10), 91, 77.

*4-Hydroxy-3-(3-methylbut-3-en-1-ynyl)benzyl Alcohol* (**5**). To **1** (0.186 g, 1 mmol) in 1% aq. NaOH soln. (25 ml) was added dropwise a 10% aq. NaOH soln. (2 ml) of $NaBH_4$ (50 mg, 1.3 mmol). After 2 h, the mixture was diluted with AcOEt and acidified with 5% aq. HCl soln. The org. layer was then washed with aq. $NaHCO_3$ soln., dried ($MgSO_4$), and evaporated, and the residue purified by CC ($CH_2Cl_2$/AcOEt 9:1): **5** (179 mg, 95%). White needles. M.p. 63–65°. FT-IR: 3600–3100 (OH), 2955, 2890, 2200, 1715, 1610, 1510, 1430, 1375, 1320, 1290, 1240, 1180, 1120, 1010, 985, 815. $^1$H-NMR (400 MHz, $CDCl_3$): 7.34 (*d*, $J = 1$, H–C(2)); 7.23 (*dd*, H–C(6)); 6.92 (*d*, $J = 8$, H–C(5)); 5.43–5.35 (2*m*, $J = 0.5$, C=$CH_2$); 4.58 (*s*, $CH_2OH$); 2.01 (*m*, $J = 0.5$, Me). EI-MS: 188 (100, $M^+$), 171 (60, $[M - OH]^+$), 131, 91, 77.

*4-Methoxy-3-(3-methylbut-3-en-1-ynyl)benzyl Alcohol* (**6**). As described for **5**, **6** was prepared by reduction of **2**. Yield 90%. FT-IR: 3500–3200 (OH), 2930, 2840, 2190, 1670, 1605, 1500, 1460, 1420, 1385, 1280, 1255, 1180, 1160, 1130, 1030, 895, 815. $^1$H-NMR (400 MHz, $CDCl_3$): 7.46 (*d*, $J = 1$, H–C(2)); 7.28 (*dd*, H–C(6)); 6.89 (*d*, $J = 9$, H–C(5)); 5.45–5.33 (2*m*, $J = 0.5$, C=$CH_2$); 4.62 (*s*, $CH_2OH$); 3.91 (*s*, MeO); 2.02 (*dd*, $J = 0.5$, Me); 1.70 (br. *s*, OH). EI-MS: 202 (100, $M^+$), 201 (20, $[M - H]^+$), 185 (10), 161(10), 91, 77.

*4-Hydroxy-3-(3-hydroxybut-1-ynyl)benzyl Alcohol* (**7**). To 5-(hydroxymethyl)benzofuran (**16**; 0.9 g, 6 mmol) in dry THF (30 ml) was added 1.6M BuLi/hexane (8 ml, 12 mmol) at 0°. After 1 h, acetaldehyde (0.27 g, 6 mmol) was added and the mixture stirred for 1 h. Again, 1.6M BuLi/hexane (4 ml, 6 mmol) was added and stirred at r.t. for 3 h. The soln. was then quenched with aq. $NH_4Cl$ soln. and concentrated under vacuum. The aq. layer was extracted with $Et_2O$ and the org. layer extracted with 2% aq. NaOH soln. The aq. layer was then acidified with 5% aq. HCl soln. and extracted with AcOEt, the org. phase dried and evaporated, and the residue purified by CC ($CH_2Cl_2$): **7** (0.61 g, 53%). $^1$H-NMR (400 MHz, $CD_3OD$): 7.27 (*d*, $J = 2$, H–C(2)); 7.15 (*dd*, H–C(6)); 6.80 (*d*, $J = 8$, H–C(5)); 4.70 (*q*, $J = 7$, C*H*(OH)Me); 4.46 (*s*, $CH_2OH$); 1.49 (*d*, $J = 7$, Me). EI-MS: 192 (30, $M^+$), 177 (100, $[M - Me]^+$), 91 (70), 84 (40).

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