

Natural Acetylenes. Part XXXVII.¹ Polyacetylenes from the Campanulaceae Plant Family. Tetrahydropyranyl and Open Chain C₁₄ Polyacetylenic Alcohols from *Campanula pyramidalis* L. and *Campanula medium* L.

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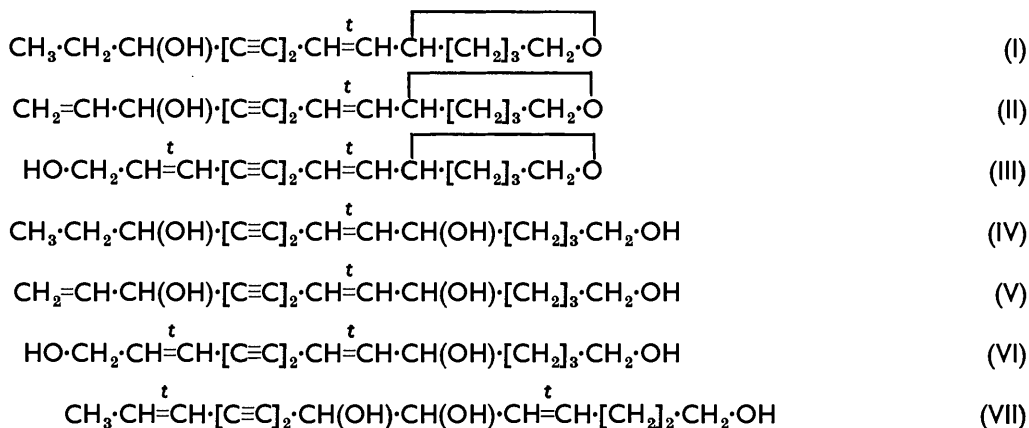
The new mono-ols $RCH(OH) \cdot [C \equiv C]_2 \cdot CH = CH \cdot \overbrace{CH \cdot [CH_2]_3 \cdot CH_2}^t \cdot O$ (R = Et or CH=CH₂) and the triols $R[C \equiv C]_2 \cdot CH = CH \cdot CH(OH) \cdot [CH_2]_3 \cdot CH_2 \cdot OH$ [R = EtCH(OH), CH₂=CH·CH(OH), or HO·CH₂·CH=CH] have been found in *C. pyramidalis* L. and *C. medium* L. (the Canterbury bell) and synthesised. A known mono-ol (III) and a known triol (VII) were also present.

THE widespread occurrence of polyacetylenes in the Campanulaceae plant family and the analysis of the polyacetylene content of *C. glomerata*² and *C. oblongifolia*³ have been reported. We now describe the polyacetylenes of two more representatives, *C. pyramidalis* L. and *C. medium* L. (the Canterbury bell), in which a considerable number of similar polyacetylenes are present in low concentrations (each less than 5 mg per kg of fresh plant material). Their isolation by repeated column and complex thin-layer chromatography was a formidable task which incurred appreciable loss of material. Eventually, the unambiguous allocation of structures to seven polyacetylenes was possible by direct comparison with synthetic specimens or samples

low concentrations from the triol fraction, and some high polarity polyacetylenes remained in the aqueous phase after the ether extraction.

C. medium was found to produce the largest variety of polyacetylenes yet encountered in the Campanulaceae; in the roots, in addition to the mono-ols (I)—(III), it contained traces of several less polar polyacetylenes with enediynes, enediynene, and more unsaturated chromophores. An apparent enediynene diol, different from the one detected in *C. pyramidalis*, appeared in the roots, but with the small amounts obtained its structure could not be elucidated. The triols (IV)—(VI) are the main polyacetylenic components of the stems of *C. medium*.

The new polyacetylenes were synthesised from the



isolated from other sources. To this end the R_F values and u.v. and mass spectra of the polyacetylenes themselves, of their acetyl and trimethylsilyl derivatives, and of their manganese dioxide oxidation products were used.

In *C. pyramidalis* the polyacetylenes were distributed over all parts of the plant in varying concentrations, but the root extract was easiest to analyse. Of the seven polyacetylenes identified, the mono-ols (I) and (II) and the triols (IV)—(VI) were new. The mono-ol (III) had been isolated from *C. glomerata*² and the triol (VII) from *Lobelia* species.¹ In addition, at least one non-polar polyacetylene was present in the least polar fractions, an apparent enediynene diol was separated in

tetrahydropyran (VIII) and the diol (IX) by Chodkiewicz couplings with the appropriate bromoacetylenes.

EXPERIMENTAL

For general techniques see Part XXXVI.¹

General Reaction Procedure for the Chodkiewicz Coupling.—The bromoacetylene (1 mmol) in MeOH (15 ml) was added during 15 min to the terminal ethynyl compound (1.25 mmol), NH₂OH·HCl (160 mg), EtNH₂ (1.2 ml; 30% aqueous solution), and CuCl (4 mg) in MeOH (12 ml), and stirred at 0° under N₂. The cooling bath was removed and after 2 h KCN (50 mg) and then ether were added. The product, isolated *via* ether, was purified by chromatography on columns and, in the case of the triols, SiO₂ layers.

* R. K. Bentley, J. K. Jenkins, Sir Ewart R. H. Jones, and V. Thaller, *J. Chem. Soc. (C)*, 1969, 830.

³ J. Lam and F. Kaufmann, *Chem. and Ind.*, 1969, 1430.

¹ Part XXXVI, R. K. Bentley, Sir Ewart R. H. Jones, R. A. M. Ross, and V. Thaller, preceding paper.

General Procedure for the Acetylation of the Alcohols.—With Ac_2O –pyridine (2 : 1), 40–48 h at 20°, purification by repeated chromatography on both columns and layers.

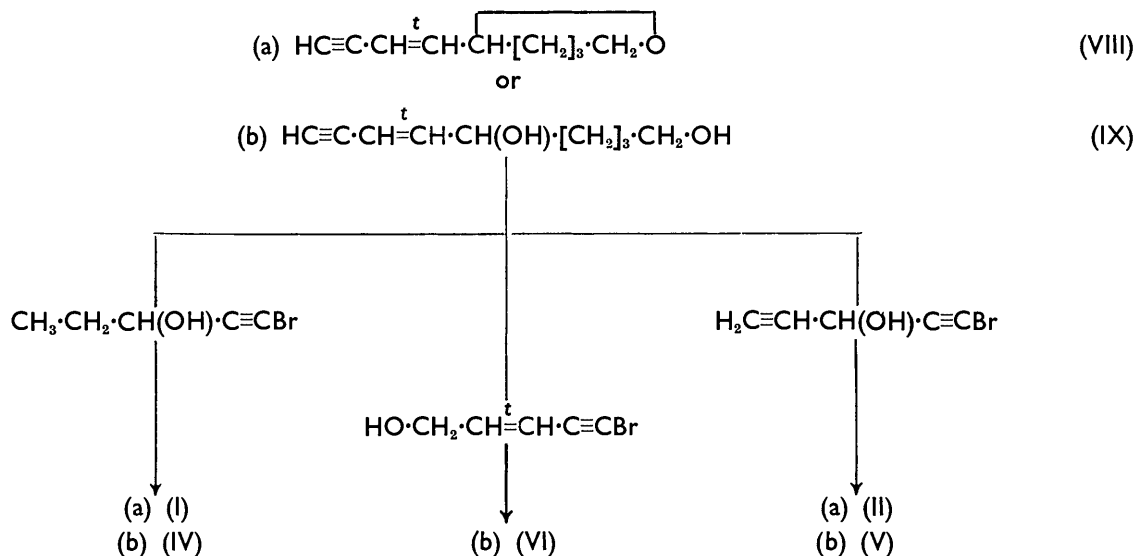
General Procedure for the Silylation of the Alcohols.—With pyridine (5 drops), $(\text{Me}_3\text{Si})_2\text{NH}$ (2 drops), and Me_3SiCl (1 drop) (in that order), 2 h at 20°, concentration *in vacuo*, and purification of the petrol extract by chromatography.

General Procedure for the Manganese Dioxide Oxidations.—The alcohol and a fivefold weight of MnO_2 in CH_2Cl_2 were shaken at 20° for 2–4 h. Filtration, concentration, and purification by chromatography.

9-(Tetrahydropyran-2-yl)-non-trans-8-ene-4,6-diyn-3-ol (I).—1-Bromopent-1-yn-3-ol (163 mg)⁴ and the tetrahydropyranyl acetylene (VIII)² gave the liquid alcohol (I) (120

and 3.69 (dd, J 16 and 5 Hz, $\text{C}\equiv\text{C}\cdot\text{CH}=\text{CH}\cdot\text{CH}\cdot\text{O}$). The alcohol (II) gave the corresponding ketone in 54% yield, M^+ 214 (100%), λ_{max} 320 (ϵ 7900), 303 (8700), 284 (7400), 267 (6700), 251 (19,200), 238 (22,800), and 206 nm (24,000), ν_{max} 2230, 2125, 1650, 1625, 1613, 995, 975, and 958 cm^{-1} , τ (CCl_4) 8.0–8.9 (m, $\text{CH}\cdot[\text{CH}_2]_3\cdot\text{CH}_2\cdot\text{O}$), 5.8–6.8 (m, $\text{CH}\cdot\text{O}\cdot\text{CH}_2$), 4.2 (dd, J 16 and 2 Hz, $\text{C}\equiv\text{C}\cdot\text{CH}=\text{CH}\cdot\text{CH}$), 3.75 (dd, J 16 and 5 Hz, $\text{C}\equiv\text{C}\cdot\text{CH}=\text{CH}\cdot\text{CH}$), and 3.3–3.95 (m, $\text{CH}_2=\text{CH}\cdot\text{CO}$). The acetylated alcohol (II) distilled at 100–120° (block) and 0.01 mmHg (Found: C, 74.15; H, 6.9. $\text{C}_{16}\text{H}_{18}\text{O}_3$ requires C, 74.4; H, 7.0%), ν_{max} (CCl_4) 2250, 2150, 1745, 1645, 1625, 970, and 955 cm^{-1} .

Tetradeca-trans-6-ene-8,10-diyn-1,5,12-triol (IV).—1-Bromopent-1-yn-3-ol (204 mg)⁴ and the acetylenic diol



mg, 55%), b.p. 150–160° (block) at 0.01 mmHg (Found: C, 76.75; H, 8.0%; M^+ , 218. $\text{C}_{14}\text{H}_{18}\text{O}_2$ requires C, 77.05; H, 8.3%; M , 218), λ_{max} 285 (ϵ 14,000), 269 (17,500), 255 (12,000), 242 (6000), and 230 nm (24,000), ν_{max} (CCl_4) 3640, 3450, 2210, 2110, 1625, 1045, and 950 cm^{-1} , τ (CDCl_3) 9.0 (t, J 7 Hz, $\text{CH}_3\cdot\text{CH}_2$), 8.0–8.8 (m, $\text{CH}_3\cdot\text{CH}_2\cdot\text{CH}\cdot\text{OH}$ and $\text{CH}\cdot[\text{CH}_2]_3\cdot\text{CH}_2\cdot\text{O}$), 6.94br (OH), 5.85–6.7 (m, $\text{CH}\cdot\text{OH}$ and $\text{CH}\cdot\text{O}\cdot\text{CH}_2$), 4.25 (d, J 17 Hz, $\text{C}\equiv\text{C}\cdot\text{CH}=\text{CH}$), and 3.72 (dd, J 17 and 5 Hz, $\text{CH}=\text{CH}\cdot\text{CH}$). The alcohol (I) (40 mg) with MnO_2 gave the corresponding ketone (24 mg, 60%), M^+ 216 (100%), λ_{max} 313 (ϵ 8100), 294 (9600), 279 (8600), 265 (7100), 250inf, and 227 nm (28,000), ν_{max} (CCl_4) 2200, 2110, 1675, 1625, 1045, and 945 cm^{-1} , τ (CCl_4) 8.85 (t, J 7 Hz, $\text{CH}_3\cdot\text{CH}_2$), 7.9–8.8 (m, $\text{CH}\cdot[\text{CH}_2]_3\cdot\text{CH}_2\cdot\text{O}$), 7.45 (q, J 7 Hz, $\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}$), 5.9–6.8 (m, $\text{CH}\cdot\text{O}\cdot\text{CH}_2$), 4.21 (dd, J 17 and 2 Hz, $\text{C}\equiv\text{C}\cdot\text{CH}=\text{CH}\cdot\text{CH}$), and 3.65 (dd, J 17 and 5 Hz, $\text{CH}=\text{CH}\cdot\text{CH}\cdot\text{O}\cdot\text{CH}_2$). The acetylated alcohol (I) had ν_{max} (CCl_4) 2220, 1740, and 955 cm^{-1} .

9-(Tetrahydropyran-2-yl)non-trans-1,8-diene-4,6-diyn-3-ol (II).—1-Bromopent-4-en-1-yn-3-ol (202 mg)⁵ and the tetrahydropyranyl acetylene (VIII) gave the liquid alcohol (II) (117 mg, 43%), M^+ 216 (100%), λ_{max} 284 (ϵ 16,000), 268 (20,200), 254 (13,500), 241 (6800), and 215 nm (28,000), ν_{max} (CCl_4) 3610, 3440, 2210, 2110, 1640, 1625, 957, and 935 cm^{-1} , τ (CDCl_3) 8.0–8.8 (m, $\text{CH}\cdot[\text{CH}_2]_3\cdot\text{CH}_2\cdot\text{O}$), 5.8–6.9 (m, $\text{CH}\cdot\text{O}\cdot\text{CH}_2$), 5.05 (d, J 5 Hz, $\text{CH}_2=\text{CH}\cdot\text{CH}\cdot\text{OH}$), 4.76 (d, J 10 Hz, *cis*- $\text{HCH}=\text{CH}\cdot\text{CH}\cdot\text{OH}$), 4.55 (d, J 18 Hz, *trans*- $\text{HCH}=\text{CH}\cdot\text{CH}\cdot\text{OH}$), 4.25 (d, J 16 Hz, $\text{C}\equiv\text{C}\cdot\text{CH}=\text{CH}$),

(IX)² gave the triol (IV) (53 mg, 18%), λ_{max} 284 (ϵ 14,900), 268 (18,700), 253.5 (12,500), 241 (6500), 230 (3200), and 217 (15,000) nm, ν_{max} (film) 2215 and 960 cm^{-1} , τ [$(\text{CD}_3)_2\text{SO}$] 9.1 (t, J 7 Hz, $\text{CH}_3\cdot\text{CH}_2$), 8.64 (m, $\text{HO}\cdot\text{CH}\cdot[\text{CH}_2]_3\cdot\text{CH}_2\cdot\text{OH}$), 8.41 (dq, J 7 and 7 Hz, $\text{CH}_3\cdot\text{CH}_2\cdot\text{CH}\cdot\text{OH}$), 6.63 (m, $\text{CH}_2\cdot\text{CH}_2\cdot\text{OH}$), 5.95 (m, $\text{CH}=\text{CH}\cdot\text{CH}\cdot\text{OH}$), 5.71 (m, $\text{CH}_3\cdot\text{CH}_2\cdot\text{CH}\cdot\text{OH}$), 5.6 (m, OH), 5.05 (d, J 5 Hz, OH), 4.5 (d, J 6 Hz, OH), 4.24 (d, J 16 Hz, $\text{C}\equiv\text{C}\cdot\text{CH}=\text{CH}$), and 3.6 (dd, J 16 and 6 Hz, $\text{CH}=\text{CH}\cdot\text{CH}\cdot\text{OH}$). (On addition of D_2O the signals at τ 4.5, 5.05, and 5.6 disappeared and the signal of the methine proton at τ 5.7 changed to a triplet, J 7 Hz.) The triacetyl derivative of the triol (IV) distilled at 170–180° (block) and 0.01 mmHg (Found: C, 66.5; H, 7.75%; M^+ , 362. $\text{C}_{20}\text{H}_{26}\text{O}_6$ requires C, 66.3; H, 7.25%; M , 362), and the tris-trimethylsilyl derivative had R_F 0.5 [petrol– Et_2O (47 : 3), 2 developments] and M^+ 452.

Tetradeca-trans-6,13-diene-8,10-diyn-1,5,12-triol (V).—1-Bromopent-4-en-1-yn-3-ol (360 mg) and the acetylenic diol (IX) gave the triol (V) (216 mg, 42%), λ_{max} 284 (ϵ 16,500), 268.5 (20,200), 254 (14,700), 241 (7400), and 213 nm (16,000), ν_{max} (film) 3440, 2210, 1640, 1624, 985, 960, and 885 cm^{-1} , τ [$(\text{CD}_3)_2\text{SO}$] 8.6 (m, $\text{HO}\cdot\text{CH}\cdot[\text{CH}_2]_3\cdot\text{CH}_2\cdot\text{OH}$), 6.6 (m, $\text{CH}_2\cdot\text{CH}_2\cdot\text{OH}$), 5.9 [m, $\text{CH}=\text{CH}\cdot\text{CH}(\text{OH})\cdot\text{CH}_2$], 5.69 (t, J 6 Hz, $\text{CH}_2\cdot\text{OH}$), 5.05 [d, J 5 Hz, $\text{CH}_2=\text{CH}\cdot\text{CH}(\text{OH})\cdot\text{C}\equiv\text{C}$], 5.04 (d, J 6 Hz, OH), 4.78 (d, J 10 Hz, *cis*- $\text{HCH}=\text{CH}\cdot\text{CH}$ –

⁴ Sir Ewart R. H. Jones, B. E. Lowe, and G. Lowe, *J. Chem. Soc.*, 1964, 1476.

⁵ F. Bohlmann and H. Bornowski, *Chem. Ber.*, 1961, 94, 3189.

OH), 4.62 (d, J 17 Hz, *trans*-HCH=CH·CH·OH), 4.19 (d, J 16 Hz, C=C·CH=CH·CH·OH), 4.12 (d, J 6 Hz, OH), 4.07 (ddd, J 17, 10, and 5 Hz, CH₂=CH·CH·OH), and 3.55 (dd, J 16 and 5 Hz, CH=CH·CH·OH). (On addition of D₂O the signals at τ 4.12, 5.04, and 5.69 disappeared; the signal at τ 6.6 remained a multiplet.) The triacetyl derivative of the triol (V) decomposed during distillation at 2×10^{-5} mmHg (M^+ 360. C₂₀H₂₄O₆ requires M , 360), and the tris(trimethylsilyl) derivative had R_F 0.4 [petrol-Et₂O (47:3), 2 developments] and M^+ 450.

Tetradeca-trans,trans-6,12-diene-8,10-diyne-1,5,14-triol (VI).—5-Bromopent-*trans*-2-en-4-yn-1-ol² (444 mg) and the acetylenic diol (IX) gave the triol (VI) (283 mg, 43%) which crystallised from Et₂O-petrol-MeOH at -40° ; m.p. 90–91° (Found: C, 72.0; H, 7.6. C₁₄H₁₈O₃ requires C, 71.75; H, 7.75%), λ_{\max} 313 (ϵ 20,000), 293.5 (24,600), 276.5 (16,400), 261.5 (8300), 247infr, 237 (33,000), and 233 nm (32,200), ν_{\max} (film) 3380, 2180, 2110, 1620, 950, and 910 cm⁻¹, τ [(CD₃)₂SO] 8.61 (m, HO·CH·[CH₂]₃·CH₂·OH), 6.57 (m, CH₂·CH·OH), 5.9 [m, CH=CH·CH(OH)·CH₂], 5.69 (t, J 5 Hz, CH₂·CH₂·OH), 5.04 [d, J 5 Hz, CH=CH·CH(OH)·CH₂], 4.99 (t, J 5 Hz, HO·CH₂·CH=CH), 4.17 and 4.13 (two d, J 16 Hz, CH=CH·[C=C]₂·CH=CH), 3.6 (dd, J 16 and 5 Hz, CH=CH·CH·OH), and 3.5 (dt, J 16 and 4 Hz, HO·CH₂·CH=CH). (On addition of D₂O the signals at τ 4.99, 5.04, and 5.69 disappeared.) The triacetyl derivative of the triol (VI) had M^+ 360 (C₂₀H₂₄O₆ requires M , 360), and the tris(trimethylsilyl) derivative had R_F 0.3 [petrol-Et₂O (47:3), 2 developments] and M^+ 450.

Isolation of Polyacetylenes from Campanula pyramidalis L.—Chopped roots (2 kg; from eight plants grown in the greenhouse and harvested at termination of flowering in late September) were extracted twice with Et₂O. The concentrated extract (4 g) was chromatographed on a SiO₂ column (250 × 3.5 mm) by gradient elution [petrol (0.5 l) was enriched first with Et₂O (1 l) and then with Et₂O-MeOH (17:3; 0.5 l)]. Fractions (50 ml) were collected and assayed spectrophotometrically; those with similar properties were combined into four groups, each of which was rechromatographed on SiO₂ layers with several solvent systems.

| Fractions | $\lambda_{\max.}/\text{nm}$ |
|-----------|-----------------------------|
| 6 | 312, 292 (traces) |
| 8–10 | 284, 268, 254, 240 |
| 11–14 | 312, 292, 276 |
| 22–26 | 312, 292infr, 284, 268, 253 |

Fractions 8–10 were separated [with petrol-Et₂O (1:1), CH₂Cl₂-EtOAc (19:1), and by continuous development with petrol-Me₂CO (10:1)] into the alcohols (I) and (II) and these were converted by MnO₂ into the corresponding ketones.

Fractions 11–14 gave on chromatography [petrol-Et₂O (1:1) and CHCl₃-MeOH (49:1)] the alcohol (III) (4 mg).

Fractions 22–26 were further separated by repeated

chromatography of the mixture itself [with Et₂O-MeOH (19:1) and CHCl₃-MeOH (19:1)], the trimethylsilylated mixture [petrol-Et₂O (24:1) and petrol-CH₂Cl₂ (47:3)], and the acetylated mixture [continuous development with petrol-Et₂O (1:1)]. The triols (IV)–(VI), as well as the triol (VII) and/or their derivatives were isolated in very small amounts (0.5–2 mg). When the triol mixture and TsOH in Me₂CO was heated under reflux for 30 min, an increase of the relative intensities of the enediynene peaks was observed and the formation of the mono-ols (I) and (III) was detected. The least polar polyacetylene band present in fractions 22–26 (*ca.* 2 mg) had λ_{\max} 284 (rel. E 0.83), 268 (1.0), 253.5 (0.6), and 241 nm (0.2) and τ (CDCl₃) 4.23 (d, J 16 Hz) and 3.73 (dd, J 16 and 5 Hz); its MnO₂ oxidation product had λ_{\max} 298.5 (rel. E 0.69), 282 (1.0), 266 (0.5), and 252 (0.25) nm and its acetylation product appeared to be a diacetate (M^+ 318), ν_{\max} 1745 and 1220–1230 cm⁻¹.

Isolation of Polyacetylenes from Campanula medium L.—Minced roots (1 kg; from twelve plants harvested near the termination of flowering in middle August) were extracted, the extract was worked up as described for *C. pyramidalis*, and the following fractions were combined.

| Fractions | $\lambda_{\max.}/\text{nm}$ |
|-----------|---|
| 5–7 | 312, 292, 279, 264, and longer wavelength |
| 10–14 | 284, 268, 254, 241 |
| 17–21 | 312, 293, 276 |
| 22–24 | 312, 293, 283, 268, 254 |
| 25–35 | 283, 268, 254 |

Fractions 5–7 gave on chromatography [petrol-Et₂O (19:1)] only two reasonably homogeneous fractions (*ca.* 0.5 mg of each), both with similar u.v. absorption (λ_{\max} 312, 293, 276, 267, and 247 nm); the less polar had M^+ 202 and the more polar 200.

Fractions 10–14 yielded the alcohols (I) and (II) (*ca.* 5 mg of each) and fractions 17–21 the alcohol (III) (4 mg).

Fractions 25–35 were chromatographed [Et₂O and CH₂Cl₂-EtOAc (3:1)] and gave what appeared to be a diol (*ca.* 1 mg), M^+ 234, λ_{\max} 284 (rel. E 0.85), 269 (1.0), 254 (0.65), and 240 nm (0.5), ν_{\max} (CHCl₃) 1730 cm⁻¹. The acetylation product had M^+ 318 and the MnO₂ oxidation product had M^+ 232, λ_{\max} 313 (rel. E 0.8), 295 (1.0), 280 (0.9), and 266 nm (0.7).

Finely cut stems of *C. medium* were extracted and the extracts were worked up as described for the roots. In the most polar fractions the presence of the triols (IV)–(VI) was detected.

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