Natural Acetylenes. Part XLVIII.[1] Absolute Configurations of a C_7 Diynol, a C_9 Diynetriol, and a C_9 Dihydroxy-diynone from Fungal Cultures

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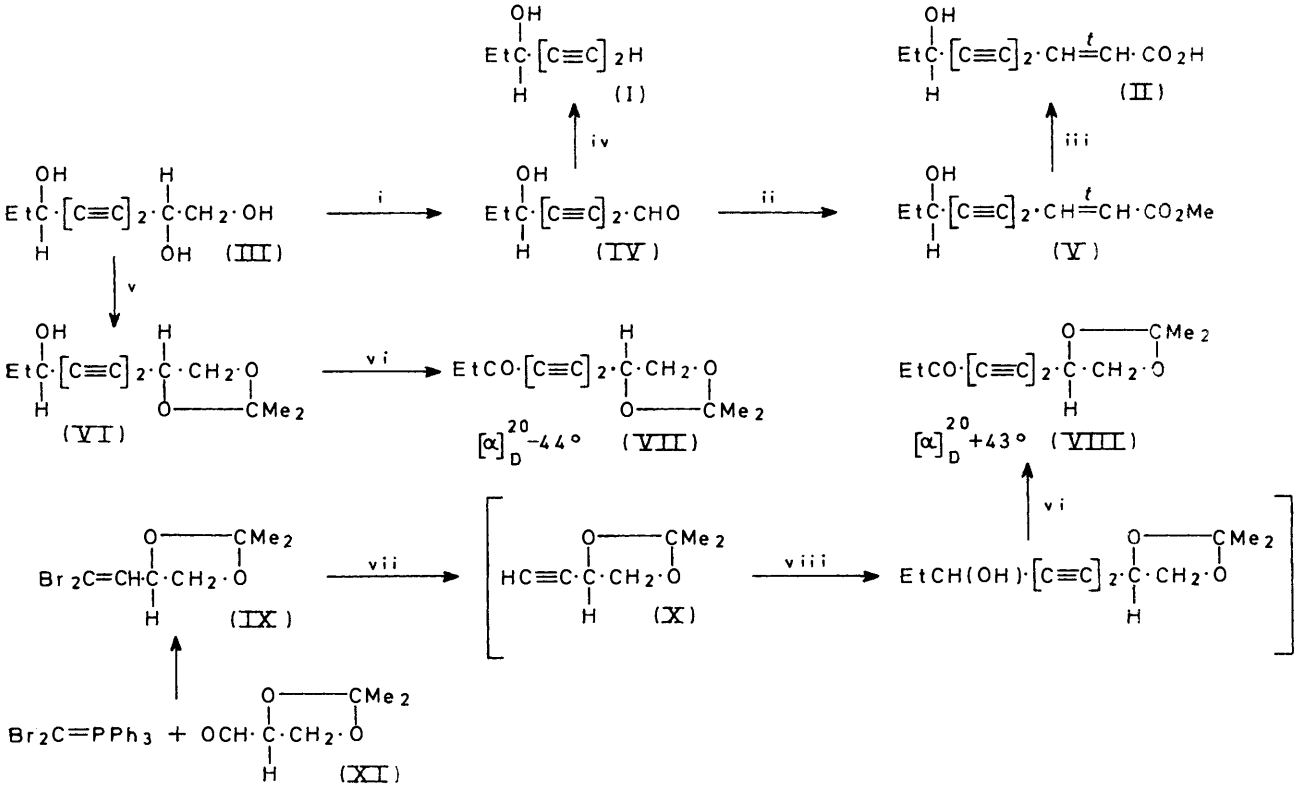
The (3*S*)-configuration has been assigned to EtCH(OH)·[C≡C]$_2$H from *Gymnopilus spectabilis* and the (2*R*,7*S*)- and (2*R*)-configurations respectively to EtCH(OH)·[C≡C]$_2$·CH(OH)·CH$_2$·OH and EtCO·[C≡C]$_2$·CH(OH)·CH$_2$·OH from *Clitocybe rhizophora* cultures.

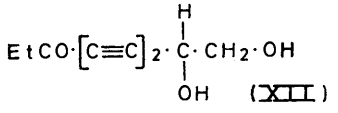
THE C_9 diynetriol (III) is the major acetylenic metabolite in *Clitocybe rhizophora* Velen cultures[2] and the C_7 diynol (I) is the major polyacetylene in those of *Gymnopilus spectabilis* (Fr.) Singer.[3] The former has been the subject of biosynthetic investigations[4] but no previous attempts have been made to elucidate the absolute configurations of the two metabolites. These have now been determined by the transformations outlined in the Scheme.



SCHEME Reagents: i, $NaIO_4$; ii, $Ph_3P{=}CH{\cdot}CO_2Me$; iii, KOH at 20°; iv, NaOH at 50°; v, Me_2CO–$CuSO_4$–TsOH; vi, MnO_2; vii, Bu^nLi; viii, CuCl–NH_2OH–$EtNH_2$–EtCH(OH)C≡CBr

The conversion of the triol (III) into both the mono-ol (I) and the (8*S*)-hydroxy-acid (II)[5,6] requires the (7*S*)- and (3*S*)-configurations respectively for the two metabolites. The keto-acetonide (VII)[2] was prepared again from the triol (III) and compared with the keto-acetonide (VIII) synthesised from D-glyceraldehyde acetonide (XI). The two derivatives had opposite rotations but were otherwise identical. The (2*R*)-configuration must be thus assigned to the keto-diol acetonide (VII), the triol (III), and, since their relationship has already been established,[2] the keto-diol (XII), a minor metabolite of *C. rhizophora*.

The method of Corey for converting the formyl into the ethynyl group[7] was used to transform D-glyceraldehyde acetonide (XI) into the ethynyl acetonide (X). This was coupled with bromopent-1-yn-3-ol and the



[1] Part XLVII, Sir Ewart R. H. Jones, V. Thaller, and J. L. Turner, *J.C.S. Perkin I*, 1975, 424.

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

[3] M. T. W. Hearn, Sir Ewart R. H. Jones, M. G. Pellatt, V. Thaller, and J. L. Turner, *J.C.S. Perkin I*, 1973, 2785.

[4] G. C. Barley, A. C. Day, U. Graf, Sir Ewart R. H. Jones, I. O'Neill, R. Tachikawa, V. Thaller, and R. A. Vere Hodge, *J. Chem. Soc.* (*C*), 1971, 3308.

[5] F. Bohlmann and G. Grau, *Chem. Ber.*, 1965, **98**, 2608.

[6] F. Bohlmann, K. M. Kleine, and C. Arndt, *Chem. Ber.*, 1964, **97**, 3469.

[7] E. J. Corey and P. L. Fuchs, *Tetrahedron Letters*, 1972, 3769.

coupling product was oxidised to the keto-diol acetonide (VIII). Attempts at isolating and fully characterising the intermediates in this synthesis were abandoned on account of their instability, and the synthesis was carried out with crude or only partly purified products. The formation of the ethynyl dioxolan (X) was easily followed by the appearance of the 3316 cm^{-1} band in the i.r. spectrum. It was possible to purify the coupling product only after manganese dioxide oxidation revealed the characteristic diynone u.v. absorption.

The pathways involved in the formation of the C_9 triol (III) and the C_7 mono-ol (I) must be related and are the subject of biosynthetic studies.

EXPERIMENTAL

For general techniques see Part XLIII.[8]

(8S)-8-*Hydroxydec*-trans-2-*ene*-4,6-*diynoic Acid* (II) *from the Triol* (III).—The triol (III) (71 mg, 0·42 mmol; m.p. 70—73°) and $NaIO_4$ in H_2O (60 mg; 4 g l^{-1}) were kept at 20° in the dark for 16 h. The mixture was extracted with CH_2Cl_2; the extract was washed with H_2O, and dried. The aldehyde (IV) solution [$\lambda_{max.}$ 286·5 (rel. *E* 1·7), 270·5 (2·0), 256·5 (1·5), and 243·5 nm (1·0); $\nu_{max.}$ 3600 (O–H), 1670 (CO), 1110, 1070, and 1040 cm^{-1} (C–O)] was concentrated to *ca.* 20 ml and added dropwise to methoxycarbonylmethylenetriphenylphosphorane (121 mg, 0·35 mmol) stirred in CH_2Cl_2 (15 ml) at −15°. Stirring was continued first at −15° (0·5 h) and then for 0·5 h without cooling. The concentrated mixture was separated by p.l.c. (petrol–Et_2O, 1 : 1) and gave the *trans*-ester (V) [38 mg, 46% from the triol (III)], R_F 0·38, $[\alpha]^{20}$ −11·5° (589 nm), −12·3° (578), −13·75° (546), and −22·5° (436) (*c* 0·76 in EtOH) (lit.,[5] $[\alpha]_{546}^{20}$ +13·9° for the *R*-ester), $\lambda_{max.}$ 302·5 (rel. *E* 3·7), 284 (3·9), 269 (2·1), and 255 nm (1·0); $\nu_{max.}$ ($CHCl_3$) 3600 (OH), 2210 and 2100 (C≡C), and 1730 cm^{-1} (ester CO); *m/e* 192 (M^+, 10%), 163 (66), 103 (65), 77 (55), 58 (98), and 57 (100); and the corresponding *cis*-isomer [12 mg, 13% from triol (III)], R_F 0·31, $\lambda_{max.}$ 304 (rel. *E* 2·4), 286 (2·5), 271 (1·75), 255 (1·0), and 224 nm (4·85).

The *trans*-ester (V) (27·8 mg, 0·145 mmol) in MeOH (2 ml) and KOH (100 mg) in H_2O (0·5 ml) were kept at 20° under N_2 for 16 h. The mixture was acidified (pH 4) with HCl (2N) and extracted with Et_2O, and the extract was washed (brine), dried, and concentrated. The solid residue gave on crystallisation (Et_2O–petrol) needles of the *trans*-hydroxy-acid (II) (10·4 mg, 40%), m.p. 97—100° (lit.,[6] 94·5°), $[\alpha]^{20}$ −27·4° (589 nm), −31·2° (578), −33·9° (546), −57·5° (436), and −87·2° (365) (*c* 0·36 in Et_2O) (lit.,[6] $[\alpha]_{546}^{20}$ −34°), $\lambda_{max.}$ 301 (rel. *E* 8·45), 283 (9·1), 267·5 (5·5), 253 (2·15), and 240 nm (1·0); $\nu_{max.}$ (CCl_4) 2240 and 2060 (C≡C) and 1740 cm^{-1} (acid CO); τ (CCl_4) 8·97 (3H, t, *J* 7 Hz, CH_3·CH_2), 8·22 (2H, m, CH_3·CH_2·CHOH), 5·54 (1H, t, *J* 6 Hz, CHOH), 3·92br (disappeared on addition of D_2O) (2H, OH + CO_2H), 3·60 (1H, d, *J* 16 Hz, CH=CH·CO), and 3·17 (1H, d, *J* 16 Hz, C≡C·CH=CH).

(3S)-*Hepta*-4,6-*diyn*-3-*ol* (I) *from the Triol* (III).—The crude aldehyde (IV) [prepared as above from 158 mg of triol (III)] was transferred into MeOH (5 ml) and swirled vigorously with NaOH–H_2O (4N; 5 ml) for 1 min at 50° (bath). The mixture was poured onto ice–brine–Et_2O, the layers were separated, the aqueous layer was extracted with Et_2O, and the combined Et_2O extracts were dried and concentrated. The residue was dissolved in Et_2O–petrol and filtered through SiO_2 (5 g). The filtrate gave on concentration the heptadiynol (I) (70 mg, 70%), $[\alpha]^{20}$ −14·5° (589 nm), −15·6° (578), −17·3° (546), −27·6° (436), and −40·0° (365) (*c* 0·972 in EtOH), identical with the natural product.

(4R)-2,2-*Dimethyl*-4-(5-*oxohepta*-1,3-*diynyl*)-1,3-*dioxolan* (VII) *from the Triol* (III).—The triol (III) (115 mg, 0·7 mmol), $CuSO_4$ (500 mg), and TsOH (10 mg) were shaken in Me_2CO (75 ml) for 16 h under N_2 in the dark. Usual work-up gave the liquid acetonide (VI) (95 mg, 68%), R_F 0·61 (Et_2O), $[\alpha]^{20}$ −55° (589 nm), −56·7° (578), −64·2° (546), and −116° (436) (*c* 0·55 in EtOH) {lit.,[2] $[\alpha]_D^{24}$ −61° (*c* 0·23 in EtOH)}; $\lambda_{max.}$ 258 (rel. *E* 1·0), 244 (1·6), and 232 nm (1·6); $\nu_{max.}$ 3610 and 3350 (OH), 2160 (C≡C), 1380 and 1350 (CMe_2), and 1150 and 1060 cm^{-1} (C–O). This and MnO_2 (1 g) in CH_2Cl_2 (5 ml) were shaken for 2 h under N_2 in the dark. Filtration and concentration gave the liquid keto-acetonide (VII) (75 mg, 81%), R_F (Et_2O) 0·62, $[\alpha]^{20}$ −44·2° (589 nm), −46·1° (578), −53·6° (546), and −102·6° (436) (*c* 0·705 in EtOH) (lit.,[2] $[\alpha]_D^{23}$ −57°), $\lambda_{max.}$ 281 (ε 4100), 266 (5600), 252 (3400), 239 (2200), and 227 nm (1700); $\nu_{max.}$ 2230 and 2140 (C≡C), 1680 (CO), 1380 and 1370 (CMe_2), 1145, 1100, and 1065 cm^{-1} (C–O); τ (CCl_4) 8·88 (3H, t, *J* 7 Hz, CH_3·CH_2), 8·69 and 8·59 (each 3H, s, CMe_2), 7·48 (2H, q, *J* 7 Hz, CH_3·CH_2·CO), 6·00 (2H, m, OCH·CH_2O), and 5·30 [1H, m, C≡C·CH(O)·CH_2].

(4S)-2,2-*Dimethyl*-4-(5-*oxohepta*-1,3-*diynyl*)-1,3-*dioxolan* (VIII) *from* D-*Glyceraldehyde Acetonide* (XI).—CBr_4 (5·11 g, 15·4 mmol) in CH_2Cl_2 (10 ml) was added slowly to Ph_3P (4·04 g, 15·4 mmol) and Zn dust (1·0 g, 15·4 mmol) stirred in CH_2Cl_2 (20 ml) under N_2 at 20°. Stirring was continued for 24 h at 20° before D-glyceraldehyde acetonide [8] (from 1·9 g, 7·25 mmol of 1,2,5,6-di-*O*-isopropylidene-D-mannitol) in CH_2Cl_2 (5 ml) was added and stirring was continued for another 2 h. Petrol (160 ml) was added to the mixture and the insoluble material was removed by decantation and filtration. It was dissolved again in CH_2Cl_2 (10 ml), the solution was treated with petrol (40 ml), and the precipitate was removed again. This process was repeated three times more. The combined petrol–CH_2Cl_2 extracts were concentrated and the residue (1·44 g, 32%) was distilled to give the dibromo-olefin (IX), b.p. 70—73° at 0·5 mmHg, R_F 0·67 (Et_2O), $[\alpha]^{20}$ −0·2° (589 nm), −0·2° (578), −0·5° (546), −2·3° (436), and −7·4° (365) (*c* 1·02 in EtOH); $\nu_{max.}$ (film) 1383 and 1375 (CMe_2), 1068 (C–O), and 677 cm^{-1} (C–Br); τ (CCl_4) 8·67 and 8·63 (each 3H, s, CMe_2), 6·40 [1H, m, O·CH·C(H)H·O], 5·88 [1H, m, O·CH·C(H)H·O], 5·47 [1H, m, =CH·CH(O)·CH_2], and 3·51 (1H, d, *J* 8 Hz, Br_2C=CH·CH). To this (740 mg, 2·58 mmol) stirred in dry Et_2O (3 ml) under N_2 at −78° was added Bu^nLi in hexane (2·3N; 2·1 ml, 4·9 mmol) in the course of 2 h and stirring was continued for 4 h at −78°. Brine (1·5 ml) was then added dropwise at −78° and the mixture was allowed to warm up to −20°. The layers were separated, the H_2O layer was extracted with Et_2O, and the combined Et_2O extracts were dried to yield a solution of the crude ethynyl acetonide (X), R_F 0·72 (Et_2O), $\nu_{max.}$ (CCl_4) 3316 cm^{-1} (C≡C–H). This was transferred into MeOH (5 ml) and added to NH_2·OH,HCl (260 mg), CuCl (20 mg), and $EtNH_2$ (40%; 2·5 ml), stirred in H_2O (3 ml)–MeOH (10 ml) under N_2 at 20°. After 10 min bromopent-1-yn-3-ol [prepared from pent-1-yn-3-ol (175 mg, 2·06 mmol) and Br_2 in NaOH solution] in MeOH

[8] M. Ahmed, G. C. Barley, M. T. W. Hearn, Sir Ewart R. H. Jones, V. Thaller, and J. A. Yates, *J.C.S. Perkin I*, 1974, 1981.

(5 ml) was added during 1 h and stirring was continued for 3 h. Usual work-up (KCN addition; H_2O–Et_2O partition) gave the crude product, which was dissolved in CH_2Cl_2 (5 ml) and shaken at 20° with MnO_2 (1 g) under N_2 in the dark for 5 h. The mixture was filtered (Celite), the MnO_2 was washed with Et_2O, the combined extracts were concentrated, and the residue was separated by p.l.c. (petrol–Et_2O, 17 : 3; continuous elution for 1·5 h). The band *ca.* 65 mm up the plate (dark purple under 254 nm light) gave on extraction the (4*S*)-keto-diol acetonide (VIII) (45 mg, 8%), $[\alpha]^{20}$ +43° (589 nm), +45° (578), +52° (546), and +102° (436) (*c* 0·975 in EtOH); u.v., i.r., and n.m.r. spectra and chromatographic behaviour identical with those of the (4*R*)-compound derived from the natural triol (III).

We thank the S.R.C. for research grant support.

[4/2102 *Received*, 10*th October*, 1974]