Total Synthesis of the Acetylenic Sesquiterpene Freelingyne

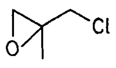
By David W. Knight and Gerald Pattenden*
(*Department of Chemistry, The University, Nottingham,* NG7 2RD)

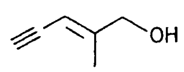
Summary The total synthesis of the acetylenic sesquiterpene, freelingyne (**11**) is described.

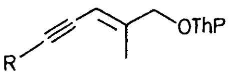
The acetylenic grouping is found only rarely in terpenoids. Freelingyne, a sesquiterpene from *Eremophila freelingii*,[1] was the first acetylenic terpene isolated, and its structure (**11**)† represents the most unsaturated furano-sesquiterpene found in Nature. We now record the total synthesis of natural freelingyne.

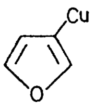
Condensation of the chloro-epoxide (**1**) with sodium acetylide afforded the *E*-enynol (**2**)[2] which was protected as its tetrahydropyranyl ether (**3**). This enyne (**3**) on sequential reaction with n-butyl-lithium and iodine yielded the iodoacetylene (**4**). A coupling reaction[3] between (**4**) and 3-furanylcopper (**5**) (formed from 3-iodofuran by treatment with n-butyl-lithium and cuprous bromide) produced (**6**) [λ_{max} 263 nm, ν_{max} 2200 cm^{-1}, τ 2·42 (1H), 2·65 (1H), 3·59 (1H), 4·14 (≡C–CH=), 5·4 (C*H*(O)O–), 5·8—6·6 (2 × C*H*$_2$–O), 8·08 (=C*Me*), 8·2—8·6 (6H)], accompanied by symmetrically coupled bis-acetylenic and bis-furan byproducts. The coupling reaction to (**6**) was an essential feature, since use of 3-iodofuran and the corresponding copper acetylide resulted in largely symmetrically coupled acetylene and iodo-bis-furans.

After cleavage of the tetrahydropyranyl ether with acid, the alcohol (**7**) was oxidised to the *E*-enynal (**8**) with manganese dioxide. Condensation of this aldehyde with the phosphorane (**10**)[4] derived from lactol (**9**)[5] by sequential reaction with phosphorus tribromide, triphenylphosphine and base gave a 6:4 mixture (by n.m.r.) of isomers, about the C_4–C_5 double bond, of freelingyne [(**11**) and (**12**)] in a total yield of 65%. The two isomers were separated by chromatography and the less polar one, m.p. 157—159°, was identical in all respects (mixed m.p., n.m.r., i.r., visible, m.s., t.l.c.) with naturally occurring freelingyne. The more polar isomer showed m.p. 158—159°, depressed to m.p. 135—140° on admixture with natural material, and spectral data [τ 2·39 (≡C–C=C*H*–O), 2·54 (CO–CMe=C*H*), 2·63 (O–C*H*=), 3·56 (≡C–$\overset{\|}{\text{C}}$–C*H*=), 3·7 (=CMe–C*H*=), 4·13 (≡C–C*H*=), 7·76 (=C*Me*) and 7·92 (=CMeCO)] consistent with the C_4–C_5 double bond isomer of natural freelingyne.‡

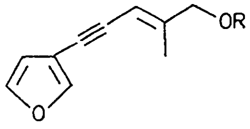

(1)

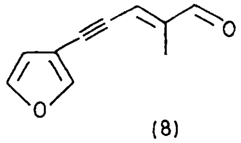

(2)

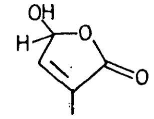

(3) R = H
(4) R = I

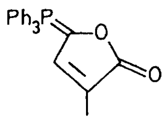


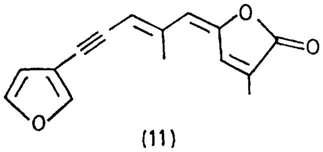
(5)

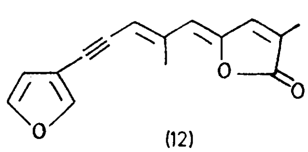

(6) R = ThP
(7) R = H


(8)


(9)


(10)


(11)


(12)

We thank Dr. Massy-Westropp for a sample of natural freelingyne, and the S.R.C. for a studentship (to D.W.K.).

(*Received*, 17*th December* 1973; *Com.* 1701.)

---

† The configurations about the C_4–C_5 and C_6–C_7 double bonds in natural freelingyne are not known with certainty. Dr. Massy-Westropp has recently proposed the revised configurational assignments shown in (**12**) (personal communication).

‡ Dr. Massy-Westropp has informed us that he has independently synthesised natural freelingyne and the C_4–C_5 double bond isomer of freelingyne (unpublished work; personal communication).

[1] R. A. Massy-Westropp, G. D. Reynolds, and T. M. Spotswood, *Tetrahedron Letters*, 1966, 1939.

[2] R. Ahmad and B. C. L. Weedon, *J. Chem. Soc.*, 1953, 3286. The *E*-configuration was unambiguously established by *X*-ray measurements on the corresponding α-naphthylurethane; we are grateful to Dr. M. J. Begley of this department for these data.

[3] *Cf.* R. Oliver and D. R. M. Walton, *Tetrahedron Letters*, 1972, 5209.

[4] *Cf.* J. E. T. Corrie, *Tetrahedron Letters*, 1971, 4873.

[5] G. Pattenden and B. C. L. Weedon, *J. Chem. Soc.*, (*C*), 1968, 1984.