Stereochemistry of Freelingyne [(4Z,6E)-9-(3-Furyl)-2,6-dimethylnona-2,4,6-trien-8-yn-4-olide] by X-Ray Analysis

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The crystal structure of freelingyne was determined by X-ray diffraction from diffractometer data by direct methods. Crystals are triclinic, space group $P\bar{1}$, with $Z = 2$ in a unit cell of dimensions: $a = 6.013 \pm 0.004$, $b = 9.184 \pm 0.005$, $c = 11.658 \pm 0.006$ Å, $\alpha = 94.93 \pm 0.07$, $\beta = 100.51 \pm 0.07$, and $\gamma = 100.35 \pm 0.07°$. The structure was refined by least squares to R 0.051 for 2 026 independent reflections. The stereochemistry of freelingyne was thus determined as 4Z, 6E.

THE total synthesis of the novel acetylenic sesquiterpene freelingyne, from *Eremophila freelingii*, was reported contemporaneously by Massy-Westropp and co-workers [1] and by ourselves.[2] Whereas our own synthesis led to a readily separable mixture of only the (4E,6E)- (1) and (4Z,6E)- (2) isomers, one of which was identical with the natural product, their route gave a more complex mixture of geometrical isomers, containing (3) and possibly (4)

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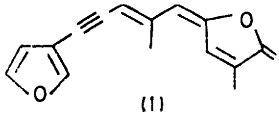
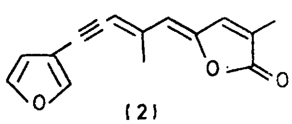
[1] C. F. Ingham, R. A. Massy-Westropp, and G. D. Reynolds, *Austral. J. Chem.*, 1974, **27**, 1477.

[2] D. W. Knight and G. Pattenden, *J.C.S. Chem. Comm.*, 1974, 188.

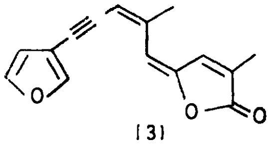
in addition to (1) and (2). N.m.r. data have suggested that natural freelingyne has the stereochemistry shown in structure (1) [3] whereas synthesis of some model compounds, and comparison of ^1H n.m.r. data have supported the stereochemistry depicted in structure (2).[4] A third stereochemical formulation [*viz.* (3)] has unfortunately been incorporated in the review literature.[5] The paucity of suitable model compounds of known stereochemistry, together with the uncertainties inherent in assigning stereochemistries to trisubstituted double bonds based on allylic coupling constants [6] has led us to examine the geometry of freelingyne by *X*-ray methods. We now report the determination of the stereochemistry shown in (2) for natural freelingyne by *X*-ray analysis.



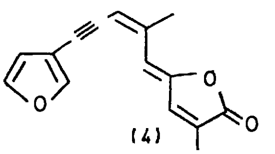
(1)



(2)



(3)



(4)

EXPERIMENTAL

Totally synthetic freelingyne, prepared according to ref. 2, was crystallised from chloroform to form suitable specimens for crystallographic analysis. Oscillation and Weissenberg photographs established the unit-cell dimensions and space group. For intensity measurement a crystal of dimensions *ca.* 0.8 × 0.5 × 0.1 mm was mounted on an automatic four-circle diffractometer. Unit-cell dimensions were refined by a least-squares fit of the positions of 12 reflections measured on the diffractometer. Intensity data were then collected by use of Mo-K_α radiation for $2\theta \leqslant 56°$, using ω—2θ scan. 2026 Independent observed reflections, with net count $> 3\sigma$ were used in the structure solution and refinement. No absorption corrections were made. Data reduction and subsequent crystallographic calculations were performed by use of the '*X*-Ray '70' program system.[7] Atomic scattering factors were taken from ref 8.

Crystal Data.—$C_{15}H_{12}O_3$, $M = 240$, m.p. 157—159 °C, Triclinic. $a = 6.013 \pm 0.004$, $b = 9.184 \pm 0.005$, $c = 11.658 \pm 0.006$ Å, $\alpha = 94.93 \pm 0.07$, $\beta = 100.51 \pm 0.07$, $\gamma = 100.35 \pm 0.07°$, $U = 618.0$ Å^3, $Z = 2$, $D_c = 1.29$ g cm^{-3}, $F(000) = 252$. Space group $P\bar{1}$ from intensity statistics and subsequent refinement. Mo-K_α radiation, $\lambda = 0.71069$ Å; μ(Mo-K_α) = 0.97 cm^{-1}.

Structure Determination.—Intensity data were first normalised by use of the SAP Programs of Ahmed *et al.* (National Research Council, Ottowa) with $k(s)$ values taken from a smooth curve drawn through the experimental points. Intensity statistics clearly indicated the presence of a centre of symmetry with $|E|$ 0.7747 and $|E^2 - 1|$ 1.0181, compared with the theoretical values [9] $|E|$ 0.798, $|E^2 - 1|$ 0.968 for centrosymmetric and $|E|$ 0.886, $|E^2 - 1|$ 0.736 for non-centrosymmetric structures. The structure was then solved by direct methods by use of the MULTAN program.[10] The 216 largest normalised structure factors ($|E| > 1.8$) were used in the direct phase-determining procedure. The initial E maps based on the best sets of phases (figures of merit 1.074 and 1.072, eliminating the all-positive set) both showed partial structures which failed to refine because they were too close to the centre of symmetry. The E maps indicated that the partial molecules were in the correct orientation, but the wrong translation with respect to the symmetry of the unit cell. The starting set of phases was therefore altered and the MULTAN program then gave a set of phases with a figure of merit of 1.086. An E map based on this set of phases revealed the structure with 18 of the highest 21 peaks corresponding to all of the non-hydrogen atom positions in the molecule.

Atomic co-ordinates, with standard deviations in parentheses

Atom	x/a	y/b	z/c
O(1)	0.4033(2)	−0.0294(2)	0.7429(1)
O(4)	0.2656(2)	0.1199(1)	0.6159(1)
O(12)	0.6449(3)	0.7255(2)	0.0231(1)
C(1)	0.2491(3)	0.0313(2)	0.7058(1)
C(2)	0.0236(3)	0.0295(2)	0.7380(1)
C(3)	−0.0862(3)	0.1124(2)	0.6669(1)
C(4)	0.0611(3)	0.1703(2)	0.5898(1)
C(5)	0.0163(3)	0.2599(2)	0.5063(1)
C(6)	0.1585(3)	0.3242(2)	0.4294(1)
C(7)	0.0640(3)	0.4084(2)	0.3504(2)
C(8)	0.1787(3)	0.4829(2)	0.2701(2)
C(9)	0.2724(3)	0.5477(2)	0.2015(2)
C(10)	0.3802(3)	0.6255(2)	0.1192(2)
C(11)	0.2720(4)	0.7000(3)	0.0273(2)
C(12)	0.4384(4)	0.7567(3)	−0.0268(2)
C(13)	0.6044(4)	0.6454(2)	0.1120(2)
C(14)	0.4006(3)	0.3017(2)	0.4379(2)
C(15)	−0.0454(3)	−0.0514(2)	0.8352(2)
H(3)	−0.235(3)	0.131(2)	0.665(2)
H(5)	−0.127(3)	0.280(2)	0.498(2)
H(7)	−0.096(4)	0.419(2)	0.348(2)
H(11)	0.109(5)	0.698(3)	0.004(2)
H(12)	0.447(5)	0.816(3)	−0.096(3)
H(13)	0.738(4)	0.613(2)	0.155(2)
H(14a)	0.476(4)	0.359(3)	0.391(2)
H(14b)	0.400(4)	0.197(3)	0.417(2)
H(14c)	0.500(5)	0.338(3)	0.518(2)
H(15a)	0.071(5)	−0.021(3)	0.904(2)
H(15b)	−0.071(5)	−0.155(3)	0.813(2)
H(15c)	−0.179(6)	−0.026(4)	0.853(3)

Initially two cycles of block-diagonal least-squares refine-

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

[4] C. F. Ingham and R. A. Massy-Westropp, *Austral. J. Chem.*, 1974, **27**, 1491.

[5] V. Herout, in 'Aspects of Terpenoid Chemistry and Biochemistry,' ed. T. W. Goodwin, Academic Press, New York, 1971, p. 53.

[6] *Cf.* G. P. Newsoroff and S. Sternhell, *Austral. J. Chem.*, 1972, **25**, 1669.

[7] '*X*-Ray '67' system of programs, ed. J. M. Stewart, University of Maryland Technical Report TR 67 58, 1967, revised 1970, ed. J. M. Stewart, F. A. Kundell, and J. C. Baldwin.

[8] 'International Tables for *X*-Ray Crystallography,' vol. III, Kynoch Press, Birmingham, 1962.

[9] I. L. Karle, K. S. Dragonette, and S. A. Brenner, *Acta Cryst.*, 1965, **19**, 713.

[10] G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.

ment of atomic positions and isotropic temperature factors were performed with all the data and unit weights, treating all atoms as carbon. The refined temperature factors enabled the three oxygen atoms to be readily identified and a difference map showed no prominent features, confirming the correct placing of all non-hydrogen atoms. Four more cycles of least-squares refinement, with oxygen atoms identified, reduced the value of R to 0.134. The temperature factors of all atoms were then allowed to vary anisotropically and two further cycles of refinement reduced R to 0.088. At this stage a difference map was calculated which revealed the positions of all 12 hydrogen atoms in the 14 highest peaks in the map. The hydrogen atoms were then included in the refinement with isotropic temperature factors and four more cycles reduced R to 0.062. Analysis of the agreement between $|F_o|$ and $|F_c|$ suggested the adoption of a weighting scheme of the form $w = 1$ for $|F_o| \leqslant 6.0$ and $w = (6.0/|F_o|)^2$ for $|F_o| > 6.0$. Finally, eight cycles of full-matrix least-squares refinement were performed using the weighting scheme and these reduced the value of the agreement factor R to 0.051. At this stage the largest parameter shifts were of the order of 0.4σ indicating that refinement had converged after a total of 20 cycles. A final difference map showed no peaks or depressions >0.2 eÅ^{-3} confirming the correctness of the final structure. Final atomic co-ordinates are listed in the Table; thermal parameters, and observed and calculated structure factors are listed in Supplementary Publication No. SUP 21508 (16 pp., 1 microfiche).*

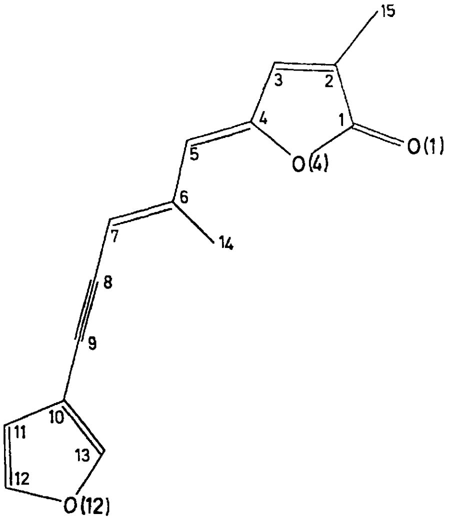

FIGURE 1 Crystallographic numbering scheme

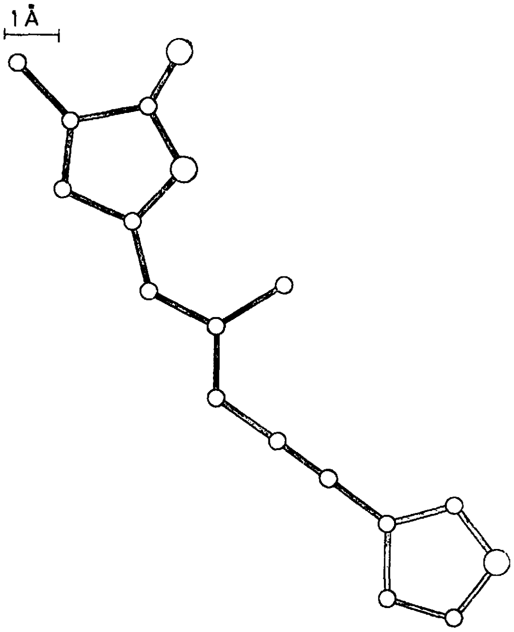

FIGURE 2 General view of freelingyne molecule

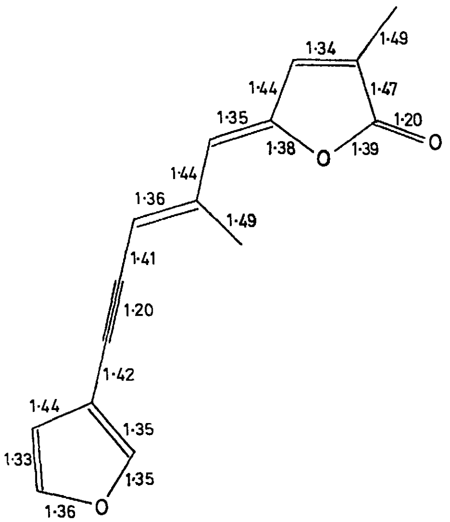

FIGURE 3 Bond lengths (Å); largest standard deviation 0.004 Å

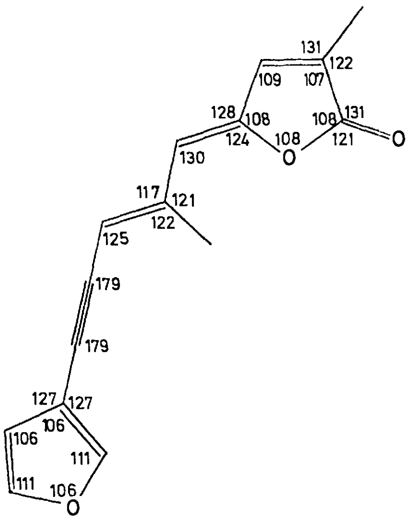

FIGURE 4 Bond angles (°); largest standard deviation 0.3°

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* See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1974, Index issue.

DISCUSSION

For crystallographic purposes the atomic numbering scheme shown in Figure 1 was adopted. A general view of the resulting molecular structure is shown on Figure 2. This confirms the structure of freelingyne as the (4*Z*,6*E*)-isomer (2). Bond lengths and angles, displayed in Figures 3 and 4 together with an indication of their standard deviations, are all as expected for such a highly conjugated structure. The bond angles show several significant deviations from the theoretical value of 120° for sp^2 hybridised carbon atoms. These can all be explained in terms of the angular strain in the two five-membered rings and the van der Waals repulsions between neighbouring non-bonded atoms. For example the large C(4)–C(5)–C(6) (130°) and C(6)–C(7)–C(8) (125°) bond angles can be explained in terms of van der Waals repulsions. For clarity the refined bond lengths and angles to hydrogen atoms are not displayed in the Figures although these all had expected values (C–H 0.90 to 1.01 Å, H–C–H 102 to 113°).

The arrangement of the molecules within the unit cell is shown in Figure 5 projected along the *x* axis. This view emphasises the planar nature of the molecule and reveals that the molecular planes are packed approximately parallel to the (011) plane within the unit cell. There are no intermolecular interactions, however, other than van der Waals attractions, as there are no intermolecular contact distances <3.4 Å.

The overall structure of the molecule is planar with no atom further than 0.18 Å from the mean plane through the whole molecule. The small derivations from planarity can best be described in terms of rotations of each of the five membered rings about the C(4)–C(5) and C(9)–C(10) bonds respectively, in opposite senses. The dihedral angle between the mean plane through the molecule and the furan ring is 9.0°, and the angle to the lactone ring is 3.6°. Both the lactone ring and the furan ring are themselves planar with χ^2 29.1 for the former and 1.6 for the latter. The planarity of the furan ring is further emphasised by the torsion angles about the bonds within the ring, none of which differ significantly from 0°. The torsion angles about the remainder of the bonds in the molecule are all very small, the largest of which, about the C(5)–C(6) bond, is 2.5°, confirming the high degree of planarity of the freelingyne molecule.

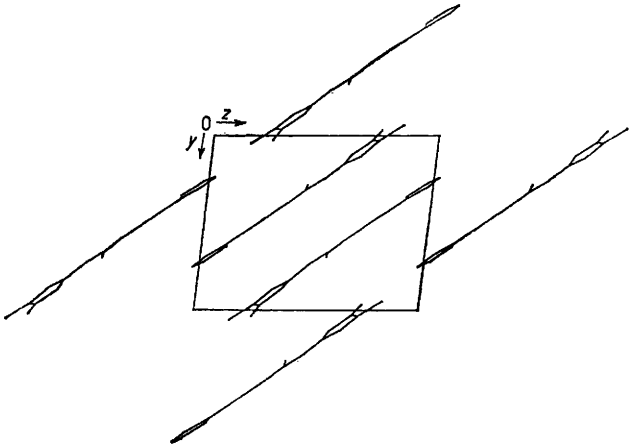

FIGURE 5 The arrangement of molecules within the unit cell; projection along *x* axis

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