

Phototransformations of 4,5-diphenylisoxazole

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Abstract. Sunlight photolysis of 4,5-diphenylisoxazole (1) in methanol sensitized by benzophenone gives 4,4',5,5'-tetraphenyl-2,2'-bioxazole, (4). On irradiation at 350 nm in acetone or at 253.7 nm in absolute alcohol, isoxazole (1) yields α -benzoylphenylacetone nitrile (6) besides the expected phenanthro [9, 10-*d*]-oxazole (5). The bioxazole and the ketonitrile have been identified by single crystal X-ray studies.

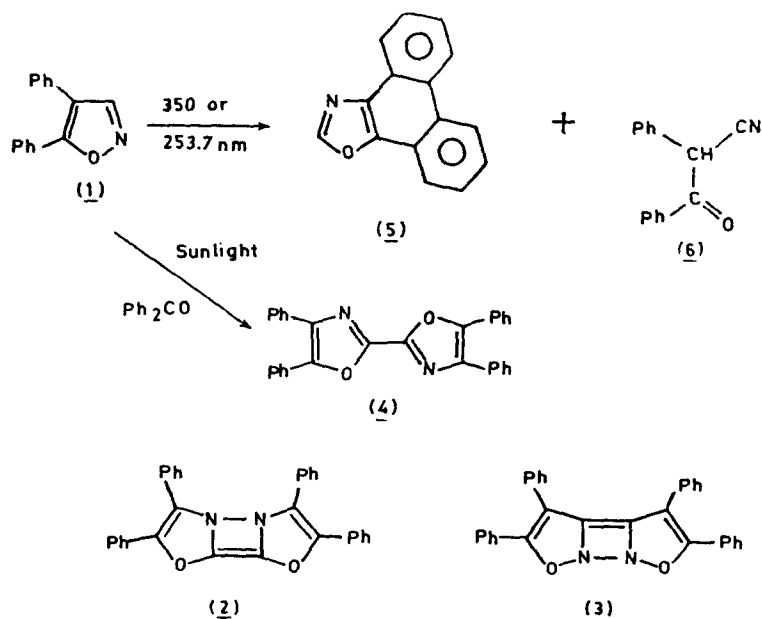
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1. Introduction

Isoxazoles are photochemically active in the UV region due to the weak nature of the N–O link. Ullman and Singh (1966, 1967) in their pioneering study elucidated the mechanism of the photoisomerisation of isoxazole to oxazole. This transformation was found to proceed through an azirine intermediate. It was shown that the photochemical behaviour of the azirines depends dramatically on the wavelength of the radiation used. Implicating the same intermediate, Kojima and Maeda (1969) converted 2,5-diphenyloxazole to a photolysate consisting mostly of 3,5-diphenylisoxazole, 4,5-diphenyloxazole and phenanthro [9, 10-*d*]-oxazole. One of us has shown that the attempted photoelectrocyclic ring closure of 4-benzalamino-5-styrylisoxazole results in an imidazole, another process initiated by N–O scission (Keshava Rao *et al* 1988). In continuation of our interest in the photochemistry of this nucleus, we wish to report the phototransformations of 4,5-diphenylisoxazole, (1) (Subba Raju and Rao 1987).

2. Results and discussion

Exposure of methanolic solutions of (1) to sunlight in the presence of a few crystals of benzophenone turned the clear colourless solution lemon yellow (scheme 1). Pure crystals of (4) were deposited after 8h (yield 20%). The mass spectrum of the latter showed a molecular ion peak at m/z 440, clearly indicating that (1) (M^+ m/z 221) underwent oxidative dimerization on irradiation. The product exhibited blue fluorescence (emission at 418 nm) in chloroform. Therefore, we inferred that the dimer might have a fused structure (2) or (3). The ^1H NMR spectrum which showed only two singlets in the aromatic-region (δ 7.4 and 7.8) did not resolve the ambiguity, but clearly indicated that the product does not contain a hydrogen in the 3-position (δ 8.3 in 4,5-



Scheme 1. Phototransformations of 1.

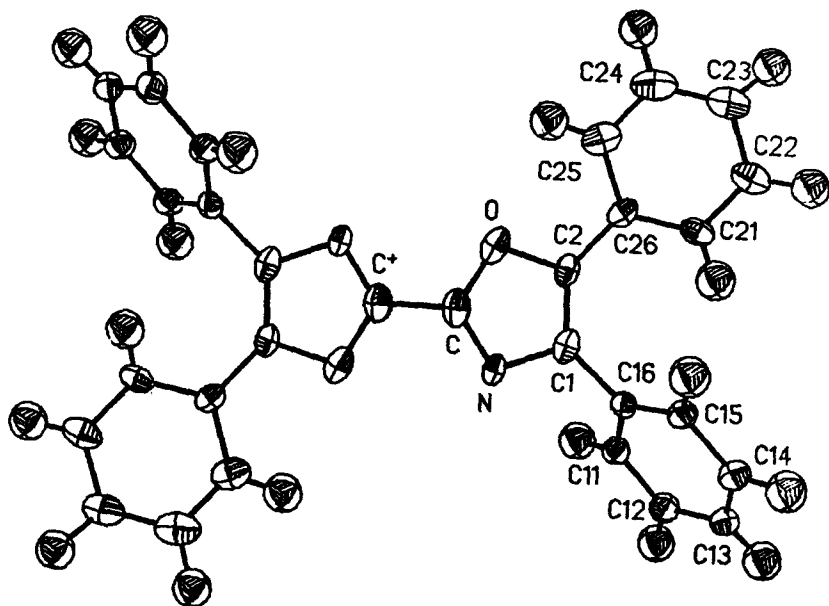


Figure 1. Structure of bioxazole (4) showing atom labelling.

diphenylisoxazole). The structure could be deciphered only by single crystal X-ray crystallography (figure 1 and tables 1 and 2) which showed that it is 4,4',5,5'-tetraphenyl-2,2'-bioxazole (4). Compound (4) has been synthesized earlier from α -aminobenzyl phenyl ketone (Heinze and Baumgartel 1970), but this method, which employs an uncommon starting material and reagents such as oxalyl chloride,

Table 1. Atom coordinates ($\times 10^4$) and equivalent isotropic temperature factors ($\text{\AA}^2 \times 10^3$)* for bioxazole (4).

Atom	X	Y	Z	U_{eq}
N	4032(6)	5861(4)	8786(3)	21(1)
O	2310(5)	3730(4)	9558(2)	36(1)
C	4103(8)	4922(6)	9573(4)	33(2)
C(1)	1962(7)	5249(5)	8189(3)	26(1)
C(11)	2951(7)	6054(5)	6378(3)	27(1)
C(12)	2549(8)	6882(6)	5486(4)	34(2)
C(13)	571(8)	7740(6)	5418(4)	33(2)
C(14)	-966(8)	7774(6)	6271(4)	32(2)
C(15)	-562(7)	6930(5)	7159(3)	28(1)
C(16)	1389(7)	6062(5)	7215(3)	22(1)
C(2)	919(7)	3927(5)	8646(3)	25(1)
C(21)	-2716(8)	2812(5)	7525(4)	30(2)
C(22)	-4699(8)	1672(6)	7286(4)	34(2)
C(23)	-5142(8)	367(6)	7931(4)	39(2)
C(24)	-3578(10)	227(6)	8777(4)	42(2)
C(25)	-1634(9)	1379(6)	9017(4)	38(2)
C(26)	-1161(7)	2708(5)	8396(3)	25(1)

*Equivalent isotropic U defined as one third of the trace of the orthogonalised U tensor.

$U_{eq} = (U_{11} + U_{22} + U_{33} + 2U_{13} \cos \beta)/3$, (for monoclinic crystals: $\beta \neq 90^\circ$).

Table 2. Selected intramolecular bond lengths (\AA) and angles (degrees) for bioxazole (4).

<i>Bond lengths</i>			
N-C	1.304(6)	C-C ⁺	1.436(9)
N-C(1)	1.394(5)	C(1)-C(2)	1.356(9)
O-C	1.334(5)	C(1)-C(16)	1.481(6)
O-C(2)	1.395(5)	C(2)-C(26)	1.464(6)
<i>Bond angles</i>			
C-N-C(1)	104.4(3)	N-C(1)-C(16)	117.4(3)
C-O-C(2)	104.4(3)	N-C(1)-C(2)	108.8(4)
N-C-O	115.0(4)	C(16)-C(1)-C(2)	133.7(4)
N-C-C ⁺	125.9(5)	C(26)-C(2)-C(1)	136.2(4)
O-C-C ⁺	119.1(5)	O-C(2)-C(1)	107.4(3)

phosphorous pentachloride and phosphorous oxychloride, is not only laborious but also gives low yields. Another advantage of the present photochemical method is that it gives the pure bioxazole straightaway without any need for work-up, purification or even crystallization. The bioxazole is an efficient dye laser.

Irradiation at 350 nm of (1) in acetone for 6h furnished three products which were separated by column chromatography. Two solids (m.p. 94°, 152°C) were isolated along with a very small quantity of a gummy substance whose physical state could not be improved. Structural investigation of the gum was therefore abandoned. The higher melting compound is phenanthro [9, 10-*d*] oxazole (5), a not unexpected product

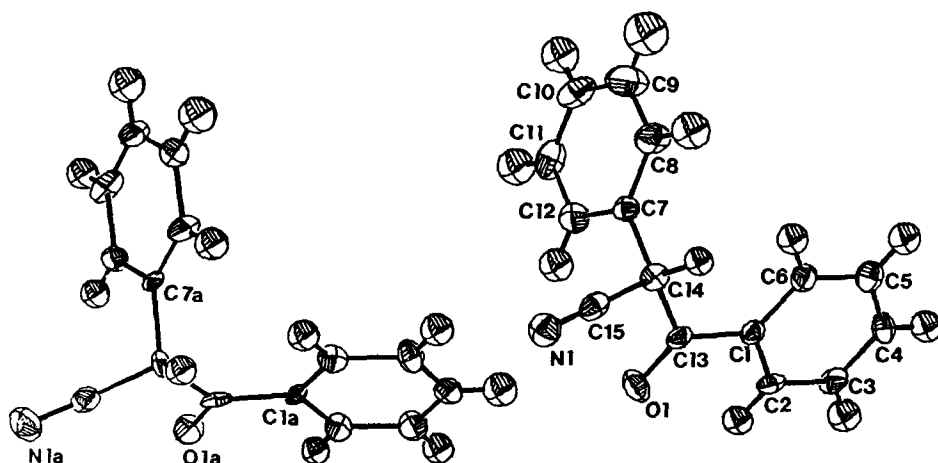
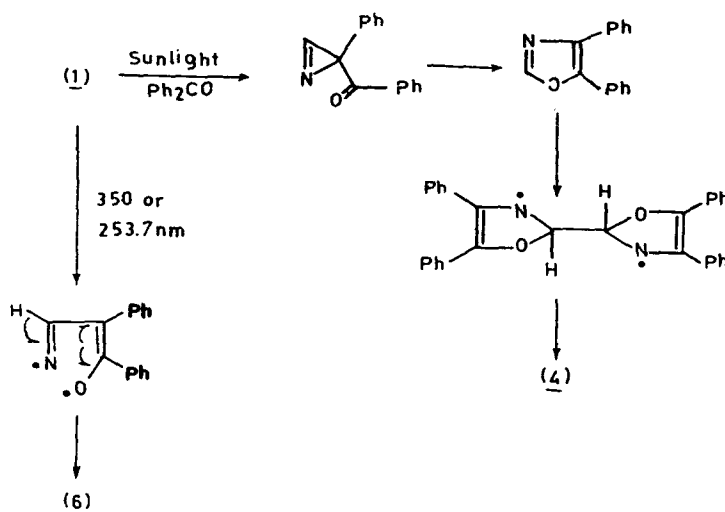


Figure 2. Structure of ketonitrile (6) showing atom labelling. The two symmetry-independent molecules are shown.



Scheme 2. Mechanisms for the formation of 4 and 6.

obtained in 40% yield (Kojima and Maeda 1969). The lower melting compound obtained in low yields (< 35%) was found by X-ray crystallography (figure 2 and tables 3 and 4) to be α -benzoylphenylacetonitrile ((6), $M^+ m/z$ 421), the formation of which is an interesting as well as an unexpected observation (scheme 2). A sharp singlet at δ 5.6 in the ^1H NMR spectrum of (6) indicates a tertiary proton which is deshielded by carbonyl and cyano groups. The same methine carbon appears at 46.8 ppm in the ^{13}C NMR spectrum which also has peaks at 116.7 and 200.0 ppm due to the cyanide and ketone functions, respectively. This is the first reported observation of the formation of ketonitrile (6) in the photolysis of an isoxazole. The 3-unsubstituted isoxazoles have hitherto been known to undergo isomerization to ketonitriles only under the influence

Table 3. Atom coordinates ($\times 10^4$) and equivalent isotropic temperature factors ($\text{\AA}^2 \times 10^3$)* for ketonitrile (6).

Atom	X	Y	Z	U_{eq}
O(1)	2382(2)	5306(3)	1281(3)	32(1)
N(1)	3662(3)	7313(4)	303(4)	42(2)
C(1)	2248(3)	5290(4)	3148(4)	16(2)
C(2)	2553(4)	5629(4)	4146(4)	25(2)
C(3)	2131(4)	5291(5)	5053(4)	30(2)
C(4)	1389(3)	4639(4)	4971(4)	29(2)
C(5)	1068(4)	4317(5)	3993(4)	32(2)
C(6)	1499(3)	4632(4)	3082(4)	24(2)
C(7)	4300(3)	5691(4)	2420(4)	17(2)
C(8)	4729(3)	5820(5)	3377(4)	28(2)
C(9)	5482(4)	5225(5)	3592(4)	36(2)
C(10)	5818(4)	4517(5)	2832(4)	35(2)
C(11)	5382(3)	4376(4)	1877(4)	32(2)
C(12)	4631(3)	4972(4)	1664(4)	25(2)
C(13)	2653(3)	5622(4)	2144(4)	21(2)
C(14)	3479(3)	6374(4)	2167(4)	22(2)
C(15)	3557(4)	6913(4)	1121(5)	27(2)
O(1a)	570(2)	4621(3)	7571(3)	36(1)
N(1a)	2137(3)	6673(4)	7617(3)	31(2)
C(1a)	399(3)	3772(4)	9215(4)	21(2)
C(2a)	728(4)	3510(4)	10230(4)	27(2)
C(3a)	256(4)	2856(4)	10926(4)	30(2)
C(4a)	-545(4)	2450(4)	10615(4)	27(2)
C(5a)	-881(4)	2714(5)	9615(4)	32(2)
C(6a)	-419(3)	3356(4)	8932(4)	24(2)
C(7a)	2444(3)	3970(4)	8586(4)	21(2)
C(8a)	3025(4)	3695(5)	9383(5)	36(2)
C(9a)	3633(4)	2861(5)	9230(5)	54(3)
C(10a)	3678(4)	2296(5)	8295(5)	38(2)
C(11a)	3097(4)	2571(5)	7485(5)	40(2)
C(12a)	2482(4)	3398(5)	7630(4)	31(2)
C(13a)	868(3)	4464(4)	8450(5)	21(2)
C(14a)	1779(3)	4893(4)	8746(4)	21(2)
C(15a)	1981(3)	5905(5)	8110(4)	25(2)

*Equivalent isotropic U defined as one third of the trace of the orthogonally-lised U tensor.

$U_{eq} = (U_{11} + U_{22} + U_{33} + 2U_{13}\cos\beta)/3$, (for monoclinic crystals: $\beta \neq 90^\circ$).

of a base (Claisen 1903). Homolysis of the N–O linkage followed by the migration of the hydrogen atom in the 3-position to the adjacent carbon leads to the nitrile. This photochemical reaction could be of interest in solid state chemistry because of the generation of an asymmetric centre in the product. If an isoxazole crystallises in an enantiomorphous space group, it should, in principle, be possible to prepare an optically active ketonitrile by the photolysis of such a crystal (Elgavi *et al* 1973). Under these conditions, hydrogen migration can be controlled on one side, that is, a stereoselective attachment made on the adjacent carbon atom. However, solid state irradiation of (1) was inconclusive, i.e. the glass plate coated with the substrate turned pale yellow when irradiated with either 3500 or 2537Å. TLC examination of the material showed no conversion at all.

Table 4. Selected intramolecular bond lengths (Å) and angles (degrees) for ketonitrile (6).

<i>Bond lengths</i>			
C(13)–O(1)	1.220(6)	C(13a)–O(1a)	1.220(6)
C(15)–N(1)	1.151(8)	C(15a)–N(1a)	1.138(7)
C(13)–C(14)	1.566(7)	C(13a)–C(14a)	1.543(7)
C(14)–C(15)	1.476(8)	C(14a)–C(15a)	1.490(7)
C(1)–C(13)	1.480(7)	C(1a)–C(13a)	1.475(7)
C(7)–C(14)	1.544(7)	C(7a)–C(14a)	1.529(7)
<i>Bond angles</i>			
C(1)–C(13)–O(1)	122.4(4)	C(1a)–C(13a)–O(1a)	121.7(5)
C(14)–C(13)–O(1)	117.6(4)	C(14a)–C(13a)–O(1a)	118.9(4)
C(14)–C(15)–N(1)	176.4(6)	C(14a)–C(15a)–N(1a)	179.4(6)
C(13)–C(14)–C(15)	108.4(4)	C(13a)–C(14a)–C(15a)	110.0(4)

Irradiation of (1) at 253.7 nm in absolute alcohol gave a mixture of the phenanthrooxazole (5), the ketonitrile (6) in better yields and the same gum obtained earlier which again could neither be improved nor identified. It is also important to note that bioxazole (4) has been obtained only in the presence of benzophenone, a sensitizer.

3. Experimental details

3.1 Instruments

NMR spectra were run on a Varian FT-80A and Varian 300 MHz, with TMS as internal reference. The chemical shifts (δ) are reported in ppm. Mass spectra were recorded on a Varian MAT CH-7 instrument using the electron impact (EI) method at 70 eV. IR spectra were recorded on a Perkin–Elmer 283B spectrophotometer using KBr pellets and a NaCl cell. A Cary 17 spectrophotometer was used to obtain the UV spectral data. Fluorescence spectra were recorded on an Aminco xy recorder at room temperature.

3.2 Materials

Compound (1) was prepared as described by Kojima and Maeda (1969). Solvents were used after purification by distillation and other standard methods. Silica gel (100–200 mesh) was used for column chromatography.

3.3 Photochemical irradiation experiments

4,5-Diphenylisoxazole (1.7 g in 60 ml MeOH) was exposed to sunlight for 3–4 h. There was no reaction. Addition of a few crystals of benzophenone to the solution brought about a change within an hour in the sunlight. The clear colourless solution turned lemon yellow and began depositing crystals. The irradiation was continued for 8 h. The crystals were filtered and washed with a few millilitres of acetone. The product 4,4',5,5'-tetraphenyl-2,2'-bioxazole was obtained in a TLC-pure state (100 mg, m.p. 261°C). Identification was made by elemental analysis, ¹H NMR, MS and single crystal X-ray

diffraction. $^1\text{H NMR}$, δ 7.4, 7.8(s); analysis, calculated for $\text{C}_{30}\text{H}_{20}\text{O}_2\text{N}_2$: C, 81.81, H, 4.54, O, 7.27, N, 6.36; found: C, 81.35, H, 4.50, O, 7.29, N, 6.32%.

3.3a *Irradiation of (1) in acetone*: The isoxazole (600 mg in 60 ml dry acetone) was irradiated for 6 h with RUL 350 nm lamps in a multilamp Rayonet reactor (Model, RPR-208). Ice cold water was circulated through a cold finger immersed in the quartz tube. The solvent was removed under vacuum and the residue was separated into 3 compounds (including a gum) on a silica gel column.

Compound (5) (m.p. 152°C, 240 mg) was identified as phenanthro [9, 10-*d*] oxazole, collected from petroleum ether–benzene (20:80).

Compound (6) (m.p. 94°C, 210 mg) was identified as α -benzoylphenylacetone nitrile, collected from benzene. MS, M^+ m/z 221, IR, 2240, 1670 cm^{-1} , $^1\text{H NMR}$ δ 5.6 (s, 1H), 7.3–7.9 (m, 10H), $^{13}\text{C NMR}$ 46.8, 116.7, 128.34, 129.10, 129.75, 134.56, 200.0 ppm. Analysis: calculated for $\text{C}_{15}\text{H}_{11}\text{ON}$: C, 81.44; H, 4.97; O, 7.24; N, 6.33; found: C, 81.24; H, 4.99; O, 7.21; N, 6.30%.

3.3b *Irradiation of (1) in absolute alcohol*: The isoxazole (500 mg in 60 ml absolute alcohol) taken in a quartz tube was irradiated for 6 h with 253.7 nm lamps in a multilamp Rayonet reactor. Cold finger was used to prevent warming. The solvent was removed under vacuum and the residue was separated into the same 3 components obtained from photolysis in acetone. The only noticeable difference was that the yield of ketonitrile (6) was better (30 mg).

3.4 X-ray analysis

3.4a *Determination of the crystal structure of compound (4)*: $\text{C}_{30}\text{H}_{20}\text{N}_2\text{O}_2$, $M_r = 440$, triclinic, $P\bar{1}$, $Z = 1$, $a = 5.846(2)$, $b = 7.798(2)$, $c = 12.182(4)$ Å, $\alpha = 99.82(2)$, $\beta = 91.75(3)$, $\gamma = 95.22(3)^\circ$, $V = 544.3(3)$ Å³, $F(000) = 232$, $D_x = 1.34$ mg m^{-3} , $\lambda(\text{MoK}\alpha) = 0.7108$ Å, $\mu(\text{MoK}\alpha) = 0.79$ cm^{-1} , $T = 150$ K. Intensity data were collected on a plate-like crystal $0.48 \times 0.22 \times 0.04$ mm^3 on a Nicolet R3 diffractometer. Unit cell parameters were obtained from 25 reflections in the range $3 < 2\theta < 25^\circ$. The ω scan method was used with a scan width of 1.6° , 0.10 background/count ratio and a scan speed of $4.88^\circ/\text{min}$. A total of 2317 reflections was collected with $(\sin \theta/\lambda)_{\text{max}} = 0.62$ and in the range $0 < h < 8$, $-10 < k < 10$, $-16 < l < 16$. Of these, 921 unique reflections were found to be non-zero with $I > 3.0\sigma(I)$. Three standard reflections (300), (030), (003) were measured every 97 reflections and showed less than 3% variation. The structure was solved by direct methods and refined with full-matrix least-squares refinement and unit weights on F_o using the SHELXTL package of programs. The hydrogen atoms, located from a difference map, were refined isotropically while the other atoms were refined anisotropically. Refinement converged at $R = 0.048$, error-of-fit = 4.94, $\Delta/\text{max} = 0.13$, the maximum peak in the final Fourier = $1 e \text{ \AA}^{-3}$. Table 1 contains the positional parameters and table 2 shows some intramolecular bond lengths and angles. Figure 1 is a view of the molecule showing the atom numbering scheme. The molecule lies on an inversion centre and the bond lengths and angles appear normal.

3.4b *Determination of the crystal structure of compound (6):* $C_{15}H_{11}NO$, $M_r = 221$, monoclinic, $P2_1/c$, $z = 8$, $a = 15.530(10)$, $b = 11.95(5)$, $c = 12.620(8)$ Å, $\beta = 91.08(5)^\circ$, $V = 2343(2)$ Å³, $F(000) = 928$, $D_x = 1.25$ mg m⁻³, $\lambda(MoK_\alpha) = 0.7108$ Å, $\mu(MoK_\alpha) = 0.79$ cm⁻¹, $T = 150$ K. Intensity data were collected on an irregular chip $0.40 \times 0.28 \times 0.12$ mm³ on a Nicolet R3 diffractometer. Unit cell parameters were obtained from 25 reflections in the range $3 < 2\theta < 25^\circ$. The ω scan method was used with a scan width of 1.4° , 0.30 background/count ratio and a scan speed of $7.32^\circ/\text{min}$. A total of 3478 reflections was collected with $(\sin \theta)/\lambda$ max = 0.54 and in the range $0 < h < 17$, $0 < k < 13$, $-14 < l < 14$. Of these 1244 unique reflections were found to be non-zero with $I > 3.0 \sigma(I)$. Three standard reflections (600), (060), (006) were measured every 97 reflections and showed less than 4% variation. The structure was solved by direct methods and refined with full-matrix least-squares refinement on F_o using the SHELXTL package of programs. The hydrogen atoms were placed in calculated positions and allowed to ride on the bonded carbon atom while the other atoms were refined anisotropically. Refinement converged at $R = 0.048$, $WR = 0.045$, error-of-fit = 5.01, Δ/σ max = 0.03, the maximum peak in the final Fourier = $0.19 e \text{ \AA}^{-3}$. Table 3 contains the positional parameters and table 4 shows some intramolecular bond lengths and angles. Figure 2 shows the atom numbering scheme and a view of the two symmetry-independent molecules. The bond lengths and angles in these two molecules do not show any substantial variation.

Acknowledgements

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