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REACTION OF SeO_2 WITH DIENES: 1. LINALYL ACETATE

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Abstract.- The reaction of linalyl acetate with SeO_2 in alcoholic media affords some selenium containing substances, among the usual allylic oxidation products. The structural determination of products and a proposal for the reaction mechanism are discussed.

INTRODUCTION

In a previous work[1] we carried out the oxidation of linalyl acetate (1) with SeO_2 as the first step in the synthesis of linalolic acid and its esters. This reaction gave essentially the expected products of allylic oxidation. A more careful investigation of the secondary products of the reaction in MeOH or mixtures of MeOH/EtOH, has allowed us to identify some Se-containing compounds. The isolation and structural determination of such products have afforded us results similar to those observed by Grigoryeva *et al*[2,3] for this reaction in aprotic media, but some new oxidation products containing selenium, whose structures have been determined by exhaustive NMR studies and in one case by X-ray diffraction methods, were isolated. An explanation for their formation is presented.

METHODS AND RESULTS

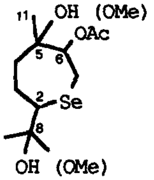
The oxidation of linalyl acetate (1) with SeO_2 in MeOH under refluxing conditions essentially affords mainly the alcohol and the aldehyde resulting from oxidation on the trans methyl group[1], and a number of selenium compounds. The presence of this element was confirmed by oxidation with perchloric acid followed by reduction to metallic Se by treatment of the oxidized material with hydrazine [4].

One of the compounds (2) proving to be positive in the Se assay is a crystalline solid with m.p.=112°. Its MS has several molecular ions with proportions corresponding to that of Se isotopes, the most abundant among them being those at *m/z* 324 and 322, coinciding with the molecular formulas $C_{13}H_{24}O_4{}^{80}Se$ and $C_{13}H_{24}O_4{}^{78}Se$.

The IR spectrum of this substance displays absorptions of hydroxyl and acetoxyl groups, and in its ^{13}C NMR spectrum (Table 1) the absence of olefinic bonds may be seen. As compared with the ^{13}C NMR spectrum of 1, that of compound 2 reveals the persistence of three methyls, two methylenes, the oxygenated quaternary carbon atom and the acetate group, the two double bonds being substituted by a methylene (17.54 ppm), two methines (50.90 and 82.91 ppm) and an oxygenated tertiary carbon atom (77.73 or 71.42 ppm); at the same time the entrance of a methoxyl group can be seen. These findings show that one is dealing with a cyclic compound with three oxygenated functions, alcohol, methylether and acetate, on the carbon atoms at 71.42, 77.73 and 82.91 ppm, and that the Se must be bonded to the two remaining carbons that have changed their chemical shifts (the methine absorbing at 50.90 and the methylene at 17.54 ppm).

The ^1H-NMR spectrum of the compound (Table 2) shows signals that can be assigned to an AMX system: 2.25 (J=13.7 and 2.1 Hz), 3.16 (J=13.7 and 10.7 Hz) and 4.84 ppm of a -CH(OAc)-CH_2-Se- grouping, in which it is possible to observe the deshielding due to the acetate group and an important difference (0.93 ppm) in the chemical shift of the two geminal hydrogen atoms of the methylene group, owing to the diamagnetic anisotropy produced by the selenium atom. Of the rest of the signals, the three methyls, the methoxyl and the acetoxyl groups are clearly differentiated, and the remaining are those corresponding to a $-CH_2-CH_2-\underset{|}{C}H-Se$ grouping, among which an overlapping signal at 3.18 ppm could be assigned to the methine supporting the Se atom.

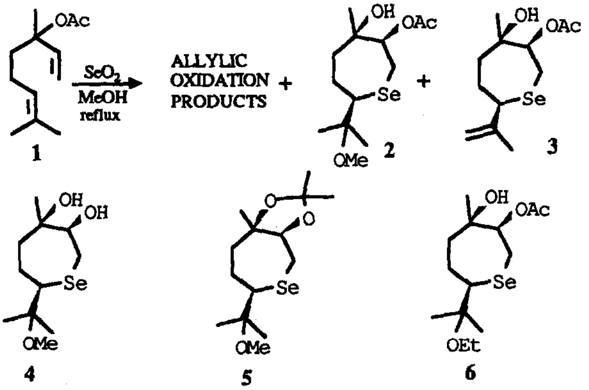
These NMR data indicate that the carbon skeleton of the original linalyl acetate is maintained; this was confirmed by a 2D-INADEQUATE correlation experiment[5]. Accordingly, 2 must have the molecular constitution depicted below; the position occupied, respectively, by the hydroxyl and methoxyl groups and the stereochemistry of the chiral centers remain to be elucidated.



The study of one-bond and long-range heteronuclear 2D-NMR correlations confirmed the earlier assignments and allowed us to locate the methoxyl group on the central carbon atom of the ispropyl group upon observing a correlation between the methoxyl hydrogens and that carbon atom absorbing at 77.73 ppm.

The positions occupied by the oxygenated sustituents were confirmed in the conversion of the hydroxyacetate 2 into the diol 4 and of the latter into the isopropyliden ketal 5, which implies the proximity of hydroxyl and acetoxyl groups. The very small change observed in the chemical shift of H-6 and C-6 in 2, 4 and 5 agrees with these structures. The formation of 5 from 4 and the similarity of the coupling constants of H-6 and H-7 in compounds 2, 4 and 5 suggest a *cis* disposition for the two neighbouring oxygenated functions in the three compounds, which would have the structures shown in scheme 1.

Another by-product (3) from the oxidation of 1 with SeO_2, in which the presence of Se was observed, has molecular ions in the MS at *m/z* 292 and 290, corresponding to the molecular formulas of $C_{12}H_{20}O_3{}^{80}Se$ and $C_{12}H_{20}O_3{}^{78}Se$. This substance shows strong structural analogies with compound 2. The differences lie in the presence of an isopropenyl grouping at position 2 instead of the 2-methoxy-2-propyl grouping, as may be observed from its spectroscopic data (Tables 1 and 2). This compound is identical to that obtained by oxidation of 1 with SeO_2 in aprotic solvents[2,3].



Scheme 1

The structure of 3 was confirmed by X-ray diffraction, as will be described below, also observing the *cis* disposition for the hydroxyl, the acetoxyl and the isopropenyl groups.

The formation of compounds 2 and 3 in a proportion of about 10% of the reaction product,was observed each time that 1 was treated with SeO_2. In some occasions a mixture of EtOH/MeOH was used as solvent, obtaining an analogous compound 6, with an ethoxyl group at position 8 instead of the methoxyl group shown by compound 2. The spectroscopic properties of 6 (Tables 1 and 2) are identical to those of 2,except for the small variations expected from the structural change.

Table 1. ^{1}H-NMR data for compounds **2-6**.

H	2	3	4	5	6
2	3.18 *m*	3.68 *dd* (13.1; 4.4)	3.20 *m*	3.10 *dd* (10.3; 6.1)	3.18 *m*
6	4.84 *dd* (10.7; 2.1)	4.88 *dd* (10.7; 2.3)	3.62 *dd* (9.5; 1.6)	4.05 *dd* (10.1; 3.5)	4.86 *dd* (10.7; 2.3)
7	3.16 *dd* (13.7; 10.7)	3.23 *dd* (13.8; 10.7)	3.04 *dd* (14.0; 9.5)	2.97 *dd* (13.3; 10.1)	3.15 *dd* (13.7; 10.7)
7'	2.25 *dd* (13.7; 2.1)	2.36 *dd* (13.8; 2.3)	2.42 *dd* (14.0; 1.6)	2.65 *dd* (13.3; 3.5)	2.26 *dd* (13.7; 2.3)
9	1.24 *s*	4.84 *dd* (1.5; 0.8) 4.65 *dd* (1.5; 1.5)	1.26 *s*	1.30 *s*	1.26 *s*
10	1.23 s	1.84 *s*	1.24 *s*	1.24 *s*	1.24 *s*
11	1.19 s	1.20 *s*	1.24 *s*	1.22 *s*	1.20 *s*
OMe	3.17 s		3.18 *s*	3.17 *s*	3.37 *q* (6.9) 1.13 *t* (6.9)
Ac	2.10 s	2.11 *s*			2.10 *s*
Acetonide				1.41 *s* 1.46 *s*	

δ values in ppm. J values in Hz. CDCl3 with TMS as int. st.

Table 2. ^{13}C NMR data for compounds **2-6**

C	2	3	4	5	6
2	50.90	47.00	51.82	50.40	51.44
3	20.86	25.20	23.11	21.01	21.01
4	37.86	37.60	37.29	35.76	37.95
5	71.42	72.00	72.90	83.35	71.77
6	82.91	83.00	78.78	82.90	83.11
7	17.54	18.70	22.23	24.05	17.66
8	77.73	148.40	77.83	77.63	77.73
9	21.43	110.00	22.07	22.71	22.22
10	22.36	19.05	22.72	23.33	23.35
11	29.05	29.45	28.48	28.63	29.37
OMe	49.05		49.25	49.29	
OEt					56.70 16.05
OAc	20.86 169.32	21.12 169.50			21.01 169.56
Acetonide				27.54 29.93 107.51	

δ values in ppm. $CDCl_3$ with TMS as int. st.

CRYSTALLOGRAPHIC STUDIES

The X-ray diffraction was carried out on compound **3** from which a good quality monocrystal was obtained.The final atomic coordinates are listed in Table 3. The structure consists of two crytallographically independent molecules; both are

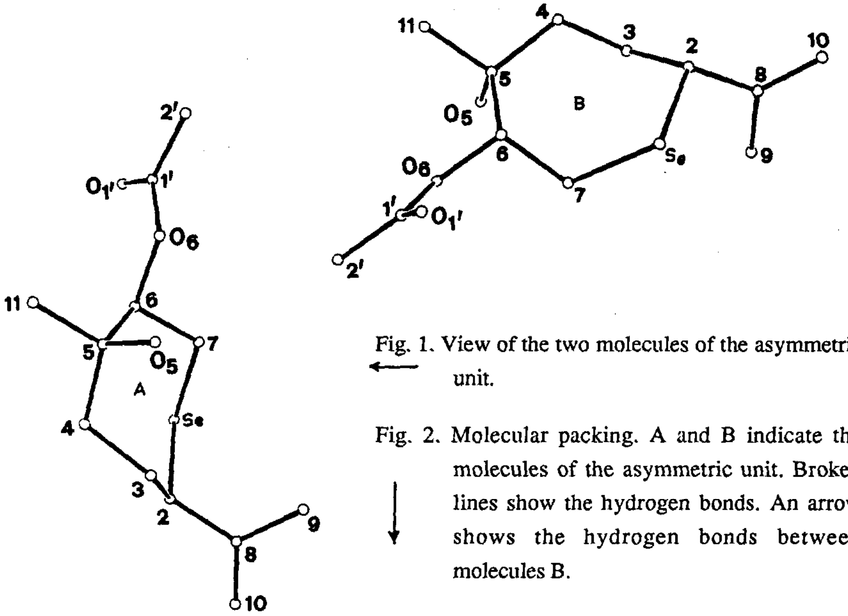


Fig. 1. View of the two molecules of the asymmetric
← unit.

Fig. 2. Molecular packing. A and B indicate the molecules of the asymmetric unit. Broken lines show the hydrogen bonds. An arrow shows the hydrogen bonds between molecules B.
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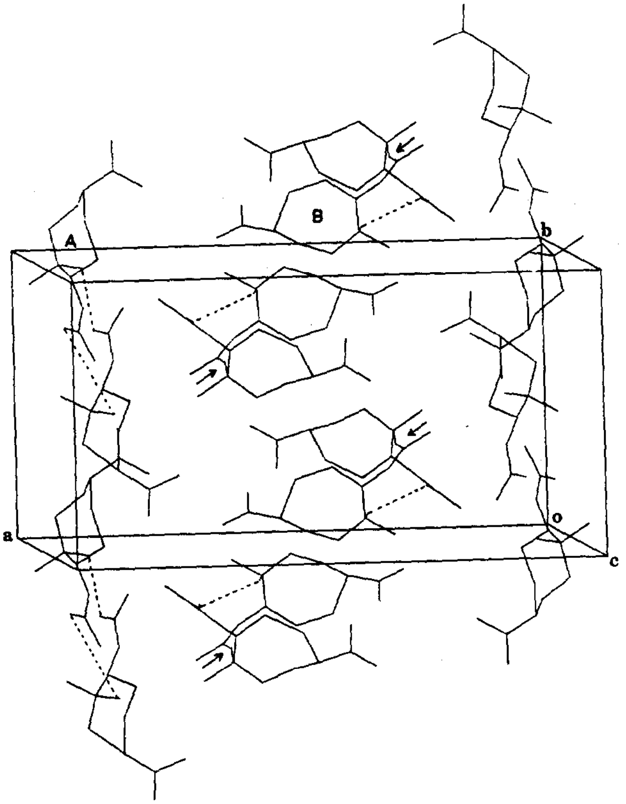


almost identical. Figure 1 shows the a symmetric unit with molecules A and B together with the numbering scheme. The conformation adopted for the hetero-ring was deduced from analysis of the torsion angles. In both molecules the conformation adopted is a twist-chair. Table 4 shows the torsion angles for this ring; they follow a clock-wise direction, starting at C-6, the dominant symmetry being rotational through C-2 in both molecules[6,7].

Table 5 gives the bond distances and angles for the Se-C atoms. It is seen that the observed values for the Se-C distances are different and rather large, although they are in agreement with values of 1.97 Å reported by Dulegeard[8] and 2.01 Å reported by Kivekash[9]

Table 3. Fractional atomic coordinates (x 10^4) and equivalent temperature factors (Å x10^4) with e.s.d.'s in parentheses

Atom	X	Y	Z	U .
Se A	8531(0)	886(0)	9394(0)	522(5)
O5 A	9084(1)	-234(2)	13632(3)	433(9)
O6 A	8886(1)	-1851(2)	11844(3)	459(10)
O1′ A	9034(2)	-2732(2)	10013(4)	717(16)
C2 A	8691(2)	2097(3)	10709(4)	431(13)
C3 A	8984(2)	1722(3)	12153(4)	411(12)
C4 A	9534(2)	967(3)	12298(4)	439(13)
C5 A	9410(2)	-224(3)	12562(4)	387(12)
C6 A	9043(2)	-810(3)	11310(4)	417(13)
C7 A	8440(2)	-299(3)	10617(4)	453(13)
C8 A	8124(2)	2750(3)	10665(4)	478(14)
C9 A	7621(2)	2247(4)	11201(6)	670(19)
C10 A	8087(2)	3743(3)	10166(5)	633(18)
C11 A	10016(2)	-815(3)	13044(5)	590(16)
C1′ A	8886(2)	-2735(3)	11093(4)	445(13)
C2′ A	8673(2)	-3690(3)	11758(5)	573(16)
Se B	5143(0)	-3114(0)	14106(1)	592(6)
O5 B	6116(1)	-3972(3)	10891(3)	617(13)
O6 B	6739(1)	-2634(3)	12763(3)	571(12)
O1′ B	7133(2)	-2068(4)	14872(4)	882(19)
C2 B	4730(2)	-4318(4)	12967(5)	536(15)
C3 B	5063(2)	-4648(3)	11864(5)	542(15)
C4 B	5708(2)	-5060(3)	12414(5)	588(17)
C5 B	6229(2)	-4303(3)	12299(5)	515(15)
C6 B	6278(2)	-3295(3)	13208(4)	477(14)
C7 B	5714(2)	-2602(3)	13058(4)	492(14)
C8 B	4077(2)	-4020(5)	12439(6)	695(20)
C9 B	3198(3)	-3918(7)	11329(8)	1043(30)
C10 B	3660(3)	-4490(7)	12990(10)	1151(37)
C11 B	6825(2)	-4932(5)	12654(7)	864(25)
C1′ B	7133(2)	-2081(4)	13678(5)	541(16)
C2′ B	7564(2)	-1467(4)	13039(6)	696(20)

Table 4. Torsion angles (°) in the seven-membered ring.e.s.d.'s. in parentheses

Molecule A		Molecule B	
C5-C6-C7-Se	80.9(4)	C5-C6-C7-Se	83.2(4)
C6-C7-Se-C2	-85.0(3)	C6-C7-Se-C2	-78.7(3)
C7-Se-C2-C3	27.1(3)	C7-Se-C2-C3	13.4(3)
Se-C2-C3-C4	49.0(4)	Se-C2-C3-C4	61.4(4)
C2-C3-C4-C5	-104.7(4)	C2-C3-C4-C5	-105.2(5)
C3-C4-C5-C6	72.8(4)	C3-C4-C5-C6	68.0(5)
C4-C5-C6-C7	-54.2(4)	C4-C5-C6-C7	-54.3(5)

Table 5. Bond distances (Å) and angles (°) at Se.

Se A -C2 A	1.977(4)	Se A -C7 A	1.950(4)
Se B-C2 B	1.984(4)	Se B-C7 B	1.936(4)
C2 A-Se A-C7 A	100.4(2)		
C2 B-Se B-C7 B	102.7(2)		

The configuration adopted by the substituents at C-2, C-5(O-5) and C-6 are: ß,ß,ß for both molecules. The crystal structure is shown in Figure 2. The intermolecular contacts are between atoms O-5 and O-1′; the links produce an infinite chain of molecules A and B along the b axis. The scheme below shows the geometry of the H-bonds for molecules of A and B, respectively.

	donor	donor-aceptor	H-aceptor	·donor-H---aceptor
(1)	O5-H	O5...........O1′	H.........O1′	O5-H.........O1′
	0.959 Å	2.886 Å	1.924 Å	167.9°
(2)	O5-H	O5...........O1′	H.........O1′	O5-H.........O1′
	0.922 Å	2.996 Å	2.088 Å	168.1°

(1) X, 1/2-Y, 1/2+Z

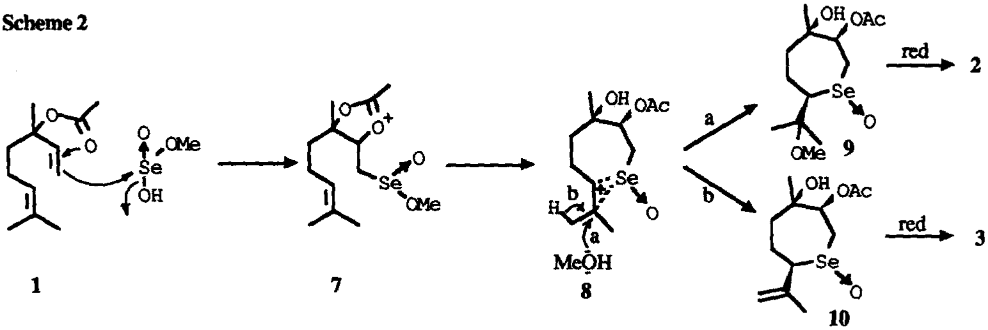
(2) X, -1/2-Y, 1/2-Z

DISCUSSION

In view of the results obtained by us, the course of the reaction can be explained in terms of two electrophilic attacks by a selenium species on the double bonds of linalyl acetate **1**. The attack on the Δ^7 double bond, favoured by the anchimeric assistance of the acetate group, is completed with the emigration of this group, whereas the attack on the Δ^2 double bond is produced with the addition of selenium and a molecule of the alcohol used as solvent. In this way the reaction would occur as indicated in scheme 2.

The electrophilic nature of SeO_2 or its solvated derivatives has been reported to be responsible for several reactions of SeO_2 with olefins[10] and carbonyls[11] and has even served to explain some stereochemical results of the usual allylic oxidation of olefins[12], such that it may be the cause of the first electrophilic attack, that affords the intermediate **7**. A new electrophilic attack on the Δ^2 double bond would lead to an intermediate **8**, which by addition of MeOH or by deprotonation may lead to the selenoxides **9** and **10**. In agreement with this proposal the reaction of SeO_2 with two double bonds to give selenoxides has been reported for several substrates[11,13], and the reduction of selenoxides to selenides, corresponding to the conversion of **9** and **10** into **2** and **3**, is a transformation that occurs through the exhange of the oxygen between selenoxides and species of Se(II)[14] and has been mentioned as a method for transforming alcohols into aldehydes in the presence of SeO_2 as catalyst[15] and as method for achieving the Kornblum oxidation[16].

Scheme 2



Although this mechanism accounts reasonably well for the conversion of 1 into 2 and 3, a species of Se(II), whose origin lies in the solvolysis of compounds having Se(II) formed in the [2,3] rearrangement during allylic oxidation[17,18] may also act as the electrophile responsible for the first attack on the Δ^7. In this case, the second electrophilic attack on Δ^2 would lead directly to the formation of the final selenides. In either of the two possibilities, the reaction sequence must be as indicated; otherwise, an initial attack on Δ^2 would lead to the formation of the two epimers at C-2, which is not the case in any of our experiments.

The reaction of SeO_2 with olefins and aromatic compounds through a double electrophilic attack, leading to the formation of two C-Se bondings with such substrates and giving rise to several selenides, has been observed on different occasions[19,20,21]. In view of the results in this report, the reaction seems to have a general nature and is perfectly well encompassed within the reactivity of selenium species, which together with ene reactions and others acting as electrophiles they also produce redox reactions.

EXPERIMENTAL

General experimental procedures. Mps were determined in capillaries and are uncorrected. Optical rotations were measured in $CHCl_3$. IR spectra were obtained in $CHCl_3$. ϑ_{max} values are expressed in cm^{-1}. ^1H NMR (200.13 MHz) and ^{13}C NMR (50.3 MHz) spectra were measured in $CDCl_3$ with TMS as internal standard. δ values are expressed in ppm. EIMS were obtained at 70 ev. *m/z* values followed by relative abundance (%) are stated. Flash chromatography was run on silica gel (Merck Nº 9385)

Oxidation of 1. General method. To a solution of 1 (25 g, 0.128 mol) in MeOH (30 ml) a solution of SeO_2 (16 g., 0.144 mol) in MeOH (500 ml) was slowly added, and the reaction was refluxed by 5 h. Once the Se was eliminated by filtration and the MeOH evaporated, the reaction mixture dissolved in hexane and washed with diluted $NaHCO_3$ gave 27 g of the reaction product as a brown-orange oil. By CC unreacted 1 (25-45 %), allylic oxidation products (70-45 %), 2 (~7%) and 3 (~2%) were isolated. When the reaction reflux was maintained by 15 h. the proportion of allylic oxidation products increased, that of unreacted 1 decreased whereas that of Se-containing by-products was maintained.

6-acetoxy-2(2-methoxy-2-propyl)-5-methylselenepan-5-ol (2). White crystals. M.p. 112° (hex-CH_2Cl_2). IR(KBr): 3480, 1735, 1245, 1140, 1070. MS *m/z* : 324, 265, 252. Treatment of 180 mg of 2 with 2 ml of KOH/MeOH (5%) afforded 140 mg of 4. IR: 3400, 1130, 1070, 1005, 835. To 60 mg of 4 in 3 ml of Me_2CO, 1 ml of 2,2-dimethoxypropane and a catalytic amount of Me_3SiCl were added; from the reaction mixture 63 mg of 5 were obtained. IR(film): 1230, 1135,1065, 1025, 835.

6-acetoxy-5-methyl-2(2-propenyl)selenepan-5-ol (3). White crystals. M.p.108°(hex-CH_2Cl_2). IR: 3460, 3030, 1730, 1235, 960, 940, 885. When the SeO_2 is solved in EtOH instead MeOH, 6 was obtained in ~2% while 2 decreased to ~5%. *6-acetoxy-2(2-ethoxy-2-propyl)-5-hydroxy-5-methylselenepano* (6). White crystals, M.p. 116° (hex-CH_2Cl_2). IR(KBr): 3475, 1735, 1250, 1130, 1065.

Crystallographic techniques. Colourless prysmatic crystal with approximate dimensions 0.2x0.23x0.10 mm. was used for data collection. Unit cell parameters from least-squares refinement of 2θ values of 41 reflexions: a=22.594(1), b=12.578(1), c=10.0132(3) Å, ß=102.372(2)º, space group P21/c, deduced from systematic absences, Z=4.

Phylips PW 1100 four-circle diffractometer, graphite monochromated CuKα radiation (λ=1.5418Å). The intensities of 4929 reflexions were collected in the range of $2<2\theta<65^\circ$, ω-2θ scan technique, scan width 1.5, scan speed 0.06° seg. Two reference reflexions monitored every 90 measured reflexions, no variation was observed. Corrections for Lorentz and polarization was applied. 4341 intensities were considered observed with $I>2\sigma(I)$ criterion, and they were used in the subsequent calculations; the number of variables is 288.

The structure was solved by standard Patterson and Fourier synthesis and refined by full-matrix least-squares with anisotropic temperature factors for all non-H atoms, this led to R=0.064. Difference-electron density maps computed at this stage revealed positions of the H atoms in the structure and assigned isotropic temperature factor of the heavier atoms to which they are attached, and they were considered as fixed isotropic contributors; quantity minimized is $\Sigma w([Fo]-[Fc])^2$ were w was empirically calculated preventing bias in $<w\Delta^2F>$ vs. $<Fo>$ and vs $<\text{sen } \theta/l>$. The last cycle of refinement gave R=0.049 and Rw=0.053, the final difference map revealed no residuals greater than 0.37 e Å^{-2}. Atomic scattering factors and anomalous dispersion corrections from International Tables for X-Ray Crystallography[22]. All calculations performed with X-Ray 76 System[23], on a VAX 11/750 computer. [Lists of structure factors, anisotropic thermal parameters, have been deposited as supplementary material].

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REFERENCES

1.- A. San Feliciano, M. Medarde, J.L.López and J.M. Miguel del Corral; *An. Quim.* Ser C **82**, 195 (1986)
2.- N.Y. Grigoryeva, A.V. Lozanova, A. I. Lutsenko and A.M. Moiseenkov; *Izv. Akad. Nauk. SSR Ser. Khim.* **11**, 2514 (1986)
3.- A.M. Moiseenkov, N.Y. Grigoryeva and A.V. Lozanova; *Dokl. Akad. Nauk. SSSR* , **289**, 114 (1986)
4.- F. Feigl; *Anal. Chim. Acta* , **24**, 501 (1961)
5.- T.H. Mareci and R. Freeman; *J. Magn. Reson.*, **48**, 158 (1982)
6.- E. Toromanoff; *Tetrahedron*, **36**, 2809 (1980)
7.- W.L. Duax, C.M. Weeks and D.C. Rohrer; "Topics in Stereochemistry" v.9, p. 271-383. (E.L. Eliel and N. Allinger Eds.), John Wiley, New York, 1976.
8.- Y. Dulegeard, Y. Le Pouzat-Guinier-Manach and J. Meinnel; *Cryst. Struct. Comm.*, **3**, 387 (1974)
9.- R. Kivekash, M. Klinga, R. Ugla, M. sundberg, T. Laitalainen and T. Simonen; *Cryst. Struct. Comm.*, **7**, 441 (1978)
10.- K.B. Wiberg and S.D. Nielsen; *J. Org. Chem.*, **29**, 3353 (1964)
11.- K.B. Sharpless and K.M. Gordon; *J. Am. Chem. Soc.*, **98**, 300 (1976)
12.- L.M. Stephenson and D.R. Speth; *J. Org. Chem.*, **44**, 4683 (1979)
13.- J.M. Marx and R. Norman; *Tetrahedron Lett.*, 2867 (1973)
14.- H.J. Reich J. M. Renga and I. L. Reich; *J. Am. Chem. Soc.*, **97**, 5434 (1974)
15.- F. Ogura, T. Otsubo, K. Ariyoshi and H. Yamaguchi; *Chem. Lett.*, 1833 (1983)
16.- F. Ogura, T. Otsubo, K. Ariyoshi and H. Yamaguchi; *Chem. Lett.*, 892 (1984)
17.- K.B. Sharpless and R.F. Lauer; *J. Am. Chem. Soc.*, **94**, 7153 (1972)
18.- D. Arigoni, A. Vasella, K. B. Sharpless and H.P. Jensen; *J. Am. Chem. Soc.*, **95**, 7917 (1973)
19.- D.H. Olson; *Tetrahedron Lett.*, 2053 (1966)
20.- G. Menta and V.R. Nayak; *J. Chem. Sect. B*, **15B**(5), 419 (1977)
21.- S.S. Krishnamurthy and S. Soundzrarajan; *J. Organomet. Chem.*, **15**, 367 (1968)
22.- International tables for X-Ray Crystallography. Tome IV. Kynoch Press. Birminghan (1974)
23.- J.M. Stewart, P.A. Machin, H.L. Ammon, H. Dickinson and H. Flack. "The X-Ray System". Computer Science Center, Univ. of Maryland, College Park, Maryland (1976).