

Structural Resolution of the Stereochemistry of a Spirooxirane Derived from an α -Arylidene Heterocyclic Carbonyl. The Crystal and Molecular Structure of 2-(*p*-Chlorophenyl)-5-phenyl-7-methyl- 1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one

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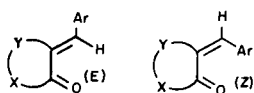
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The stereochemical assignment of molecular geometry for α -arylidene carbonyl compounds and spirooxirane derived from them have continued to be a challenging problem for which the most satisfactory solution continues to be an x-ray diffraction structure determination. In that regard, the title compound (a spirooxirane) has been found to crystallize in the monoclinic space group $P2_1/c$ with cell dimensions of $a = 5.989(1)\text{\AA}$, $b = 27.625(4)\text{\AA}$, $c = 9.374(2)\text{\AA}$, $\beta = 99.06(1)^\circ$. The structure of the compound has been determined, with the refinement to $R = 0.059$. The previous, tentative assignment of structure has been confirmed substantiating our prediction that the oxidation of the enone system proceeds with rotation of the phenyl group on the β -carbon away from the carbonyl group, minimizing adverse steric interactions and allowing orbitals of the carbonyl group to overlap with those of the carbanionic center during the closure of the oxirane ring. The agreement between predictions based on nmr data and the x-ray diffraction determination will support a stronger reliance on the nmr data predictions in subsequent studies.

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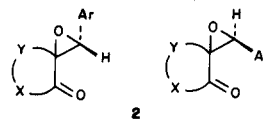
Introduction.

The assignment of stereochemistry to diastereomeric (*Z* or *E*) isomers of α -arylidene carbonyl compounds continues to present a challenging problem (1). Numerous



physical and chemical techniques (ir, uv, nmr, photochemical, thermal and acid-catalyzed *Z/E* isomerization) have been brought to bear on the problem and successful assignment of arylidene geometry in α -arylidene- γ -lactones (2), 3-arylidene-2-pyrrolidones (3), 3-arylidene-*N*-arylsuccinimides (4), α -arylidene-1-tetralones (5), 3-arylidene-thianaphthen-2-ones (6) and α -arylideneindanones (5a,7) and auronones (8) has been achieved. However, ambiguity in the assignment of geometry may arise, for example, in the case of 2-aryl-4-arylidene-5(4*H*)-oxazolones (1b,9) and 4-arylidene-1-aryl-2-pyrazolin-5-ones (10) due to the ease with which *Z/E* thermal and/or acid-catalyzed isomerization may occur. Furthermore, the problems associated with assigning stereochemistry in such systems may be compounded by the availability of only one isomer of the pair and/or the close similarity of their spectral data when both may be isolated.

The assignment of molecular geometry becomes more complex for the spirooxiranes **2**, derived from **1**, since neither the chemistry nor spectral parameters may necessarily parallel those of the α -arylidene compounds.



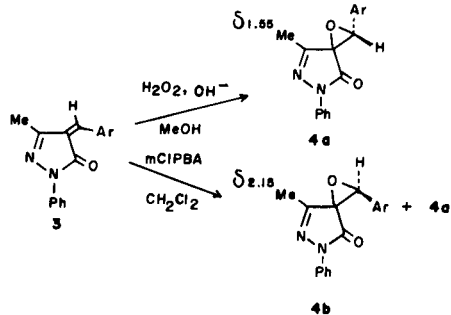
In the course of our work on the photochemistry of heterocyclic spirooxiranes (11), we prepared the pyrazolinone oxiranes from the corresponding α -arylidene pyrazolinone oxiranes **4** from the corresponding α -pyrazolinone **3** having the *Z* configuration (10). The stereochemistry of the α -arylidene pyrazolinone **4** has been secured unequivocally by (i) detailed ^1H nmr studies where both the *Z* and *E* isomers of **3** were available (10) and (ii) by ^{13}C nmr spectroscopy and analysis of the long-range $^3\text{J}_{\text{C,H}}$ coupling constants observed between the vinyl proton and the carbonyl carbon as well as the azomethine carbon, respectively (11c). The vinylic hydrogen is coupled to the carbon atom of the carbonyl group with the larger of the two coupling constants, an observation consistent with the trans-orientation of the hydrogen atom to the carbonyl group (11c). Basic hydrogen peroxide oxidation of the arylidene compounds **3** gives primarily oxiranes **4a**, while *m*-chloroper-

Table Ia

Fractional Coordinates and Anisotropic Thermal Parameters
(Anisotropic thermal parameters $\times 10^4$, estimated standard deviations in Parentheses refer to last decimal place.)

Atom	X	Y	Z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Cf	-0.7162(2)	0.0317(0)	0.2955(2)	535(6)	16(0)	282(3)	-20(1)	119(3)	6(1)
N1	0.1198(5)	0.2967(1)	0.3812(3)	284(12)	14(1)	115(5)	-8(2)	83(6)	-2(1)
N2	-0.0557(5)	0.2860(1)	0.4632(3)	293(12)	14(1)	110(5)	-10(2)	87(6)	-4(1)
C3	-0.0708(6)	0.2397(1)	0.4740(4)	251(14)	16(1)	84(5)	-2(3)	41(7)	-4(2)
C4	0.0903(6)	0.2151(1)	0.3938(4)	288(15)	13(1)	114(6)	-1(3)	70(8)	3(2)
O4	0.2140(5)	0.1729(1)	0.4449(3)	354(11)	16(0)	159(5)	11(2)	45(6)	7(1)
C5	0.2154(6)	0.2556(1)	0.3358(4)	258(14)	15(1)	122(6)	0(3)	57(8)	1(2)
O5	0.3672(5)	0.2526(1)	0.2637(3)	351(11)	20(1)	205(5)	1(2)	167(7)	0(1)
C6	0.1608(7)	0.3463(1)	0.3533(4)	349(17)	14(1)	94(6)	-11(3)	39(8)	0(2)
C7	0.3515(7)	0.3590(2)	0.2940(4)	327(17)	18(1)	157(7)	-15(3)	89(9)	0(2)
C8	0.3864(8)	0.4077(2)	0.2698(5)	451(21)	23(1)	192(9)	-32(4)	91(11)	9(2)
C9	0.2399(8)	0.4426(2)	0.3018(5)	595(25)	17(1)	222(9)	-16(4)	42(12)	20(2)
C10	0.0531(8)	0.4292(2)	0.3603(5)	457(21)	15(1)	252(10)	9(3)	76(12)	15(2)
C11	0.0138(7)	0.3811(1)	0.3847(5)	313(17)	16(1)	185(8)	4(3)	67(9)	6(2)
C12	-0.2385(7)	0.2167(1)	0.5546(4)	332(16)	15(1)	127(6)	-11(3)	102(8)	0(2)
C13	0.0568(7)	0.1682(1)	0.3113(4)	373(17)	14(1)	128(4)	9(3)	90(9)	1(2)
C14	-0.1377(7)	0.1355(1)	0.3130(4)	374(17)	11(1)	103(6)	0(3)	67(8)	-1(2)
C15	-0.3095(7)	0.1355(1)	0.1965(4)	432(19)	13(1)	103(6)	0(3)	74(9)	4(2)
C16	-0.4880(7)	0.1038(1)	0.1900(4)	386(18)	13(1)	132(7)	-1(3)	46(9)	2(2)
C17	-0.4876(7)	0.0716(1)	0.3038(4)	478(20)	9(1)	173(8)	-3(3)	127(10)	-1(2)
C18	-0.3207(8)	0.0709(1)	0.4201(4)	568(22)	14(1)	126(7)	-2(3)	67(10)	10(2)
C19	-0.1444(8)	0.1025(1)	0.4250(4)	443(19)	14(1)	127(7)	1(3)	29(9)	9(2)

benzoic acid oxidation of **3** when Ar is phenyl, gives a mixture of **4a** and **4b** (11c). The geometry indicated for **4a** and **4b** was tentatively assigned on the basis of the proton chemical shift of the methyl group bonded to the pyrazolinone ring. This assumes that the anisotropy of the phenyl ring when *syn* to the methyl group shields the methyl substituent and thus the isomer with the lower chemical shift (δ 1.55) is assigned structure **4a**. To substantiate this as-



sumption, geometry was determined independently and unequivocally for **4a** (Ar = *p*-chlorophenyl) using the techniques of single crystal x-ray diffraction. The oxirane used in the crystal structure analysis was prepared by basic hydrogen peroxide oxidation of the corresponding arylidene-pyrazolinone **3** (Ar = *p*-chlorophenyl) (10b) and purified by recrystallization from hexane, mp 118-119° (11b).

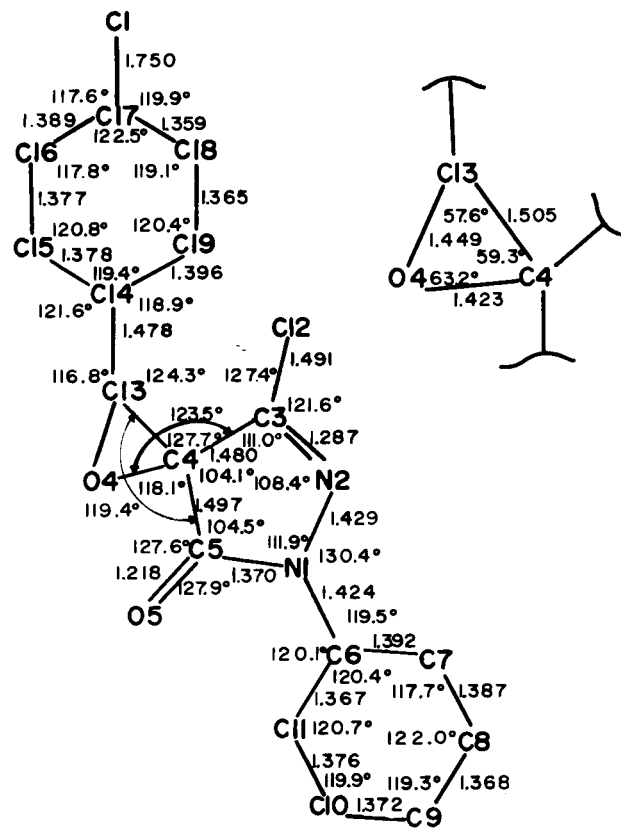


Figure 1

Table Ib
Hydrogen Fractional Coordinates

Atom	X	Y	Z	β
H7	0.4880(0)	0.3370(0)	0.2830(0)	5.0(0)
H8	0.5450(0)	0.4170(0)	0.2330(0)	6.5(0)
H9	0.2472(0)	0.4822(0)	0.2790(0)	7.6(0)
H10	-0.0596(0)	0.4551(0)	0.3811(0)	5.5(0)
H11	-0.1390(0)	0.3720(0)	0.4200(0)	4.6(0)
H12.1	-0.3060(0)	0.2410(0)	0.6130(0)	4.8(0)
H12.2	-0.3736(0)	0.1993(0)	0.4953(0)	5.2(0)
H12.3	-0.1602(0)	0.1874(0)	0.6170(0)	4.6(0)
H13	0.1562(0)	0.1630(0)	0.2216(0)	5.4(0)
H15	-0.3010(0)	0.1620(0)	0.1150(0)	4.5(0)
H16	-0.6340(0)	0.1055(0)	0.1107(0)	5.5(0)
H18	-0.3150(0)	0.0420(0)	0.5000(0)	5.1(0)
H19	0.0056(0)	0.0979(0)	0.5012(0)	6.2(0)

Table II
Closest Intermolecular Distances

Contact Atoms	Distance (Å)
H18 — C ℓ	2.84
H10 — C ℓ	2.89
H12.1 — O5	2.60
H12.2 — O4	2.55
— C5	3.09
H12.3 — N1	2.80
— C6	2.83
H11 — C15	2.94
H13 — C16	2.74
H16 — C11	2.79
— C10	2.93

Limits for C ℓ —H are 3.30 Å

Limits for X—H are 3.10 Å, x \neq C ℓ or H

Number on Hydrogen refers to non-hydrogen to which it is attached.
Thus, Number H12.1, H12.2, H12.3 refer to methyl hydrogens on C12.

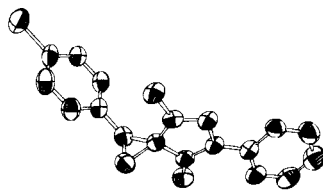
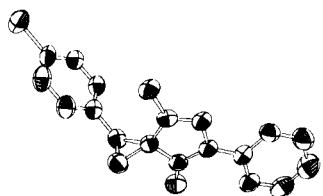


Figure 2

X-Ray Structural Investigation.

A single crystalline platelet of **4a** measuring 0.30 mm \times 0.10 mm \times 0.60 mm was chosen for analysis. All crystallographic measurements were performed on a modified General Electric XRD-490 fully automated single crystal diffractometer. This device employs the stationary counter-stationary crystal technique and utilizes balanced nickel and cobalt filters in conjunction with a copper target x-ray generator.

The title compound was found to crystallize in the monoclinic space group $P2_1/c$. Unit cell parameters were obtained through careful measurement of Bragg reflections having $2\theta > 65^\circ$ where the $\text{CuK}(\alpha_1 - \alpha_2)$ is resolvable, under fine conditions (*i.e.*, employing a 2° take off angle and 0.05° slit). A least squares fit of the measured 2θ values for 51 reflections which satisfied this requirement led to the lattice constants: $a = 5.989(1)\text{Å}$, $b = 27.625(4)\text{Å}$, $c = 9.374(2)\text{Å}$, $\beta = 99.06(1)^\circ$. The calculated density of 1.373 g/cc assuming four molecules per cell is in good agreement with the experimentally measured density of $1.39 \pm .02$ g/cc (using flotation methods). Since $P2_1/c$ is a centrosymmetric space group the unit cell of the crystal consists of an equal number of d, ℓ pairs of molecules. This would be in accord with the chemical expectations of a $d\ell$ mixture from the creation of a chiral carbon, C4, non-stereospecifically *via* the oxidation reaction.

A total of 2667 independent reflections were collected to a 2θ maximum of 140° (0.82Å). Of these 1921 (72%) were considered to be statistically significant for use in least squares refinement. The statistical criterion which is employed in the rejection of weak or unobserved data is expressed as:

$$[|N_i - 2\sigma(N_i)| - |I_{C_0} + 2\sigma(I_{C_0})|] > N$$

in which the sigmas are calculated solely on the basis of counting statistics and N is a constant for a given crystal and is established by the measurement of scattered intensities in the region of symmetry extinct reflections. Anomalous background and $\alpha_1 - \alpha_2$ splitting corrections were applied as functions of 2θ . Additionally the normal $1/LP$ corrections were applied and the resultant intensities were reduced to structure factor amplitudes in the usual manner.

The correct trial solution was obtained by symbolic addition using the program FAZC (12). Coordinates of all non-hydrogen atoms except the one later labelled C-9 were located in this manner. This atom was subsequently located by examination of the resultant electron density map following 5 cycles of isotropic least squares refinement. Inclusion of this atom and assignment of appropriate scattering factors for all atoms led to an initial reliability factor of 0.132 (13). This was followed by 5 cycles of anisotropic refinement producing an R value of 0.090.

Hydrogen atoms were next located by differences Fourier synthesis and appended to the coordinate list. Inclusion of these atoms and subsequent refinement, fixing positional and isotropic thermal vibrational (arbitrarily set = 4.0) parameters for all 12 hydrogen atoms resulted in a further reduction to 0.067. Five additional cycles of refinement, introducing a $1/\sigma^2$ weighting scheme for observed reflections, converged to an R of 0.059. At this stage restraints on the hydrogen coordinates and isotropic thermal parameters were removed for three cycles of refinement. This produced reasonable bonding and thermal parameters for all hydrogen atoms (with the exception of those bound to the chlorinated phenyl substituent), and converged to the final weighted reliability factor of 0.055. Those hydrogen atoms attached to the substituted phenyl were assigned their original coordinates derived by earlier difference Fourier synthesis and six subsequent cycles of least squares refinement were performed, again fixing the hydrogen positional and thermal parameters. Estimated shifts were then observed to be less than 0.05σ and examination of a difference Fourier electron density map yielded no peaks greater than $0.2 e/\text{\AA}^3$ and therefore the structure refinement was concluded. Observed interatomic bonding distances and angles are summarized in Figure 1 and a stereo ORTP view of the molecule is supplied in Figure 2. Estimated standard deviations calculated for the interatomic spatial parameters range from 0.0004 to 0.007 Å for bond distances and 0.2 to 0.4° for bonding angles. Each of the rings displays at least a moderate degree of planarity. The pyrazolinone ring (esd = 0.009 Å) intersects the plane defined by the oxirane ring with a dihedral angle of 91.1° and the chlorinated phenyl ring (Å, esd = 0.003 Å) at an angle of 93.0°. Final atomic coordinates and their respective thermal parameters are supplied in Table Ia (non-hydrogens) and Table Ib (hydrogens). Table II lists the closest intermolecular contacts. It is evident that the unusual shape of the cell results from the accommodation of a relatively long molecule with the packing distances determined by the minimal contact distances necessary to accommodate the chlorine and the hydrogens of the methyl carbon (C12).

Discussion.

The x-ray crystallographic structure determination reported here confirms the tentative assignment of structure **4a** to the pyrazolinone spirooxiranes obtained by basic hydrogen peroxide oxidation of arylidenepyrazolinones **3**. Thus the oxidation of the enone system in **3** proceeds as predicted (14,8b) with rotation of the phenyl group on the β -carbon away from the carbonyl group to minimize adverse steric interactions and to allow orbitals of the carbonyl group to overlap with those of the carbanionic center at carbon-4 during the closure of the oxirane

ring. The two stereoisomeric oxiranes formed in the slow reaction with *m*-chloroperbenzoic acid arise from a stereospecific oxidation of enones of differing configuration present in solution (10c,11c). The different stereochemical outcomes of the two oxidation reactions reflect different mechanisms for the formation of the oxirane ring, and not necessarily the relative stabilities of the two possible oxiranes.

Pyrazolinone spirooxiranes undergo photochemical opening of the oxirane ring to give carbonyl ylides (11a). The conversion of the three membered heterocycle, a 4n system, to the open chain dipolar form is an electrocyclic reaction and is expected from orbital symmetry considerations to occur in a disrotatory fashion in the excited state and in a conrotatory manner in the ground state (15,16). The stereochemistry of the formation of carbonyl ylides thermally and photochemically has been examined. Preliminary experiments with the *cis*- and *trans*-2,3-diphenyloxiranes indicate that the carbonyl ylides are formed photochemically in a disrotatory fashion (17). Orbital symmetry restrictions appear to be less stringent in the case of the reactions of oxiranes in the ground state (18).

The x-ray crystallographic data presented here provide accurate knowledge of the stereochemistry of pyrazolinone spirooxiranes **4**, information that is essential in the light of the observations made on other oxirane systems, to our study of the photochemical and thermal reactions of these compounds.

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(12) The programs used are part of the crystallographic package for the PDP-10 developed at UNO by J. N. Brown, L. R. Towns, R. J. Majeste and L. M. Trefonas (1966-1976). The package includes a series of direct methods programs, among them FAZC for centrosymmetric crystals and MULTANII for general cases.

(13) The conventional reliability index (R), or the weighted reliability index (r) are cited throughout the paper

$$R = \frac{\sum w \ ||kF_o| - |F_c||}{\sum w \ |kF_o|}$$

$$r = \left(\frac{\sum w \ ||kF_o| - |F_c||^2}{\sum w \ |kF_o|^2} \right)^{1/2}$$

where w is a weighting factor equal either to 1 or $1/\sigma^2$, and

$$\sigma = 0.5 F_o [(1 + I_{N_i}/I_{C_o})(1 - I_{N_i}/I_{C_o})]^{1/2}$$

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