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## Structural Studies of Radical Reaction Products.

### I. The Structure of an Asymmetrically Substituted Diazene: 3-(*p*-Chlorophenyl)-4-(*p*-chlorophenylazo)-4-methyl-2-pentanone, C<sub>18</sub>H<sub>18</sub>Cl<sub>2</sub>N<sub>2</sub>O

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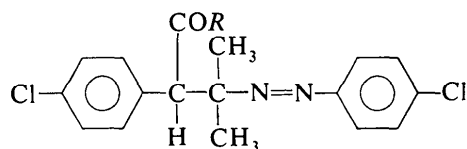
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**Abstract.**  $M_r = 349.26$ , triclinic, space group  $P\bar{1}$ ,  $Z = 2$ ,  $a = 15.863$  (7),  $b = 10.226$  (4),  $c = 5.765$  (4) Å,  $\alpha = 92.30$  (8),  $\beta = 88.37$  (8),  $\gamma = 108.70$  (9)° (least-squares-refined values),  $U = 885.0$  (9) Å<sup>3</sup>,  $D_m = 1.30$ ,  $D_x = 1.31$  g cm<sup>-3</sup>,  $\mu(\text{Mo } K\alpha) = 3.71$  cm<sup>-1</sup>,  $F(000) = 364$ . The final conventional  $R$  factor is 0.0415 for 2176 observed reflections [having  $I \geq 3\sigma(I)$ ]. The distance between the N atoms of the azo group [1.240 (3) Å] is equal to the expected bond length between doubly bonded  $sp^2$ -hybridized N atoms, and there is no evidence of  $\pi$  delocalization between the azo group and the phenyl rings. This structure proves unambiguously that aryl radical addition to a sterically hindered olefin is governed by steric factors.

**Introduction.** The homolytic arylation of olefins has not been extensively investigated even though significant synthetic results have been obtained using diazonium salts as the aryl radical source (Rondestvedt, 1960, 1976; Citterio & Vismara, 1980).

During a systematic study of this class of reactions (Citterio, Minisci, Albinati & Brückner, 1980; Citterio, Minisci & Vismara, 1982), we have carried out an X-ray structural determination of the compound obtained from decomposition of 4-chlorobenzene-diazonium chloride by Ti<sup>III</sup> ions in the presence of 4-methyl-3-penten-2-one (a sterically hindered olefin).

This product has the formula:



The formation of this compound is unexpected having been assumed, on the basis of previous work (Kellogg, 1967; Warren & Thaler, 1967; Huyser, 1970), that radicals (*e.g.* RS·, Br·, RCO·) add exclusively in the  $\beta$  position of olefins conjugated with electron-withdrawing groups. This structure is consistent with an aryl-group addition to the  $\alpha$  position to the CO group and the formation of a bond between the olefinic  $\beta$  carbon and the  $\beta$  nitrogen of the diazonium ion, and demonstrates that factors affecting the regioselectivity of the reaction are related rather to steric hindrance than to resonance stabilization (Citterio *et al.*, 1980). This is in agreement with recent results of gas-phase addition of carbon radicals to olefins (Tedder & Walton, 1980), but opposite to the results obtained in solution where resonance stabilization is considered the dominant factor.

**Experimental.** Pale-yellow crystals with a prismatic habit and stable to air obtained by slow evaporation of

a concentrated methanolic solution; crystal of approximate dimensions  $0.2 \times 0.3 \times 0.3$  mm chosen for the X-ray analysis; cell constants from counter data with a least-squares fitting of  $2\theta$  values of 25 high-angle reflections ( $2\theta \geq 25^\circ$ ); Philips PW1100 diffractometer (graphite-monochromated Mo  $K\alpha$  radiation,  $\lambda = 0.71060 \text{ \AA}$ ),  $2\theta \leq 50^\circ$ ,  $\omega/2\theta$  scan, scan speed of  $0.04^\circ \text{ s}^{-1}$ , scan width of  $1.20^\circ$ ; two background counts measured at each side of the peaks for 10 s and the values averaged; 3233 independent reflections of which 2176 were considered as observed on the criterion  $I \geq 3\sigma(I)$  (based on counting statistics) and subsequently used for the refinement; Lorentz and polarization corrections, no absorption or extinction correction; three standard reflections, evenly distributed in reciprocal space, measured every 100 min to check the stability of the crystal and the experimental conditions; no significant variations detected.

Structure solved using *MULTAN* (Main, Lessinger, Woolfson, Germain & Declercq, 1976);  $E$  map calculated from the set with the highest figure of merit revealed all but the H atoms; refinement by full-matrix least squares, anisotropic temperature factors for C, N, O and Cl atoms; H atoms in their idealized positions included in the last cycles of the refinement and their positions adjusted at the end of each cycle to maintain a C—H bond length of  $1.08 \text{ \AA}$ .

$\sum w(|F_o| - |F_c|)^2$  minimized, with  $w = k/[\sigma^2(F_o) + gF_o^2]$  where  $\sigma$  is based on counting statistics and  $k$  and  $g$  are optimized in the least-squares procedure ( $k = 0.0285$ ,  $g = 0.042534$ ); final conventional  $R$  is  $0.0415$  for the observed reflections, the weighted  $R_{2w}$  factor is  $0.0576$ ; difference-Fourier map at the end of the refinement showed no significant features; scattering factors from *International Tables for X-ray Crystallography* (1974) with the real part of the anomalous dispersion taken into account; calculations performed on a Univac 1100 computer (*SHELX* system, Sheldrick, 1976).

The final atomic coordinates and equivalent isotropic temperature factors are given in Table 1. Bond lengths and angles are shown in Table 2 and torsion angles in Table 3.\*

**Discussion.** A perspective view of the molecule is given in Fig. 1 ( $R = \text{CH}_3$ ). The azo group is in the *trans* configuration as usually found in similar molecules (Allmann, 1974).

The distance N(1)—N(2) [ $1.240(3) \text{ \AA}$ ] is equal to the value  $1.24 \text{ \AA}$  expected for a double bond between  $sp^2$ -hybridized N atoms (Allmann, 1974) and signifi-

cantly different from the value of  $1.287(8) \text{ \AA}$  found in *p*-carboxyphenylazoxycyanide (Viterbo, Gasco, Serafino & Mortarini, 1975) or the value of  $1.266(4) \text{ \AA}$  in *S*-methylthiozone (Preuss & Gieren, 1975). In the latter case an extensive  $\pi$  delocalization has been

Table 1. Final positional parameters (e.s.d.'s on the last significant figure in parentheses) and  $B_{eq}$  values ( $\text{\AA}^2$ ) (Willis & Pryor, 1975)

$$B_{eq} = \frac{8}{3} \pi^2 \sum_i U_{ij} a_i^* a_j^* a_i \cdot a_j$$

	$x$	$y$	$z$	$B_{eq}$
Cl(1)	0.5646 (1)	0.8358 (1)	0.8981 (2)	7.3
Cl(2)	0.9227 (1)	-0.2056 (1)	1.6994 (3)	9.2
C(1)	0.6067 (3)	0.7167 (3)	1.0194 (6)	4.5
C(2)	0.6772 (3)	0.6887 (4)	0.9146 (6)	5.0
C(3)	0.7094 (2)	0.5918 (4)	1.0093 (6)	4.8
C(4)	0.6686 (2)	0.5226 (3)	1.2049 (5)	3.6
C(5)	0.5992 (3)	0.5558 (4)	1.3102 (6)	5.5
C(6)	0.5675 (3)	0.6533 (4)	1.2176 (8)	7.0
C(7)	0.6908 (2)	0.2308 (3)	1.5025 (5)	3.5
C(8)	0.7844 (2)	0.2457 (3)	1.3979 (5)	3.4
C(9)	0.8208 (2)	0.1339 (3)	1.4747 (5)	3.4
C(10)	0.8680 (2)	0.1480 (3)	1.6818 (5)	4.3
C(11)	0.9000 (2)	0.0444 (4)	1.7491 (6)	5.3
C(12)	0.8844 (2)	-0.0733 (4)	1.6113 (7)	5.5
C(13)	0.8397 (3)	-0.0890 (4)	1.4071 (8)	5.7
C(14)	0.8085 (2)	0.0150 (3)	1.3393 (6)	4.7
C(15)	0.6218 (2)	0.0997 (4)	1.4056 (7)	4.5
C(16)	0.6852 (3)	0.2294 (4)	1.7692 (6)	4.7
C(17)	0.8532 (2)	0.3883 (4)	1.4404 (7)	4.1
C(18)	0.9175 (3)	0.4446 (5)	1.2449 (7)	5.2
N(1)	0.7039 (2)	0.4195 (3)	1.2820 (4)	3.6
N(2)	0.6574 (2)	0.3446 (3)	1.4326 (5)	4.1
O	0.8593 (2)	0.4488 (2)	1.6275 (5)	4.7

Table 2. Bond lengths ( $\text{\AA}$ ) and angles ( $^\circ$ ) (e.s.d.'s on the last significant figure in parentheses)

N(1)—N(2)	1.240 (3)	C(7)—C(15)	1.530 (4)
N(1)—C(4)	1.432 (5)	C(7)—C(16)	1.538 (5)
N(2)—C(7)	1.498 (5)	C(8)—C(9)	1.522 (5)
Cl(1)—C(1)	1.742 (4)	C(8)—C(17)	1.531 (4)
Cl(2)—C(12)	1.748 (4)	C(9)—C(10)	1.405 (4)
C(1)—C(2)	1.360 (6)	C(9)—C(14)	1.380 (4)
C(1)—C(6)	1.368 (5)	C(10)—C(11)	1.385 (6)
C(2)—C(3)	1.387 (6)	C(11)—C(12)	1.372 (5)
C(3)—C(4)	1.386 (5)	C(12)—C(13)	1.369 (6)
C(4)—C(5)	1.372 (5)	C(13)—C(14)	1.383 (6)
C(5)—C(6)	1.382 (7)	C(17)—C(18)	1.501 (5)
C(7)—C(8)	1.549 (5)	C(17)—O	1.212 (5)
N(1)—N(2)—C(7)	114.3 (3)	Cl(2)—C(12)—C(11)	119.1 (3)
N(2)—N(1)—C(4)	114.1 (3)	Cl(2)—C(12)—C(13)	119.5 (3)
N(1)—C(4)—C(3)	115.8 (3)	C(1)—C(2)—C(3)	119.1 (3)
N(1)—C(4)—C(5)	124.8 (3)	C(1)—C(2)—C(5)	118.9 (4)
N(2)—C(7)—C(8)	112.0 (2)	C(2)—C(3)—C(4)	120.1 (4)
N(2)—C(7)—C(16)	106.4 (3)	C(2)—C(3)—C(6)	121.8 (4)
N(2)—C(7)—C(15)	103.8 (3)	C(3)—C(4)—C(5)	119.3 (4)
Cl(1)—C(1)—C(2)	119.3 (3)	C(4)—C(5)—C(6)	120.7 (3)
Cl(1)—C(1)—C(6)	118.9 (3)	C(7)—C(8)—C(9)	112.7 (2)
C(7)—C(8)—C(17)	114.2 (3)	O—C(17)—C(18)	121.5 (3)
C(8)—C(7)—C(15)	110.6 (3)	C(9)—C(8)—C(17)	110.0 (3)
C(8)—C(7)—C(16)	114.7 (3)	C(9)—C(10)—C(11)	120.7 (3)
C(15)—C(7)—C(16)	108.6 (3)	C(9)—C(14)—C(13)	121.2 (3)
C(8)—C(9)—C(10)	121.7 (3)	C(10)—C(9)—C(14)	118.1 (3)
C(8)—C(9)—C(14)	120.2 (3)	C(10)—C(11)—C(12)	119.1 (3)
C(8)—C(17)—C(18)	116.6 (3)	C(11)—C(12)—C(13)	121.4 (4)
C(8)—C(17)—O	121.7 (3)	C(12)—C(13)—C(14)	119.4 (4)

\* List of structure factors, anisotropic thermal parameters, Table 3 and some relevant least-squares planes have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38062 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

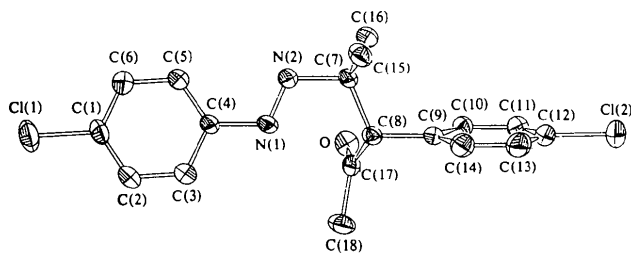


Fig. 1. An ORTEP (Johnson, 1965) drawing of the molecule. H atoms have been omitted for clarity.

postulated on the basis of spectroscopic and structural evidence. This N—N distance is, on the other hand, comparable with the values found in azobenzene (Brown, 1966), *trans-p,p'*-dichloroazobenzene [1.247 (3) and 1.252 (5) Å respectively] and other substituted azo compounds (Hope & Victor, 1969).

There is no evidence for any  $\pi$  delocalization between the azo group and the phenyl ring or the other atoms of the backbone. The distance N(1)—C(4), 1.432 (5) Å, is equal to the expected value of 1.43 Å (Allmann, 1974), for a single bond between  $sp^2$ -hybridized atoms. The N(2)—C(7) bond length is 1.498 (5) Å, comparable with the value of 1.479 (5) Å found in paraffinic bonds (*Molecular Structures and Dimensions*, 1972) and with 1.492 (3) Å found in azoisobutyronitrile or 1.496 (4) Å in 3,3'-azopentane-3,3'-dicarbonitrile (Jaffe, Malament, Slisz & McBride, 1972); on the other hand it is significantly longer than the accepted value of 1.391 (4) Å for a shortened C—N bond (partial double-bond character) (Preuss & Gieren, 1975).

The other C—C and C—O bond lengths in the molecule fall within the expected range; the average C—Cl bond length is  $1.745 \pm 0.003$  Å.\* It has already been pointed out that substitution of the benzene ring may affect its geometry in a way that reflects the inductive and resonance effect of the substituent (Domenicano, Vaciago & Coulson, 1975; Domenicano, Mazzeo & Vaciago, 1976; Domenicano & Murray-Rust, 1979); in particular the deformations from ideal  $D_{6h}$  geometry are more marked nearest to the substituents. Thus, though the average of the C—C bond lengths in the two phenyl rings [ $1.379 (5) \pm 0.012$  Å] and the average of the C—C—C bond angles [ $120.03 (4) \pm 1.14^\circ$ ] fall in the expected range, significant distortions from the idealized symmetry may be found. In particular the angles C(2)—C(1)—C(6) and C(11)—C(12)—C(13) [121.8 (4) and 121.4 (4)° respectively] are equal to the value of 121.4° predicted when a Cl substituent is present (Domenicano *et al.*, 1976). It may be noted that, also in this case, the changes in bond angles induced by substitution are

much more pronounced and significant than those in bond lengths (Domenicano *et al.*, 1975; Norrestam & Schepper, 1981) or in the planarity of the phenyl rings which, for the present structure, are hardly significant. The value of 120.0° expected for a —N=N— substituent is comparable with the 119.3 (4)° found here for the angle C(3)—C(4)—C(5).

It may be interesting to note the large deviations from the ideal values for the angles N(1)—C(4)—C(5) and N(1)—C(4)—C(3) [124.8 (3) and 115.8 (3)° respectively] which may be compared with the values of 125.9 and 114.2° found for the similar angles in *p,p'*-dichloroazobenzene (Hope & Victor, 1969) or 124.1 (4) and 115.5 (4)° in azobenzene (Brown, 1966). This type of distortion (in which the N—C—C angle defined by the C—C bond *cis* to the double bond is greater than the other) is a common feature of azo compounds and may be due to steric repulsion between atoms C(5) and N(2) [the C(5)···N(2) distance being 2.730 (6) Å].

The molecule is not planar, with the phenyl ring bound to the azo group making an angle of 11.4 (2)° with the plane containing C(4), N(1), N(2) and C(7) (the maximum distance of these atoms from the least-squares plane they define is 0.023 Å). The torsion angle N(1)—N(2)—C(7)—C(8) is 8.8 (8)° (see Table 3), while larger deviations from planarity are indicated by the dihedral angles C(7)—C(8)—C(17)—O and C(7)—C(8)—C(9)—C(10) [43.1 (9) and —86.6 (10)° respectively] and the angle of 68.7 (1)° between the two phenyl rings.

No short intermolecular contacts have been detected and the packing of the molecules in the crystal is due to van der Waals interactions.

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\*  $\pm$  refers to the root-mean-square deviation from the mean.

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## Studies of Monoclinic Hen Egg White Lysozyme.

### II. The Refinement at 2.5 Å Resolution – Conformational Variability between the Two Independent Molecules

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**Abstract.** Monoclinic hen egg white lysozyme crystals (*M1* form) [Hogle, Rao, Mallikarjunan, Beddell, McMullan & Sundaralingam (1981). *Acta Cryst.* **B37**, 591–597] containing two independent molecules in the asymmetric unit have been refined to an *R* value of 0.26 for 6045 reflections in the resolution range  $5.0 > d > 2.5$  Å. The electron density is strong and clearly defined for the entire backbone and side chains of both molecules, except for the residues 62–63 and 125. The  $\alpha$ -carbon atoms of the two independent molecules have an r.m.s. deviation of 0.70 Å. With the SEWFA (systematic elimination of the worst-fitting atoms) procedure, the conserved part of the structure is shown to consist of the helical residues as well as residues in the active site. A comparison of this structural variability with the average thermal parameters shows that all regions of large thermal factors occur in the variable part of the structure, except for residues 61–65; these apparently have internal motions.

**Introduction.** A question of paramount importance in protein structure analysis is the degree of variability a protein undergoes in a crystal field. Such information can be gleaned by studying the structure of a protein which crystallizes in different crystalline forms or, even

better, if multiple copies of the protein occur in the asymmetric unit of the crystal. The former would give some idea of the degree of deformation experienced by the protein molecule in different crystalline environments, but usually suffers from the difficulty that the data collection and the refinement procedures may not all be carried out under the same conditions and some of the observed variability may arise from such effects. If there are two or more independent molecules in the crystal, these problems are circumvented.

Hen egg white lysozyme (HEWL) is an ideal candidate for such studies since it crystallizes in many polymorphic forms (*e.g.* tetragonal, triclinic, monoclinic and orthorhombic) that diffract to high resolution (Steinrauf, 1959). Furthermore, the monoclinic form has the additional advantage that it contains two independent molecules. In part I, we reported the 4 Å MIR structure determination of this form (Hogle, Rao, Mallikarjunan, Beddell, McMullan & Sundaralingam, 1981) and a 6 Å study has also been recently reported by Artymiuk, Blake, Rice & Wilson (1982). We have now refined the structure at 2.5 Å resolution using the constrained least-squares procedure (Konnert, 1976; Hendrickson & Konnert, 1980*a,b*). The atomic thermal parameters were allowed to vary with tight constraints. In this paper, we discuss the variations in the positions and thermal factors of the residues in the two independent molecules.

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