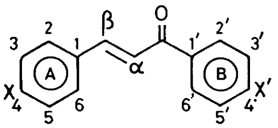
# Configurations and Conformations of the Oximes, *O*-Methyl Oximes, and *N*-Methylnitrones derived from Chalcones

By **Denis W. Clack, Nadir Khan, and David A. Wilson,*** University College, Cathays Park, Cardiff CF1 1XL

The *E*- and *Z*-oximes, *O*-methyl oximes, and *N*-methylnitrones of (*E*)-chalcone and its 4-MeO, 4-$NO_2$, 4'-MeO, and 4'-$NO_2$ derivatives have been synthesised and examined by u.v. and $^1H$ and $^{13}C$ n.m.r. spectroscopy. It is concluded that all these compounds exist in solution in the antiperiplanar (*s-trans*) conformation about the Cα–C=N bond, with the aryl ring B (on the C=N carbon) approximately orthogonal to the plane of the rest of the molecule. Electron densities and total energies have been calculated by CNDO/2 methods for the *E*- and *Z*-nitrones, and $^{13}C$ chemical shifts for the αβ-unsaturated nitrone system are discussed in the light of these electron densities and are compared with similar treatments for the parent chalcones. The effects of substituents at C-4 or -4' on the electronic structure of the nitrone group are discussed in terms of resonance contributors. Rates of thermal isomerisation of *E,Z*-nitrones to *E,E*-nitrones, and the position of the equilibrium between them, are reported. The $\lambda^d$ value for the *E*-styryl group was found to be *ca.* 1.1.

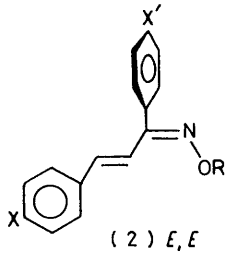
*E*-CHALCONES (benzalacetophenones, 1,3-diarylprop-2-en-1-ones) in solution have predominantly the synplanar conformation † with both aryl rings conjugated with the enone system [1] (1). (This numbering system is also used for all the compounds discussed in this paper.) Substituents X and X' each affect the position of the long-wavelength maximum in the u.v. spectra of chalcones [2] (examples in Table 1). In the $^1H$ n.m.r. spectra of chalcones, β-H ($\delta_H$ *ca.* 8.0) lies at lower field than α-H ($\delta_H$ *ca.* 7.4),[1,3] while in the $^{13}C$ n.m.r. spectra β-C ($\delta_H$ *ca.* 144) lies at lower field than α-C ($\delta_C$ *ca.* 120).[4-6] These assignments, although correct, were not formally proved by isotopic labelling: we describe this proof. Correlations have been reported between Hammett substituent constants (σ) for X and X' and the $^{13}C$ chemical shifts of α- and β-C, and between the $^{13}C$ chemical shifts and calculated total electron densities [6] and calculated π-electron densities [5] (except for α-C and X'-substituted chalcones, indicating that resonance effects are largely localised in ring B).



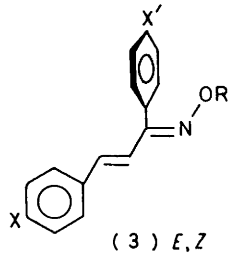
( 1 )

Conversion of a ketone into an oxime not only provides a derivative, but introduces a group with its own interesting chemistry and an additional element of geometrical isomerism. In the chalcone series, we demonstrate that substantial conformational changes are consequent upon this conversion.

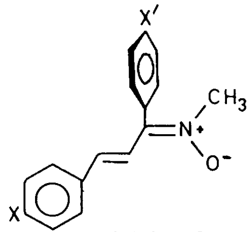
We have used a previously described method [7] of isomerising chalcone *E*-oximes to their *Z*-isomers to provide samples of both series of compounds (2; R = H) and (3; R = H). These oximes have been methylated and the mixtures of products separated to provide both series of *O*-methyl oximes (2; R = Me) and (3; R = Me) and of *N*-methylnitrones (4) and (5). The spectroscopic results for these compounds, supported by electron density and total energy calculations, indicate that they exist in solution in the antiperiplanar conformation about the α-C–C=N bond, and with aryl ring B out of conjugation and essentially orthogonal to the rest of the molecule, as shown. These conformations are those that examination of molecular models indicates as involving the least steric interactions.



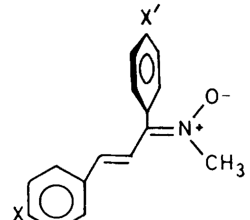
( 2 ) *E,E*



( 3 ) *E,Z*



( 4 ) *E,E*



( 5 ) *E,Z*

*E,E*-Oximes (2; R = H) were prepared by acid-catalysed oximation of the ketone. Sodium hydroxide in dimethyl sulphoxide isomerised [7] oximes (2; X = X' = H; X = MeO, X' = H; X = H, X' = MeO) to mixtures containing 70—90% of the *E,Z*-isomers, from which pure samples were obtained. Attempts to apply this method to oximes (2; X = $NO_2$, X' = H, and X = H, X' = $NO_2$) gave only polymeric material, and

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† The terms *s-cis* (or *cisoid*) and *s-trans* (or *transoid*) have the same ambiguitities that *cis* and *trans* themselves have. Therefore synplanar (*sp*) and antiperiplanar (*ap*) are used in conjunction with the normal sequence rules (*Pure Appl. Chem.*, 1976, **45**, 13; Rule E-5.6). However, these terms have their own imprecision in that ±30° from planarity is accommodated. To indicate true coplanarity of the groups we suggest *s-E* and *s-Z*, using the sequence rules and the original abbreviation for ' single bond ' (R. S. Mulliken, *Rev. Modern Phys.*, 1942, **14**, 265). Mixing English and German should cause no disquiet to those happy to accept mixing English and Latin or Latin and Greek.

the $E,Z$-oximes were obtained by careful chromatography or fractional crystallisation of products from acid-catalysed oximation, which usually contained up to 30% of the $E,Z$-isomers if the preparations were heated for at least 72 h.

Alkylation of oxime anions generally gives a mixture of *O*- and *N*-alkylation, with the former predominating.[8] However, we have found that alkylation of chalcone oximes with methyl iodide in benzene–aqueous sodium hydroxide using benzyltriphenylphosphonium bromide as phase-transfer catalyst[9] gave 60—80% *N*-methylation (nitrones) and only *ca.* 10% *O*-methylation. Using dimethyl sulphate instead of methyl iodide gave less *N*- and more *O*-methylation, and considerably more hydrolysis to chalcones. The methylation products were separated by column chromatography to provide compounds (2—5; X,X′ = H, MeO, $NO_2$) for spectroscopic examination.

*U.v. Spectra.*—From the results given in Table 1, it can be seen that whilst substituents X and X′ on chalcones (1) both lead to shifts to longer wavelength for the longest wavelength absorption band, only substituents on ring A of the oximes, *O*-methyl oximes, and nitrones lead to similar shifts. Substituents on ring B lead either to no significant shift or to a small shift to shorter wavelength. Absence of conjugation between ring B and the rest of the molecule is indicated for compounds (2)—(5).

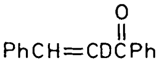
TABLE 1

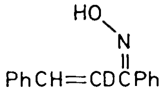
U.v. maxima (nm) (and molar extinction coefficients) in ethanol

| X, X′ | H,H | MeO,H | $NO_2$,H | H,MeO | H,$NO_2$ |
|---|---|---|---|---|---|
| Chalcones (1) | 309 | 236<br>342 | 316 | 229<br>322 | 268<br>321 |
| $E,E$-Oximes (2; R = H) | 290 (20 500) | 303 (21 500) | 236 (14 700)<br>335 (18 900) | 281 (21 500) | 291 (27 900) |
| $E,Z$-Oximes (3; R = H) | 288 (34 000) | 298 (20 000) | 240 (13 800) ‡<br>335 (18 400) | 283 (28 200) | 288 (32 000) |
| $E,E$-*O*-Ethers (2; R = Me) | 294 (19 400) | 316 (19 400) | 237 (18 000)<br>335 (25 300) | 282 (26 700) | 292 (28 500) |
| $E,Z$-*O*-Ethers (3; R = Me) | 292 (36 500) * | 300 (25 100) | 240 (22 000) ‡<br>337 (30 000) | 290 (27 700) | 293 (30 300) |
| $E,E$-Nitrones (4) | 238 (12 500)<br>266 (8 500)<br>333 (24 600) | 244 (12 500)<br>349 (31 300) | 295 (14 400)<br>359 (17 900) | 231 (16 700)<br>287 (11 300) †<br>327 (21 900) | 240 (17 300)<br>246 (17 200) †<br>334 (24 400) |
| $E,Z$-Nitrones (5) | 238 (8 900)<br>271 (8 700)<br>330 (27 000) | 243 (8 400)<br>280 (7 100) †<br>348 (23 900) | 302 (17 000)<br>357 (13 300) | 226 (12 100)<br>290 (14 600 †<br>329 (24 700) | 248 (12 400)<br>263 (11 900)<br>329 (31 500) |

* R = $CH_2SCH_3$. † Shoulder. ‡ Samples actually contained *ca.* 10% of the $E,E$-isomer.

$^1$H *N.M.R. Spectra.*—The α,β-protons of the chalcones form AB systems and the lower-field signals have been assigned to β-H. The chemical shifts of the α,β-protons of the oximes *etc.* (2), (3), and (5), but not nitrones (4), were at higher fields than in the chalcones, and at higher fields in the $E,Z$-isomers than in the $E,E$-isomers, and confirmation was required as to which proton gave which signal in each series. The α-deuteriated compounds (6)—(10) were prepared, allowing the assignments in Table 2 to be made unambiguously. The previous assignments for chalcone itself were confirmed and doubts expressed[10] concerning assignments in chalcone oximes are now dispelled, and some assignments are corrected.[11]


(6)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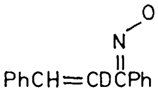
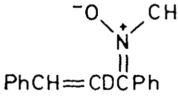
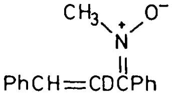

(8)


(9)


(10)

Thus, α-H appeared at lower field than β-H in compounds (2)—(5) in contrast to chalcones, and also appeared at lower field in the $E,E$-isomers than in the $E,Z$-isomers. These observations point to the antiperiplanar geometry for the α-C–C=N carbon–carbon bond. The oxygen atom or lone pair of electrons on nitrogen deshield α-H, whilst β-H is shielded by the out-of-plane aryl ring B. Ring B thus avoids steric interactions between its *ortho*-protons and β-H and the methyl or oxygen of the nitrone group (*cf.* u.v. data above, energy calculations below). Three other pieces of evidence showing this are to be found in Table 2. The methyl signals were at higher field in the $E,Z$-isomers of the *O*-methyl oximes (3; R = Me) than in the $E,E$-isomers (2; R = Me), whilst the methyl signals of the $E,Z$-nitrones (5) were more markedly at lower field than those of the $E,E$-nitrones (4). Both cases are a result of shielding by the out-of-plane aryl ring B. Also, β-H for oximes (2; R = H) and (3; R = H) were at higher field than β-H in the oximes of 4-phenylbut-3-en-2-one[12] which lack the aryl ring B. The $E,Z$-nitrones (5) do not show the *ortho*-protons of ring B significantly deshielded compared to the *meta*- and *para*-protons (other than by the effect of substituent X′), whereas in nitrones with a phenyl ring *cis* to the oxygen atom and essentially conjugated with the nitrone group, the *ortho*-protons are deshielded by *ca.* 0.7 p.p.m.[13]

$^{13}$C *N.M.R. Spectra.*—Heteronuclear spin-decoupling showed the lower-field proton of the α,β-system to be

TABLE 2

$^1$H N.m.r. spectra ($\delta_H$) for $CDCl_3$ solutions *

| X, X′ | | H,H | MeO,H | $NO_2$,H | H,MeO | H,$NO_2$ |
|---|---|---|---|---|---|---|
| Chalcones (1) | α-H | 7.33 | 7.40 | ∼7.65 | 7.47 | 7.43 |
| | β-H | 7.82 | 7.78 | ∼7.75 | 7.79 | 7.85 |
| | Aryl | 7.7—7.3 | 7.58, 6.90 | ∼8.25 | 7.8—7.3 | 7.7—7.3 |
| | Aryl′ | ∼8.0, 7.7—7.3 | ∼8.0 | ∼8.02 | 8.02, 6.92 | 8.34, 8.11 |
| *E,E*-Oximes (2; R = H) | α-H | 7.68 | 6.89 | 7.20 | 7.03 | 7.11 |
| | β-H | 6.7 | 6.34 | 6.53 | 6.51 | 6.28 |
| | Aryl | 7.5—7.3 | ∼7.3, ∼6.8 | 8.12, ∼7.5 | 7.5—7.2 | 7.5—7.2 |
| | Aryl′ | | 7.5—7.3 | 7.7—7.4 | 7.35, 6.99 | 8.31, 7.51 |
| *E,Z*-Oximes (3; R = H) | α-H | 7.07 | 6.89 | 7.20 | 7.03 | 7.11 |
| | β-H | 6.46 | 6.34 | 6.52 | 6.51 | 6.28 |
| | Aryl | 7.5—7.3 | ∼7.3, ∼6.8 | 8.12, ∼7.5 | 7.5—7.2 | 7.5—7.2 |
| | Aryl′ | | 7.5—7.3 | 7.7—7.4 | 7.35, 6.99 | 8.31, 7.51 |
| *E,E-O*-Ethers (2; R = Me) | α-H | 7.57 | 7.46 | 7.70 | 7.53 | 7.52 |
| | β-H | 6.71 | 6.66 | 6.77 | 6.63 | 6.69 |
| | $CH_3$ | 3.99 | 3.99 | 4.03 | 3.99 | 4.05 |
| | Aryl | 7.5—7.3 | 7.32, 6.78 | 8.19, 7.59 | 7.5—7.2 | 7.5—7.3 |
| | Aryl′ | | 7.5—7.3 | ∼7.5 | 7.43, 6.90 | 8.27, 7.70 |
| *E,Z-O*-Ethers (3; R = Me) | α-H | 7.04 | 6.90 | 7.17 † | 7.02 | 7.03 |
| | β-H | 6.40 | 6.35 | 6.46 | 6.48 | 6.33 |
| | $CH_3$ | 3.86 | 3.84 | 3.90 | 3.87 ‡ | 3.87 |
| | Aryl | 7.6—7.2 | 7.27, 6.78 | 8.26, ∼7.5 | 7.5—7.2 | 7.5—7.2 |
| | Aryl′ | | 7.5—7.2 | 7.8—7.4 | ∼7.4, ∼7.0 | 8.30, 7.45 |
| *E,E*-Nitrones (4) | α-H | 8.02 | 7.91 | 8.10 | 8.02 | 7.97 |
| | β-H | 6.39 | 6.32 | 6.42 | 6.40 | 6.27 |
| | $CH_3$ | 3.54 | 3.51 | 3.58 | 3.54 | 3.55 |
| | Aryl | 7.6—7.2 | 7.36, 6.77 | 8.05, 7.55 | 7.5—7.2 | 7.4—7.2 |
| | Aryl′ | | 7.6—7.2 | 7.6—7.2 | 7.19, 6.98 | 8.37, 7.51 |
| *E,Z*-Nitrones (5) | α-H | 7.20 | 7.06 | 7.37 | 7.16 | 7.20 |
| | β-H | 6.37 | 6.24 | 6.33 | 6.37 | 6.25 |
| | $CH_3$ | 4.06 | 4.00 | 4.09 | 4.00 | 4.04 |
| | Aryl | 7.5—7.3 | 7.32, 6.84 | 8.16, 7.50 | 7.4—7.2 | ∼7.3 |
| | Aryl′ | | 7.43 | 7.35 | 7.45, 6.96 | 8.32, 7.66 |

* Two precise figures for some aryl groups are the shifts for the AA′BB′ systems. † In a mixture with *E,E*-isomer. ‡ Or 3.81.

TABLE 3

$^{13}$C N.m.r. spectra ($\delta_C$) for $CDCl_3$ solutions

| X, X′ | | H,H | MeO,H | $NO_2$,H | H,MeO | H,$NO_2$ |
|---|---|---|---|---|---|---|
| *E,E*-Oximes (2; R = H) | C=N | 157.6 | 157.7 | 155.6 | 157.2 | 154.2 |
| | β-C | 139.8 | 139.2 | 134.7 | 139.4 | 137.4 |
| | α-C | 117.2 | 115.1 | 121.7 | 117.6 | 116.9 |
| | C-1 | 136.1 | 129.1 | 143.0 | 136.3 | 135.9 |
| | C-1′ | 134.6 | 135.0 | 135.1 | 129.1 | 142.2 |
| *E,Z*-Oximes (3; R = H) | C=N | 159.2 | 159.2 | 158.8 | 157.4 | 155.5 |
| | β-C | 137.0 | 136.6 | 134.3 | 134.7 | 134.5 |
| | α-C | 125.7 | 123.4 | 130.1? | 128.1 | 125.9 |
| | C-1 | 136.6 | ? | 142.5 | 136.5 | 135.9 |
| | C-1′ | 131.6 | ? | 130.9 | 124.3 | 139.5 |
| *E,E-O*-Ethers (2; R = Me) | C=N | 156.9 | 157.3 | 156.0 | 156.5 | 155.0 |
| | β-C | 139.1 | 138.9 | 136.2 | 138.9 | 139.4 |
| | α-C | 117.6 | 115.6 | 121.7 | 118.1 | 116.9 |
| | C-1 | 136.2 | 128.9 | 142.6 | 136.3 | 135.7 |
| | C-1′ | 134.9 | 135.1 | ? | 126.4? | 141.4 |
| | $CH_3$ | 62.2 | 62.1 | 62.5 | 62.1 | 62.7 |
| *E,Z-O*-Ethers (3; R = Me) | C=N | 158.1 | 158.5 | 157.5 | 157.8 | 156.3 |
| | β-C | 136.2 | 136.0 | 133.6 | 136.2 | 136.7 |
| | α-C | 126.0 | 123.8 | 130.5? | 126.3 | 127.5 |
| | C-1 | ? | ? | 142.7 | 136.4 | 135.8 |
| | C-1′ | ? | 132.4 | 134.3 | 124.1 | 138.9 |
| | $CH_3$ | 62.1 | 62.2 | 62.6 | 62.3 | 62.5 |
| *E,E*-Nitrones (4) | C=N | 148.4 | 148.5 | 147.4 | 148.2 | 148.5 |
| | β-C | 139.7 | 139.3 | 136.0 | 139.4 | 139.3 |
| | α-C | 121.6 | 119.6 | 125.6 | 122.0 | 121.1 |
| | C-1 | 136.1 | 129.2 | 142.8 | 136.4 | 135.9 |
| | C-1′ | 132.0 | 133.2 | 132.4 | 125.0 | 139.4 |
| | $CH_3$ | 49.8 | 49.6 | 50.4 | 49.7 | 50.3 |
| *E,Z*-Nitrones (5) | C=N | 146.3 | 146.9 | 146.2 | 144.5 | 147.6 |
| | β-C | 135.8 | 136.0 | 132.6 | 133.9 | 134.6 |
| | α-C | 120.5 | 118.3 | 124.4 | 121.6 | 120.3 |
| | C-1 | 136.2 | ∼129 | 142.5 | 136.3 | 136.0 |
| | C-1′ | 132.3 | 132.4 | 131.7? | 124.5 | 139.5 |
| | $CH_3$ | 49.2 | 48.9 | 49.7 | 49.6 | 49.8 |

bonded to the higher-field carbon, and *vice versa*, and examination of the deuteriated compounds (6)—(10) proved that β-C gave rise to the lower-field signal in chalcones,[4-6] oximes, and nitrones. Results are given in Table 3, where the only aryl carbons listed are C-1 and -1′, and these were not always clearly separated from the aryl carbon signals. The normal substituent shifts [14] for MeO and $NO_2$ allowed consistent assignments to be made.

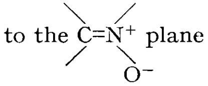
The chemical shifts for the C=N carbons fall in distinct ranges for oximes and their *O*-methyl derivatives ($\delta_C$ 154—159) and for nitrones ($\delta_C$ 144—149) as previously reported,[15] and were affected only to a small extent by substituents on the aryl rings. This was also found for the C=O carbons of chalcones,[4-6] where ring B is in conjugation with the carbonyl group, and is in line with calculated electron densities, discussed below.

With the oximes and *O*-methyl oximes, α-C was at lower field in the *E,Z*-isomers than in the *E,E*-isomers (by 8—10 p.p.m.), whereas β-C was at lower field in the *E,E*-isomers (by 2—4 p.p.m.). This trend was seen with the isomeric oximes of 4-phenylbut-3-en-2-one,[16] which we expect to have the same conformations as we describe for the chalcone derivatives. (Note that *E,E*-geometry for the chalcone oximes is *E,Z*-geometry for the butenone derivatives.) Also, β-C appeared consistently at lower field (3—5 p.p.m.) in the *E,E*-nitrones (4) than in the *E,Z*-nitrones (5) just like the oximes. There was a smaller difference (0.5—1.3 p.p.m.), in the same sense, for α-C of the nitrones, in contrast to the oximes.

Overall, the effect of substituents X and X′ on the shifts of α- and β-C was very like that found with the chalcones [4-6] but detailed comparison with the discussion of Doucet *et al.*[6] for chalcones would not be profitable because ring B of the nitrones *etc.* is no longer conjugated with the C=C–C=Z system, although the double bond of the chalcones is largely insulated by the carbonyl group from the electronic effects of ring B. The inversion of effects of substituents X on α- and β-C in chalcones, which Doucet *et al.*[6] suggest to be general for linear conjugated systems and to be in accord with theoretical models, was seen also in these oximes and nitrones. Thus, on substituting $NO_2$ for H at C-4, β-C moved upfield (*ca.* 3 p.p.m.) while β-C moved downfield (*ca.* 4 p.p.m.).

TABLE 4

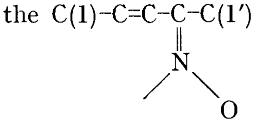
Total energies (a.u.) as a function of angle of ring B



to the $C{=}N^+$ plane $O^-$

| Angle (°) | 0 | 30 | 60 | 90 |
|---|---|---|---|---|
| *E,E*-Nitrone (4; X = X′ = H) | −149.290 | −149.470 | −149.521 | −149.522 |
| *E,Z*-Nitrone (5; X = X′ = H) | −149.334 | −149.506 | −149.524 | −149.522 |

*Calculated Electron Densities.*—With ring A coplanar with the α,β-unsaturated nitrone group, total energies were calculated by CNDO/2 methods for *s-E* conformations (*i.e.* the two double bonds coplanar rather than merely antiperiplanar, see footnote, p. 860) with ring B at several angles to this plane. The results, shown in Table 4, confirm that ring B much prefers an out-of-plane conformation. We therefore calculated π, σ, and total electron densities for each atom of the ten nitrones (4) and (5), taking ring B as orthogonal to the rest of the planar molecule. Total and π-electron densities ($q_T$ and $q_\pi$) for the atoms of the C(1)–C=C–C–C(1′) system



are given in Table 5.

C=N. There was not much variation in $^{13}C$ chemical

TABLE 5

Calculated electron densities for nitrones (4) and (5)

| X, X′ | | C=N | α-C | β-C | N | O | C-1 | C-1′ |
|---|---|---|---|---|---|---|---|---|
| *E,E*-Nitrones (4) * | | | | | | | | |
| H,H | $q_T$ | 3.974 | 3.980 | 3.982 | 4.711 | 6.490 | 3.951 | 3.971 |
| | $q_\pi$ | 1.058 | 1.004 | 1.001 | 1.183 | 1.780 | 0.993 | 1.004 |
| MeO,H | $q_T$ | 3.972 | 3.987 | 3.976 | 4.713 | 6.491 | 3.977 | 3.971 |
| | $q_\pi$ | 1.186 | 1.013 | 0.997 | 1.186 | 1.783 | 1.026 | 1.004 |
| $NO_2$,H | $q_T$ | 3.981 | 3.964 | 3.995 | 4.704 | 6.482 | 3.926 | 3.972 |
| | $q_\pi$ | 1.068 | 0.980 | 1.021 | 1.171 | 1.768 | 0.956 | 1.005 |
| H,MeO | $q_T$ | 3.971 | 3.982 | 3.982 | 4.712 | 6.490 | 3.951 | 3.998 |
| | $q_\pi$ | 1.056 | 1.003 | 1.002 | 1.183 | 1.780 | 0.993 | 1.000 |
| H,$NO_2$ | $q_T$ | 3.980 | 3.982 | 3.979 | 4.707 | 6.481 | 3.952 | 3.948 |
| | $q_\pi$ | 1.071 | 1.010 | 0.997 | 1.178 | 1.772 | 0.997 | 1.004 |
| *E,Z*-Nitrones (5) | | | | | | | | |
| H,H | $q_T$ | 3.997 | 4.004 | 3.972 | 4.710 | 6.490 | 3.954 | 3.942 |
| | $q_\pi$ | 1.059 | 1.021 | 0.991 | 1.182 | 1.775 | 0.995 | 1.002 |
| MeO,H | $q_T$ | 3.975 | 4.011 | 3.966 | 4.712 | 6.492 | 3.980 | 3.942 |
| | $q_\pi$ | 1.057 | 1.031 | 0.986 | 1.185 | 1.778 | 1.029 | 1.002 |
| $NO_2$,H | $q_T$ | 3.983 | 3.987 | 3.984 | 4.704 | 6.479 | 3.929 | 3.943 |
| | $q_\pi$ | 1.070 | 0.998 | 1.010 | 1.171 | 1.762 | 0.959 | 1.028 |
| H,MeO | $q_T$ | 3.973 | 4.005 | 3.972 | 4.712 | 6.491 | 3.954 | 3.969 |
| | $q_\pi$ | 1.058 | 1.021 | 0.991 | 1.182 | 1.775 | 0.995 | 0.997 |
| H,$NO_2$ | $q_T$ | 3.983 | 4.006 | 3.968 | 4.705 | 6.485 | 3.955 | 3.919 |
| | $q_\pi$ | 1.072 | 1.027 | 0.986 | 1.175 | 1.769 | 0.999 | 1.002 |

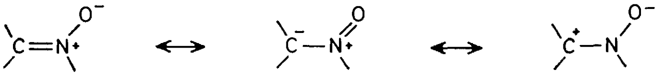
* Complete results available on request.

shifts with substituent, although *E,Z*-nitrones (5) gave signals at higher field than the corresponding *E,E*-nitrones (4), and this is just reflected in the values for $q_T$.

α-C. *E,Z*-Nitrones consistently gave this signal at higher field than the *E,E*-nitrones, and there is a corresponding greater value for $q_T$ and $q_\pi$ at α-C for the *E,Z*-nitrones. There is a good correlation between $q_\pi$ and $^{13}$C chemical shifts [slope 184 p.p.m./e, intercept ($q_\pi$ 1.000) 122.3 for *E,E* and 124.5 for *E,Z*], but a slightly better one with $q_T$ [slope 260 p.p.m./e, intercept ($q_T$ 4.000) 116.4 for *E,E* and 121.6 for *E,Z*]. Both sets of stereoisomers behave in the same way. The equivalent correlations for chalcones[6] gave 222 p.p.m./e with $q_T$ and 121 p.p.m./e with $q_\pi$. Levy *et al.*[17] reported 287 p.p.m./e for the *para*-carbon of monosubstituted benzenes, and Olah *et. al.*,[18] correlating neutral and cationic substituted benzenes, found 282 p.p.m./e for $\delta_C/q_T$ and 167 p.p.m./e for $\delta_C/q_\pi$ for the *para*-carbon.

β-C. The *E,Z*-nitrones consistently had this signal also at higher field than the *E,E*-nitrones, but here both $q_T$ and $q_\pi$ are consistently greater for the *E,E*-isomers. The $^{13}$C shifts correlate only moderately well with $q_T$ (*ca.* 200 p.p.m./e, intercept 134.8 for *E,E* and 129.5 for *E,Z*) and with $q_\pi$ (*ca.* 145 p.p.m./e, intercept 139.3 for *E,E* and 133.8 for *E,Z*). For β-C it would seem that some factor additional to π-system resonance and polarisation interactions with substituents[18] is operating. The correlations for α- and β-C give different lines ($\delta_C$ against $q_T$ or $q_\pi$) but of similar slopes, reinforcing Doucet's remark[6] that ' CNDO/2 methods correctly give the perturbations created by substituents, but less well the immediate magnetic environment of the carbons of the chain '.

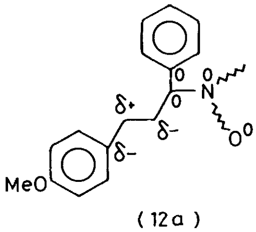
The nitrone group is usually discussed in terms of the resonance structures (11a—c)[19] and comparison between measured and calculated dipole moments[20] for *para*-substituted *C*-phenylnitrones has suggested that the nitrone group can accept electron density (from *p*-dimethylamino) and donate electron density (to *p*-nitro). Structures (12a—d) show the changes in $q_T$ for substituted nitrones relative to the unsubstituted compounds. (*E,E*- and *E,Z*-series behave in the same way; $\Delta q_T < 0.003$ is considered as zero.)



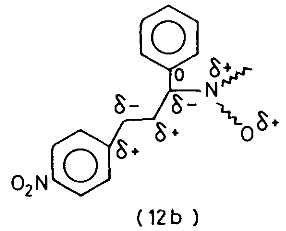
(11a) (11b) (11c)

The *p*-methoxy-group polarises the styryl system (12a), but is not a sufficiently strong electron donor to affect polarisation of the nitrone group. The *p*-nitro-group, a powerful electron acceptor, polarises the whole conjugated system (12b) increasing, in resonance terms, the importance of contributor (11b). Calculated π-bond orders for the N–O bond change from 0.415 for nitrone (4; X = X' = H) to 0.429 for nitrone (4; X = $NO_2$, X' = H), which are to be compared with a value[20] of 0.448 for (*Z*)-*C*-phenyl-*N*-methylnitrone. The *p*'-methoxyphenyl group has only a small inductive effect on the C=N carbon (12c), while the stronger inductive effect of the orthogonal *p*'-nitrophenyl group again increases (12d) the importance of resonance contributor (11b).

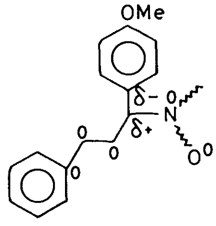
The *E,Z*-nitrones (5) were readily isomerised at 120° to equilibrium mixtures in which the *E,E*-nitrones (4) predominated. The rates of isomerisation, and equilibrium positions, were measured by $^1$H n.m.r. spectroscopy, and are given in Table 6. It had been hoped that some insight into charge character at the C=N carbon might be obtained from the effect of ring substituent on the rate of isomerisation, involving a rotation about the carbon–nitrogen bond and loss of conjugation and polar character[7] in the transition state. However, the rates were all very close, but so, we now know, are the electron densities at that carbon.



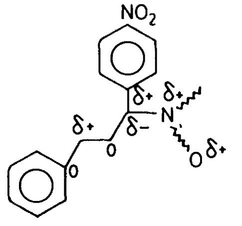
(12a)



(12b)



(12c)



(12d)

TABLE 6

Rate constants for first-order thermal isomerisation of *E,Z*-nitrones (5) to *E,E*-nitrones (4) at 120 °C in nitrobenzene, and equilibrium constants at 120°

| X, X' | H,H | MeO,H | $NO_2$,H | H,MeO | H,$NO_2$ |
|---|---|---|---|---|---|
| $10^4k/s^{-1}$ | 7.1 | 11 | 9.1 | 12 | 9.8 |
| $K$,[(4)/][(5)] | 10.8 | 11.9 | 11.5 | 11.0 | 3.7 |

With both the *E,E*- and *E,Z*-series of nitrones known to take up conformations with ring B out of the plane of the rest of the molecule, the major difference between the two series, and the reason for *E,E*-stereochemistry being preferred at equilibrium, is the steric interaction between α-H and the nitrone oxygen in the *E,E*-isomers and the larger nitrone methyl group in the *E,Z*-isomers. It is this difference in size between oxygen and methyl that may well explain the apparently broader energy minimum found in the *E,Z*-series when ring B was rotated about the C-1'–C=N bond (see Table 4).

The seemingly anomalous equilibrium constant for nitrones (X = H, X' = $NO_2$) requires comment. With the α-C–C=N bond antiperiplanar and ring B orthogonal to the rest of the molecule, the $\pi$-electron cloud of ring B (C-1′ particularly) of the *E,Z*-isomer is close to the oxygen of the nitrone group. Any attraction between ring B and this oxygen would be increased (or a repulsion lessened) by the *p*′-nitro-group, and hence influence the *E,E* : *E,Z* ratio in the way observed. An alternative consideration [21] is that the powerful electron-acceptor properties of the nitrophenyl group, and the ability of the nitrone group to donate electrons [contributor (11b)] result in ' $\pi$-electron pressure ' tending to move the nitrophenyl group a little away from orthogonality, and hence increase its effective size. This would also result in a smaller *E,E* : *E,Z* ratio, and the broader energy minimum referred to above makes this a likely explanation.

Finally, the valuable method of Knorr [22] for predicting *E* : *Z* ratios in olefins, nitrones, *etc.* does not include a $\lambda^d$ value for the *E*-styryl group. Using an equilibrium constant of 11 for these nitrones, and the figures in Knorr's tables, $\lambda^d$ *ca.* 1.1 is calculated for the *E*-styryl group.

## EXPERIMENTAL

$^1$H N.m.r. spectra were recorded at 90 MHz and $^{13}$C n.m.r. spectra at 25.2 MHz. Molecular orbital calculations were made using the CNDO self-consistent field approximate method.[23] Basis orbitals explicitly considered to contribute to the formation of the molecular orbitals were the valence orbitals $2s$, $2p_x$, $2p_y$, and $2p_z$ of the first-row elements C, N, and O, and the $1s$ orbital for hydrogen. This description therefore includes the effect of both $\sigma$- and $\pi$-electron delocalisation in determining the final charges.

Bond distances and angles for the styryl group were taken as identical to those reported for the corresponding chalcones.[24] The geometry used for the nitrone group was that previously reported.[25] All aromatic and olefinic C–H distances were taken as 1.07 Å, with the methyl C–H distance 1.10 Å. Geometries of the substituents $NO_2$ and OMe were taken from the literature.[26]

*General Synthetic Methods.*—Acid-catalysed oximation of the chalcones afforded, on crystallisation from ethanol, *E,E*-oximes (2; R = H), all known compounds. Base-catalysed isomerisation [7] (the addition of benzyltriphenylphosphonium bromide as phase-transfer catalyst gave more consistent results and rather shorter reaction times) gave *E,Z*-oximes (3; R = H) with m.p.s (from ethanol) (X = X′ = H) 118—119°, (X = MeO, X′ = H) 109—110°, (X = H, X′ = MeO) 134—135°. Fractional crystallisation of the products from prolonged (72 h) acid-catalysed oximation gave (5—10%), *E,Z*-oximes (3; R = H) with m.p.s (X = $NO_2$, X′ = H) 137—138°, (X = H, X′ = $NO_2$) 168—169°.

Typically, a mixture of oxime (2.5 g), benzyltriphenylphosphonium bromide (800 mg), and methyl iodide (6.5 g) in benzene (40 ml) was stirred vigorously with 50% aqueous sodium hydroxide (2.5 ml) for 16 h at room temperature. Normal work-up and chromatography on silica gel gave the *O*-methyl *E*-oximes (2; R = Me) with m.p.s (X = X′ = H) a gum, (X = MeO, X′ = H) a gum, (X = $NO_2$, X′ = H) 111—112°, (X = H, X′ = MeO) 63—64°, (X = H, X′ = $NO_2$) 76—77°; the *O*-methyl *Z*-oximes (3; R = Me) with m.p.s (X = X′ = H) a gum, (X = MeO, X′ = H) a gum, (X = H, X′ = MeO) 57—58°, (spectral information on the two nitro-compounds of this group was obtained from mixtures; m.p.s were therefore not obtained); *E,E*-nitrones (4) with m.p.s (X = X′ = H) 101—102°, (X = MeO, X′ = H) 85—86°, (X = $NO_2$, X′ = H) 164—165°, (X = H, X′ = MeO) 128—130°, (X = H, X′ = $NO_2$) 169—170°, and the *E,Z*-nitrones (5) with m.p.s (X = X′ = H) 146—148°, (X = MeO, X′ = H) 47—48°, (X = $NO_2$, X′ = H) 156—158°, (X = H, X′ = MeO) 163—164°, and (X = H, X′ = $NO_2$) 172—173°. Satisfactory analyses were obtained for all solid compounds.

*Deuteriated Compounds.*—Acetophenone (6.0 g) was dissolved in deuterium oxide (23 ml) and ethanol (95% OD) (13.5 ml) containing sodium hydroxide (2.6 g) and was left at 0° for 18 h. Benzaldehyde (5.3 g) was added to the solution and the mixture was stirred at room temperature for 11 h, and then left at 0° overnight. Filtration and crystallisation from ethanol gave [$\alpha$-$^2$H]chalcone [27] (8.8 g, 85%), m.p. 54—55°, containing 80% $^2$H at $\alpha$-C (by $^1$H n.m.r.). The $\alpha$-deuteriated *E,E*-oxime, *E,Z*-oxime (isomerisation without exchange of label), *E,E*-nitrone, and *E,Z*-nitrone were prepared by the general methods.

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## REFERENCES

[1] P. Baas and H. Cerfontain, *Tetrahedron*, 1977, **33**, 1509.
[2] Š. Toma, *Collect. Czech. Chem. Commun.*, 1969, **34**, 2771.
[3] J-P. Doucet, B. Ancian, and J-E. Dubois, *J. Chim. Phys.*, 1972, **69**, 188.
[4] J. Leška and P. Zahradník, *Collect. Czech. Chem. Commun.*, 1973, **38**, 3365.
[5] E. Sol'āniová, Š. Toma, and S. Gronowitz, *Org. Magn. Reson.*, 1976, **8**, 439.
[6] F. Membrey and J-P. Doucet, *J. Chim. Phys.*, 1976, **73**, 1024.
[7] N. S. Ooi and D. A. Wilson, *J. Chem. Res.*, 1980, (*S*), 394; (*M*) 4726.
[8] P. A. S. Smith and J. E. Robertson, *J. Am. Chem. Soc.*, 1962, **84**, 1197.
[9] W. P. Weber and G. W. Gokel, ' Phase Transfer Catalysis in Organic Synthesis,' Springer-Verlag, Berlin, 1977.
[10] H. Giezendanner, H. J. Rosenkranz, H-J. Hansen, and H. Schmid, *Helv. Chim. Acta*, 1973, **56**, 2588.
[11] A. T. Balaban, I. Zugrăvesu, S. Avramovici, and W. Silhan, *Monatsh. Chem.*, 1970, **101**, 704.
[12] B. Unterhalt, *Arch. Pharm.* (*Weinheim, Ger.*), 1966, **299**, 274.
[13] D. A. Kerr and D. A. Wilson, *J. Chem. Soc. C*, 1970, 1718; K. Koyano and H. Suzuki, *Bull. Chem. Soc. Jpn.*, 1969, **44**, 3306.
[14] R. J. Abraham and P. Loftus, ' Proton and Carbon-13 N.M.R. Spectroscopy,' Heyden, London, 1978, p. 28.
[15] N. S. Ooi and D. A. Wilson, *J. Chem. Res.*, 1980, (*S*) 366.
[16] B. Unterhalt and H. Koehler, *Arch. Pharm.* (*Weinheim, Ger.*), 1978, **311**, 366.
[17] G. L. Nelson, G. C. Levy, and J. D. Cargioli, *J. Am. Chem. Soc.*, 1972, **94**, 3089.
[18] G. A. Olah, P. W. Westerman, and D. A. Forsyth, *J. Am. Chem. Soc.*, 1975, **97**, 3419.
[19] H. Stamm, ' Methodicum Chemicum,' ed. F. Zymalkowski, Academic Press, New York, 1975, vol. 6, p. 334; G. R. Delpierre and M. Lamchen, *Quart. Rev.*, 1965, **19**, 329.
[20] V. I. Minikin, E. A. Medyantseva, I. M. Andreeva, and G. V. Gorshkova, *J. Org. Chem. USSR*, 1973, **9**, 148.
[21] R. Knorr, personal communication.
[22] R. Knorr, *Ber.*, 1980, **113**, 2441.
[23] J. A. Pople and D. L. Beveridge, 'Approximate Molecular Orbital Theory,' McGraw-Hill, New York, 1970.
[24] D. Rabinovich, *J. Chem. Soc. B*, 1970, 11; K. Ohkura, S. Kashino, and M. Haisa, *Bull. Chem. Soc. Jpn.*, 1973, **46**, 627.
[25] K. G. Jensen and B. Jerslev, *Acta Crystallogr.*, 1969, **25B**, 916.
[26] ' Tables of Interatomic Distances,' The Chemical Society, London, 1958.
[27] J. Ronayne, D. H. Williams, and J. H. Bowie, *J. Am. Chem. Soc.*, 1966, **88**, 4980.