1,3-Cycloadditions of 3,5-Dichloro-2,4,6-trimethylbenzonitrile Oxide to 1,1-Diphenylallene. A Reinvestigation

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The title reactions have been reported to give two monoadducts (from attack at the αβ and the βγ double bonds of diphenylallene) and a diadduct. A reinvestigation of the structure of the products by methods including an *X*-ray diffraction study, proves that isomeric formulae are required for the αβ monoadduct and therefore for the diadduct derived from it.

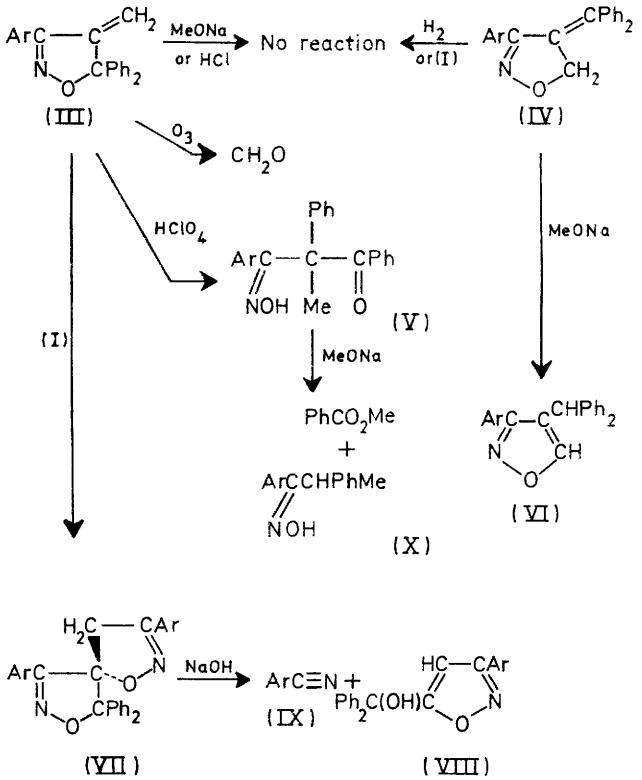
1,3-CYCLOADDITIONS of 3,5-dichloro-2,4,6-trimethylbenzonitrile oxide (I) to 1,1-diphenylallene (II) have been described [1] as giving rise to two monoadducts and a diadduct, identified as 3-aryl-5-methylene-4,4-diphenyl-2-isoxazoline, 3-aryl-4-diphenylmethylene-2-isoxazoline, and 3,3′-diaryl-4,4-diphenyl-5,5′-spirobi-2-isoxazoline (aryl = 3,5-dichloro-2,4,6-trimethylphenyl), on the basis of spectroscopic properties and chemical behaviour.

After this report, an *X*-ray diffraction analysis of the monoadducts was undertaken with the aim of studying the geometry of the crowded molecules. This analysis,[2] while confirming the structure proposed for the product of addition to the βγ double bond of (II), has shown that cycloaddition to the αβ double bond actually gives 3-aryl-4-methylene-5,5-diphenyl-2-isoxazoline (III). This has prompted a reinvestigation of some aspects of the chemical behaviour of (III), and of the structure of the diadduct derived from it.

RESULTS

Chemical reactions in the system under investigation are summarized in Scheme 1. This differs from the analogous scheme previously reported [1] in that it includes new structures for compounds (III), (V), and (VII). Furthermore, the reactivity of (V) is better specified.

The new structures are in agreement with published [1] u.v., n.m.r., and mass spectral data. In particular the absorption maximum at 268 nm (ε 8700) of adduct (III) coincides with that (ε 8600) for 5-ethoxycarbonyl-4-ethylidene-5-methyl-3-phenyl-2-isoxazolines.[3]



SCHEME 1

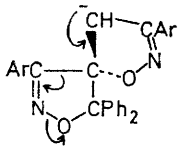
The u.v. spectrum of the oxime (V) [$\lambda_{max.}$ 240sh (ε 19,400)] can be compared with those of acetophenone oxime

[1] P. Beltrame, P. L. Beltrame, A. Filippi, and G. Zecchi, *J.C.S. Perkin II*, 1972, 1914.
[2] M. Cannas, G. Carta, and R. Destro, in preparation.
[3] P. Battioni, L. Vo-Quang, J.-C. Raymond, and Y. Vo-Quang, *Compt. rend.*, 1970, **C271**, 1468.

[$\lambda_{max.}$ (EtOH) 244·5 nm (ε 10,840)] [4] and of 1,2,3-triphenylpropane-1,3-dione [$\lambda_{max.}$ (EtOH) 247 nm (ε 26,100)].[5]

In the n.m.r. spectrum of the oxime, the methyl signal at τ 7·90 would seem to be more consistent with the previous formula,[1] containing a MeCO group,[6] than with present formula (V), containing the grouping $-N{=}C(Me)-C(Ph)-C{=}O$. Therefore model compounds have been prepared, containing the analogous chains $O{=}C(Me)-C(Ph)-C{=}O$ and $N{\equiv}C-C(Me)(Ph)-C{\equiv}N$, in order to compare the n.m.r. spectra. It has been found that the methyl group gives a signal at τ 8·13 for diethyl methyl(phenyl)malonate, and at τ 7·90 for methyl(phenyl)-malononitrile.

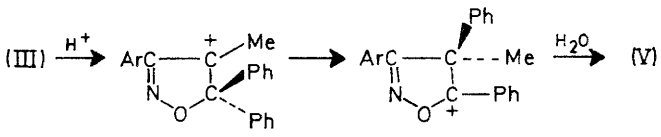
The mass spectra of compounds (III), (V), and (VII) all have a base peak at *m/e* 105, which can be attributed to the $PhCO^+$ ion, and is easily justified by the new formulations, all of which contain Ph–C–O groupings. As to the reaction giving rise to diadduct (VII), the proposed orientation (Scheme 1) is supported by the n.m.r. spectrum, which is compatible with a 4-methylene but not a 5-methylene group in a 2-isoxazoline ring.[1] Moreover, the alkaline cleavage of (VII) [1] is easily accounted for by its new formula; the carbanion (A) can be suggested as intermediate.



(A)

Chemical evidence in favour of formula (V) for the product of acidic cleavage of adduct (III) is given by the reaction with MeONa (Scheme 1). Oxime (X) has been identified by elemental analysis, and i.r., n.m.r., and mass spectra. In particular, (X) shows a band at 1665 cm^{-1} (C=N) similar to that shown by compound (V) at 1668 cm^{-1}, while the band of (V) at 1682 cm^{-1} (C=O) has disappeared. The base peak in the mass spectrum (*m/e* 105) can be attributed to the $PhCHMe^+$ ion. Methyl benzoate has also been recognised in the products by g.l.c.

The alkaline cleavage of (V) corresponds to typical



SCHEME 2

behaviour of β-diketones and of non-enolizable monoketones under similar conditions.[7] The previously reported positive iodoform test for compound (V),[1] has not been reproduced, and can be attributed to impurities (the test had been carried on a very small sample).

The reaction from (III) to (V) can be rationalized as occurring *via* protonation, phenyl shift, and ring cleavage (Scheme 2).

DISCUSSION

The correct formulation of monoadducts (III) and (IV), in both of which the central allenic carbon is at C-4, corresponds to an orientation opposite to that reported for the cycloadditions of benzonitrile oxide to allene and to phenylallene.[8]

In principle the monoadditions (which are highly regioselective, since no more than a very few percent of the missing regioisomers could have escaped detection) could proceed through a common diradical or zwitterionic intermediate, giving rise to (III) and (IV) by its two possible modes of ring closure. However, since there is no positive evidence in favour of a two-step mechanism, and the large negative value of the activation entropy and the small solvent effect [1] are in agreement with the most common concerted mechanism, our previous conclusions favouring the latter are unaltered.

We have sought justification for the observed orientation through a perturbational molecular orbital treatment. The most simplified frontier orbital approach to orientation problems predicts that of two regioisomeric adducts, that one is favoured which is obtained by the predominant frontier orbital interaction, in the direction that combines the atoms having the greatest coefficients in the relevant molecular orbitals.[9] This method correctly accounts, for instance, for the regioselectivity of the 1,3-cycloaddition of benzonitrile oxide with cyclopentadiene and with indene.[10] In our case orbital energies and coefficients for the separate molecules (I) and (II) were calculated by the CNDO/2 method.[11] Attention has been limited to the αβ cycloaddition, since strong steric interactions, which perturbation theory does not take into account, intervene in the case of βγ cycloaddition, as can be verified by molecular models. For the four π frontier orbitals, the following values of orbital energies (in hartrees) and coefficients (for atoms involved in the αβ cycloaddition) were obtained: (I) highest occupied molecular orbital (HOMO), −0·4159 ($c_C = -0{\cdot}37$; $c_O = 0{\cdot}63$); lowest unoccupied molecular orbital (LUMO), 0·0569 ($c_C = 0{\cdot}20$; $c_O = 0{\cdot}17$); (II) HOMO, −0·4042 ($c_{C_\alpha} = 0{\cdot}43$; $c_{C_\beta} = 0{\cdot}47$); LUMO, 0·1044 ($c_{C_\alpha} = -0{\cdot}31$; $c_{C_\beta} = 0{\cdot}46$). Considering the coefficient values, it is easily seen that, according to this qualitative treatment, the LUMO (I)–HOMO (II) interaction leads to regioisomer (III) ($C-C_\beta$ and $O-C_\alpha$ bonds), while the HOMO (I)–LUMO (II) interaction favours the

[4] L. Láng, 'Absorption Spectra in the Ultraviolet and Visible Region,' Vol. II, Akadémiai Kiadó, Budapest, 1964, p. 111.

[5] R. E. Lutz and C.-K. Dien, *J. Org. Chem.*, 1956, **21**, 551.

[6] H. A. Szymansky and R. E. Yelin, ' NMR Band Handbook,' I.F.I.-Plenum, New York, 1968, p. **53**.

[7] D. J. Cram and G. S. Hammond, ' Organic Chemistry,' 2nd edn., McGraw-Hill, New York, 1964, p. 472; J. March, 'Advanced Organic Chemistry: Reactions, Mechanisms and Structure,' McGraw-Hill, New York, 1968, p. 481.

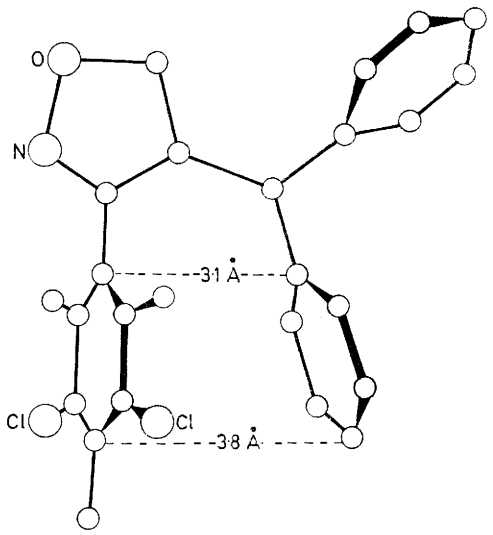
[8] G. Stagno d'Alcontres and G. Lo Vecchio, *Gazzetta*, 1960, **90**, 1239.

[9] O. Eisenstein, J.-M. Lefour, and N. T. Anh, *Chem. Comm.*, 1971, 969; K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *J. Amer. Chem. Soc.*, 1973, **95**, 7301, and previous papers.

[10] G. Bailo, P. Caramella, G. Cellerino, A. Gamba Invernizzi, and P. Grünanger, *Gazzetta*, 1973, **103**, 47.

[11] (*a*) J. A. Pople and G. A. Segal, *J. Chem. Phys.*, 1966, **44**, 3289; (*b*) D. P. Santry and G. A. Segal, *ibid.*, 1967, **47**, 158.

opposite regioisomer (C–C_α and O–C_β bonds). On the basis of the energy gaps between interacting orbitals, the interaction of LUMO (I) with HOMO (II) is slightly stronger than the other one, and isomer (III) is correctly predicted to be favoured, although high regioselectivity, as experimentally observed, would not be expected. Results of the quantitative perturbation treatment will be given elsewhere.



Schematic representation of 3-aryl-4-diphenylmethylene-2-isoxazoline from an *X*-ray diffraction study [2]

Little can be added to previous comments [1] about the βγ cycloaddition leading to (IV). The crystal structure of the product [2] shows that the three close aryl rings of the molecule can accommodate themselves at reasonable distances (Figure). In particular, the dichlorotrimethylphenyl ring at C-3 and one of the phenyl rings of the Ph_2C group at C-4 are roughly in front of each other, presenting a dihedral angle of only 13°, and a distance in the range 3·1—3·8 Å. This arrangement is similar to that found for pairs of phenyl rings almost parallel to each other in a very stable form of hexa-*o*-phenylene (m.p. 346—347 °C).[12] The stability of adduct (IV) is therefore not surprising and it can be assumed that it extends to the transition state leading to its formation.

EXPERIMENTAL

Equipment and general methods have been described.[1]

3-(3,5-*Dichloro*-2,4,6-*trimethylphenyl*)-4-*methylene*-5,5-*diphenyl*-2-*isoxazoline* (III).—This compound has been described as that labelled (III) in a previous paper.[1]

3,3′-*Bis*-(3,5-*dichloro*-2,4,6-*trimethylphenyl*)-5,5-*diphenyl*-4,5′-*spirobi*-2-*isoxazoline* (VII).—This compound has been described under numbering (VII) in the aforementioned paper.[1]

Treatment of (III) *with Perchloric Acid in Aqueous Acetic Acid.*—The procedure described under the same heading in the previous paper [1] gave 1-(3,5-dichloro-2,4,6-trimethylphenyl)-2-methyl-2,3-diphenylpropane-1,3-dione 1-oxime (V). This compound is the one labelled (V) in the previous paper,[1] τ_{OH} (CCl_4) 2·13br (s). A sample of (V) (30 mg) gave a negative iodoform test.[13]

Reaction of (V) *with Sodium Methoxide in Methanol.*—Oxime (V) (50 mg) was refluxed with sodium methoxide (0·25 mmol) in methanol (30 ml) during 3 h. Ether was added, and the mixture was washed with 5% aqueous HCl and dried (Na_2SO_4). The solvent was removed and di-isopropyl ether added to separate 1-(3,5-*dichloro*-2,4,6-*trimethylphenyl*)-2-*phenylpropan*-1-*one oxime* (X) (20 mg), as crystals, m.p. 222 °C (Found: C, 64·4; H, 5·4; N, 3·9. $C_{18}H_{19}Cl_2NO$ requires C, 64·3; H, 5·7; N, 4·2%); $\nu_{max.}$ (KBr) 3247 (OH), and 1665 (C=N) cm^{-1}; τ ($CDCl_3$) 2·60 (5H, m, aromatics), 3·40br (1H, s, exchangeable with D_2O, OH), 6·22 (1H, q, CH), 7·56 and 7·94 (3H and 6H, 2s, *Me*Ar), and 8·37 (3H, d, Me); *m/e* 77 (14%), 79 (12), 91 (11), 105 (100), 106 (36), 203 (47), 205 (29), 229 (13), 335 (22; *M*), 337 (14; *M* + 2), and 339 (2·5; *M* + 4).

The residue from the mother liquor was analysed by g.l.c. (Perkin-Elmer 800 apparatus, SE-30 3% column, temperature 110 °C) giving a peak coincident with that of an authentic sample of methyl benzoate.

Diethyl Methyl(phenyl)malonate.—This was prepared according to the literature,[14] τ ($CDCl_3$) 2·68 (5H, s, aromatics), 5·78 (4H, q, CH_2), 8·13 (3H, s, CH_3C), and 8·77 (6H, t, CH_3–CH_2).

Methyl(phenyl)malononitrile.—This was prepared according to the literature,[15] τ ($CDCl_3$) 2·50 (5H, s, aromatics) and 7·90 (3H, s, Me).

We thank the Consiglio Nazionale delle Ricerche (Rome) for financial aid.

[4/156 *Received*, 28*th January*, 1974]

[12] H. Irngartinger, *Acta Cryst.*, 1973, **29B**, 894.
[13] A. I. Vogel, 'Practical Organic Chemistry,' 3rd edn., Longmans, London, 1956, p. 1068.
[14] W. Wislicenus and K. Goldstein, *Ber.*, 1895, **28**, 815.
[15] J. C. Hessler, *Amer. Chem. J.*, 1908, **39**, 73; Beilstein's Handbuch, 1926, **IX**, 872.