The Formation of Nitriles from the Reaction between Benzaldoxime (Benzaldehyde Oxime) and Thiocarbonyl Compounds by Free Radical Mechanisms

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The reaction of benzaldoxime with thiobenzoyl and *NN*-dimethylthiocarbamoyl chlorides gives nitrile in 55—60% yield from both *E*- and *Z*-isomers. The thiobenzoyl group fragments to a mixture of biphenyl, dibenzoyl disulphide, and carbonyl sulphide, indicating a radical process. This is confirmed by studies of the decomposition of the adducts of benzaldoxime and aromatic isothiocyanates to nitrile, disubstituted urea, and carbonyl sulphide. Strong polarisations of the carbon nuclei of nitrile detected in the ^{13}C n.m.r. spectra show that elimination proceeds in a radical cage. Polarisations in the hydrogen nuclei of side products are explained by a simultaneous rearrangement of the initial adduct through a radical pair, and escape of the iminyl radical to give imine by hydrogen atom abstraction.

INVESTIGATIONS of the elimination of nitrile from acylated oximes under mildly basic conditions were crucial to the assignment of configuration to aldoximes.[1] This method is based on two important generalisations, the configurational stability of oxime derivatives and preferential *anti*-elimination.

However, Clive [2] has shown that *p*-chlorophenyl thiochloroformate reacts rapidly with aldoximes in the presence of pyridine to give nitrile in 40—60% yield. Both *Z*- and *E*-forms react under the same conditions, the yield from the former being significantly less than from the latter [*e.g.* 42.4% from (*Z*)-*p*-chlorobenzaldoxime and 60.8% from the *E*-isomer]. To explain these results rapid $E \longrightarrow Z$ isomerisation was assumed, and a symmetry allowed cyclic mechanism involving the thiocarbonate intermediate, similar to an ene reaction was postulated.

Thiocarbamoyl chlorides react in a similar manner,[3] and since ketoximes give a stable intermediate (II) analogous to (I), the formation of such an intermediate is highly probable. These intermediates (from ketoximes) rearrange [4] in solution at room temperature, probably by a free radical mechanism and it is reasonable to suppose that a similar rearrangement of (I) competes with the rearrangement process, thus reducing the yield of nitrile.

We find that the sodium salts of the *E*- and *Z*-forms of benzaldoxime react in dimethylformamide (DMF) to give 57 and 53% of nitrile, respectively, after treatment of the reaction mixture with water and extraction with ether. In addition the *Z*-form gave 9% of benzaldehyde.

Similarly, benzaldoxime reacts with thiobenzoyl chloride to give an intermediate which rapidly decomposes to give a mixture of benzonitrile, carbonyl sulphide, dibenzoyl disulphide, and biphenyl.

The isolation of biphenyl in *ca.* 20% yield suggests that free radicals are produced at some stage in the reaction, and subsequent work with the corresponding thiocarbamates show this to be the case.

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[1] P. A. S. Smith, 'Open-chain Nitrogen Compounds,' Benjamin, New York, 1966, vol. 2, p. 32.

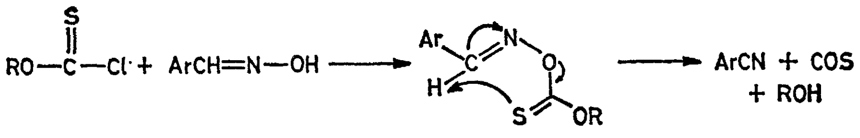
[2] D. L. J. Clive, *Chem. Comm.*, 1970, 1014.

[3] B. Cross, R. J. G. Searle, and R. E. Woodall, *J. Chem. Soc.* (*C*), 1971, 1833.

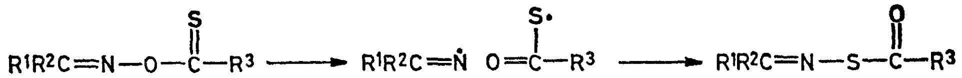
[4] R. F. Hudson, A. J. Lawson, and K. A. F. Record, *J.C.S. Perkin II*, 1974, 869.

All attempts to isolate the initial addition intermediates in these reactions were unsuccessful owing to their rapid decomposition. For this reason, an alternative method of preparation involving the addition of oximes to isothiocyanates was explored.

Nitriles are obtained, in comparable yields to the thiocarbamoyl chloride–oxime reaction, by the action of oximes on aromatic isothiocyanates,[5] together with a variety of side products, depending on the reaction conditions. At low temperatures the corresponding thiourea and carbonyl sulphide are produced. At higher temperatures, the corresponding urea is obtained and elemental sulphur eliminated. In alcoholic potassium hydroxide the urea, thiourea, and *O*-phenylimino *N*-phenylcarbamate were the main products.[5] These are obviously complex reactions, and we have investigated the reaction between benzaldoxime and *p*-tolyl isothiocyanate in some detail. Using the sodium salt of the oxime in DMF at —10°, we are able to isolate the *N*-*p*-tolyl thiocarbamate (III) and establish its structure by elemental analysis and ^{1}H n.m.r. spectroscopy.



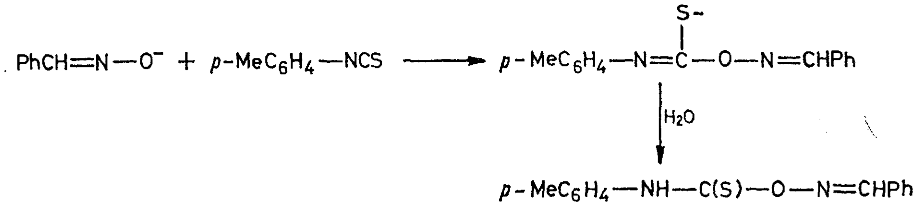
(I)



$$R^1R^2C{=}N{-}O{-}\overset{\overset{S}{\|}}{C}{-}R^3 \longrightarrow R^1R^2C{=}\dot{N}\quad O{=}\overset{\overset{S\bullet}{|}}{C}{-}R^3 \longrightarrow R^1R^2C{=}N{-}S{-}\overset{\overset{O}{\|}}{C}{-}R^3$$

(II)

$$(E)\text{-}PhCH{=}N{-}OH + PhNCS \xrightarrow{25°} PhCN + COS + (PhNH)_2C{=}S$$



$$PhCH{=}N{-}O^- + p\text{-}MeC_6H_4{-}NCS \longrightarrow p\text{-}MeC_6H_4{-}N{=}\overset{\overset{S^-}{|}}{C}{-}O{-}N{=}CHPh \xrightarrow{H_2O} p\text{-}MeC_6H_4{-}NH{-}C(S){-}O{-}N{=}CHPh$$

(III)

Low temperature n.m.r. analysis showed that *Z*- and *E*-forms of the oxime gave the same form of (III), probably due to isomerisation of the intermediate sodium salts.

The adduct (III) decomposed in solution at room temperature to give a mixture of products including di-*p*-tolylurea, carbonyl sulphide, and sulphur in addition to benzonitrile. The reaction was carried out in the cavity of an e.s.r. spectrometer but no signals were observed in the course of the reaction. Photolysis of (III) at —30° in toluene, however, gave a strong signal due to the phenyliminyl radical (g 2.002 8, a_N 1.13, a_H 7.8 mT).

Evidence for a free radical pathway was obtained by carrying out the decomposition of these adducts in the probe of an n.m.r. spectrometer, and observing the time dependent ^{1}H and ^{13}C spectra.

Strong emission was observed at δ 118 p.p.m. and enhanced absorption at δ 112 p.p.m. in the ^{13}C spectrum, the former due to the polarisation of the iminyl carbon atom, the latter to the polarisation of the C-1 atom of the phenyl ring of benzonitrile. As the nitrile is formed in primary process from the iminyl radical, Kaptein's rules[6] may be applied to these polarisations. The coupling constant a_C of the iminyl carbon atom is negative, that of the C-1 atom positive according to INDO calculations. The g value of 2.002 8 is considerably less than that of the dimethylaminothiocarbamoyl radical,[7] g *ca.* 2.05, and a similar value is assumed for the unknown PhNHCO$\dot{S}$ radical.

From the Kaptein equation (1) where μ is negative for a singlet process, ε is found to be positive for both polarisations, since $\Delta g = g(\text{iminyl}) - g(\text{thiocarbamoyl})$

$$\Gamma_{ne} = \mu\varepsilon\Delta g a_i \qquad (1)$$

is negative. The net effect, Γ_{ne}, is positive for absorption and negative for emission.

It follows from the positive value of ε that nitrile is formed within a radical cage, presumably by disproportionation to produce the unstable thiocarbamic acid, which rapidly decomposes to give amine and carbonyl sulphide.

Polarisations are observed in the ^{1}H n.m.r. spectra carried out under CIDNP conditions, in particular emission at δ 8.2 and 8.12 and enhanced absorption at

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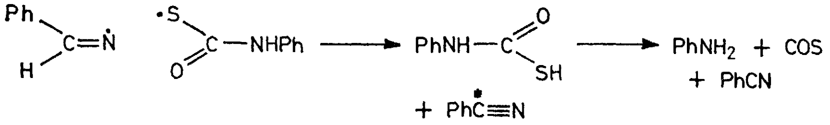
[5] A. Obregia and C. V. Gheorghiu, *J. prakt. Chem.*, 1930, **128**, 239.

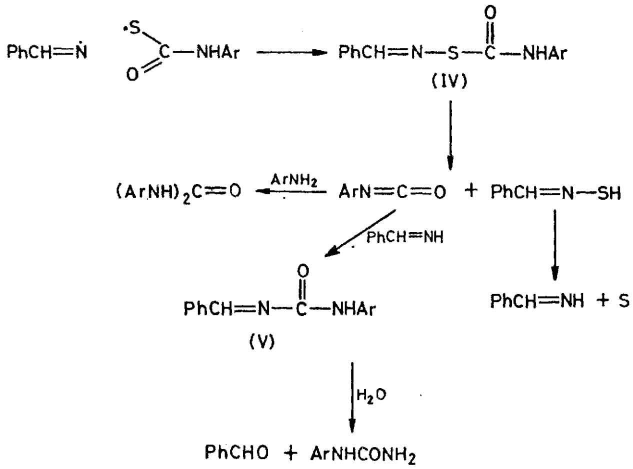
[6] R. Kaptein, *J. Amer. Chem. Soc.*, 1972, **94**, 6251.

[7] C. Brown, R. F. Hudson, and A. J. Lawson, *J. Amer. Chem.* 1973, **95**, 6500.

δ 8.45. The emission occurs at the characteristic absorption of imine, and the two peaks may be identified with the *Z*- and *E*-isomers. The coupling constant of the α-hydrogen atom of the iminyl radical is found to be positive from INDO calculations, and with the *g* values given above for iminyl and thiocarbamoyl radicals, Kaptein's equation leads to a negative value of ε, showing that the polarisation is due to iminyl radicals which have escaped from the cage.

The origin of the enhanced absorption is not known with certainty, but by analogy with the similar reaction of ketoximes,[8] a simultaneous rearrangement of the adduct (III) may give the isomer (IV), which under the conditions of the reaction undergoes elimination to give thio-oxime and isocyanate. The former is unstable[9] and decomposes to give imine and sulphur. Isocyanate then reacts rapidly with amine formed by decomposition of thiocarbamic acid. This series of processes is summarised in Scheme 1.





Scheme 1

In agreement with these proposals, a strong peak at 2 025 cm^{-1} in the i.r. spectrum of the reaction mixture due to carbonyl sulphide is observed. A carbonyl peak at 1 670 cm^{-1}, which decays in the course of the reaction, is characteristic of the rearranged product, (IV).[8] The analogous product from benzophenone oxime has been isolated in the pure state,[8] but most of these compounds decompose rapidly.

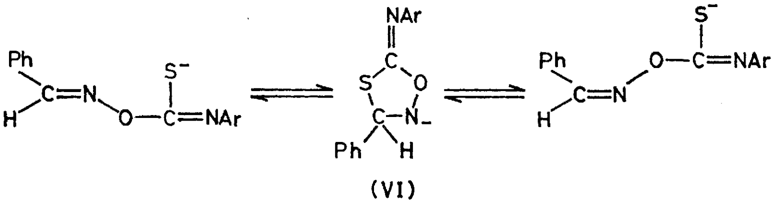
The imino hydrogen atom of (IV) may be responsible for the enhanced absorption at δ 8.5, and application of Kaptein's equation to the recombination of the geminate pair of radicals to give (IV), gives a positive value for ε in agreement with an in-cage process.

Part of the isocyanate reacts with imine in an exothermic reaction[10] to give *N*-benzylidene-*N'*-phenylurea (V; Ar = Ph). Compounds of this kind hydrolyse rapidly (even in air) to give aldehydes (or ketones) and the corresponding urea. This may account for the benzaldehyde (*ca.* 9%) formed in the reaction of *Z*-benzaldoxime with *NN*-dimethylthiocarbamoyl chloride.

Similar yields of nitrile (57 and 54%) are obtained in the reactions of *NN*-dimethylthiocarbamoyl chloride with *Z*- and *E*-oximes. There is no reason to suppose that thiocarbamoylated oximes readily isomerise at low temperatures as acylated oximes (prepared in a similar manner) are configurationally stable[11] at high temperatures.

The formation of nitrile in similar yields from *Z*- and *E*-oximes therefore supports a radical cage mechanism for the elimination.

Attempts to prove this by preparing the adducts of isothiocyanates with *Z*- and *E*-oximes were unsuccessful. These adducts can be made only through the intermediate formation of the ionised form (VI). In view of the high-nucleophilic reactivity of thiolate ions, an isomerisation by a torsional process involving the iminyl bond is highly probable (Scheme 2).



Scheme 2

The reaction between aldoximes (*Z* and *E*) with thiocarbonyl compounds to give nitrile probably proceeds mainly through a radical cage intermediate and hence the elimination is not stereospecific. This is a member of a group of reactions of oximes involving low-temperature homolysis of the N–O bond, including the

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[8] H. Dj-Forudian, R. F. Hudson, and K. A. F. Record, *J.C.S. Chem. Comm.*, 1976, 503.

[9] D. H. R. Barton, P. D. Magnus, and S. I. Pennanen, *J.C.S. Chem. Comm.*, 1974, 1007; C. Brown, B. T. Grayson, and R. F. Hudson, *ibid.*, p. 1007.

[10] G. E. P. Smith and F. W. Bergstrom, *J. Amer. Chem. Soc.*, 1934, **56**, 2095.

[11] H-O. Kalinowski and H. Kessler, *Topics Stereochem.*, 1973, **7**, 295.

reactions with sulphinyl chlorides [12] and tervalent phosphorus compounds.[13]

EXPERIMENTAL

Preparation of O-*Benzylideneamino Thiobenzoate.*—Thiobenzoyl chloride (3.7 g), prepared by the reaction of thionyl chloride on dithiobenzoic acid, was dissolved in diethyl ether (50 ml) at −10°, and sodium benzaldoximate (3.4 g) added. The suspension was allowed to stand for 1 h, sodium chloride was filtered off, and the filtrate evaporated to dryness at −10° under high vacuum to give a yellow solid. This was washed with cold light petroleum (b.p. 40—60°) to give the *product* (1.7 g, 30%), m.p. 50—53° (decomp.) (Found: C, 69.55; H, 4.45; N, 5.95%. $C_{14}H_{11}NOS$ requires C, 69.7; H, 4.55; N, 5.8%).

Decomposition of O-*Benzylideneamino Thiobenzoate.*—The thiobenzoate (4 g) was boiled in chloroform (50 ml) for 15 min. The solvent was removed to give an oily solid (4 g). Chromatography of this solid (1 g) on silica gel, eluting with 60% light petroleum (b.p. 40—60°)–40% diethyl ether gave biphenyl (0.2 g), m.p. 68—70° (lit.,[14] 69—70°), dibenzoyl disulphide (0.2 g), m.p. 132° (lit.,[15] 134—135°), and benzonitrile (0.3 g), $\nu_{max.}$ 2 210 cm^{-1}.

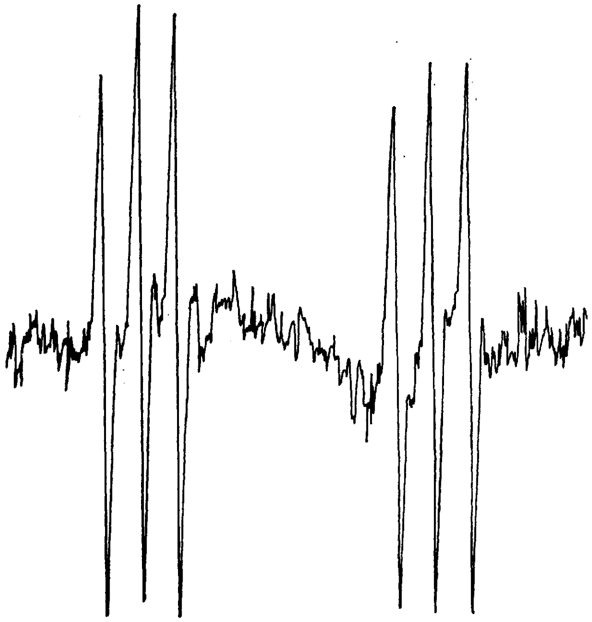
Reaction of Benzaldoxime with NN-*Dimethylthiocarbamoyl Chloride.*—(*E*)-Sodium benzaldoxime (1.4 g) was added in portions to a cold stirred solution of *NN*-dimethylthiocarbamoyl chloride (1.5 g) in DMF (20 ml). The solution was stirred for 1 h, poured into water (200 ml), and then extracted with ether to give an unstable oil. A similar oil was obtained from the reaction of (*Z*)-sodium benzaldoximate (0.85 g) with *NN*-dimethylthiocarbamoyl chloride (1.0 g). These products were analysed for benzonitrile and benzaldehyde by g.l.c. using a polypropylene glycol column at 145°. The product composition was determined by using benzyl methyl ketone as a standard. A series of mixtures of known weights of nitrile and standard were analysed, and the weight of nitrile related empirically to the ratio of their peak heights. Benzaldehyde was observed in the extract from the reaction of the *Z*-oxime, and this was estimated by a similar procedure. The following results were obtained: 57% nitrile from *E*-oxime; 54% nitrile and 9% benzaldehyde from the *Z*-oxime.

Preparation of O-*Benzylideneamino* p-*Tolylthiocarbamate* (III).—Sodium benzaldoximate (16.2 g) was added slowly to a stirred solution of *p*-tolyl isothiocyanate (16.9 g) in dry dimethylformamide (100 ml) at −10°. After stirring the mixture for 1 h at this temperature, it was poured into ice-cold 10% hydrochloric acid (600 ml). The precipitated solid was separated by filtration, and dried over silica gel. The solid was dissolved in ice-cold toluene, light petroleum (b.p. 40—60°) was added, and the solution cooled to −30°. The *product* (III) crystallised as fine needles (22.3 g, 75%), m.p. 196° (decomp.) (Found: C, 66.6; H, 5.35; N, 10.25. $C_{15}H_{14}N_2OS$ requires C, 66.6; H, 5.2; N, 10.35%), δ (60 MHz; $CDCl_3$) 9.0 (1 H, s), 7.5—8.0 (9 H, m), and 2.4 (3 H, s).

Decomposition of Compound (III).—A solution of (III) (5 g) in chloroform (50 ml) was boiled for 2 min, and allowed to cool. Di-*p*-tolylurea (1.4 g) crystallised from solution, m.p. 271° (lit.,[16] 266—268°), δ 9.05 (2 H, s), 7.3—7.8 (8 H, A_2B_2), and 2.3 (6 H, s).

The filtrate was evaporated to dryness to give a yellow oil. This was washed with ether and re-crystallised from ethanol to give di-*p*-tolylthiourea (0.5 g), m.p. 180° (lit.,[17] 182°), δ 10.2 (2 H, s), 7.4—7.9 (8 H, A_2B_2), and 2.4 (6 H, s). The ether washings were evaporated to give benzonitrile (1.8 g), b.p. 191°.

Reaction of Phenyl Isothiocyanate with (Z)- *and* (E)-*Benzaldoxime.*—Phenyl isothiocyanate (5.6 g) was added dropwise to (*E*)-sodium benzaldoximate (5.6 g) in DMF (50 ml) at 0°. The solution was stirred for 20 min, and then poured into cold dilute hydrochloric acid (20 ml concentrated HCl in 250 ml water). An oil which separated out soon solidified, and this was washed several times with water and with ethanol, and dried, m.p. 73—74° (decomp.), δ (100 MHz; −20°) δ 9.8 (NH), 8.5 (CH), and 7.2—7.7 (ArH), $\nu_{max.}(CHCl_3)$ 2 250 (PhNCO), 2 050 (COS), and 1 670 cm^{-1} (C=O).



E.s.r. spectrum of the phenyliminyl radical

The above reaction was carried out with the *Z*-form of benzaldoxime. The low temperature ^1H n.m.r. and the i.r. spectra of the product were identical to those observed for the *E*-isomer, indicating that isomerisation had occurred in the preparation of *O*-benzylideneamino phenylthiocarbamate, or that this compound rapidly isomerises.

CIDNP Experiments.—(a) A 10% (w/v) solution of the product of reaction between benzaldoxime and phenyl isocyanate in deuteriochloroform was placed in the pre-heated probe (50°) of a JEOL 100 MHz spectrometer. The spectrum was recorded immediately to show enhanced absorption at δ 8.45 and a decrease in the signal at δ 8.5. In addition emission signals at δ 8.2 and 8.12 were observed. At the end of the reaction peaks at δ 8.5 and 8.45 and a complex multiplet at δ 7.1—7.4 was observed.

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[12] R. F. Hudson and K. A. F. Record, *J.C.S. Chem. Comm.*, 1976, 831.

[13] C. Brown, A. Maron, R. F. Hudson, and K. A. F. Record, *J.C.S. Chem. Comm.*, 1976, 663.

[14] W. H. Zartman and H. Adkins, *J. Amer. Chem. Soc.*, 1932, **54**, 3398.

[15] H. E. Westlake and G. Dougherty, *J. Amer. Chem. Soc.*, 1945, **67**, 1861.

[16] T. N. Ghosh, *J. Indian Chem. Soc.*, 1945, **22**, 27.

[17] P. A. Aravindakshan, A. Bhramarambra, G. V. Nair, and C. N. V. Nambury, *Indian J. Chem.*, 1963, **1**, 395.

A similar spectrum was observed when *O*-benzylideneamino *p*-tolylthiocarbamate was decomposed in the n.m.r. spectrometer probe at the same temperature. Strong absorption was observed at δ 8.85 and emission δ 8.55.

(b) A 10% (w/v) solution of *O*-benzylideneamino phenylcarbamate in chloroform was placed in the probe of a JEOL PS 100 spectrometer preheated to 45°. The ^{13}C n.m.r. spectrum was recorded after 40 s to show enhanced absorption at δ 112 p.p.m., corresponding to the C-1 atom of the phenyl group, and emission at δ 118 p.p.m. corresponding to the imino carbon atom.

A similar spectrum was observed, with emission also at δ 136 p.p.m. in the decomposition of *O*-benzylideneamino *p*-tolylthiocarbamate under similar CIDNP conditions.

E.s.r. Measurements.—A degassed toluene solution of *O*-benzylideneamino *p*-tolylthiocarbamate was irradiated in the probe of a JEOL PE 1X spectrometer. The phenyliminyl radical was observed (Figure) with g 2.0028, a_N 1.1, and a_H 7.8 mT.

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