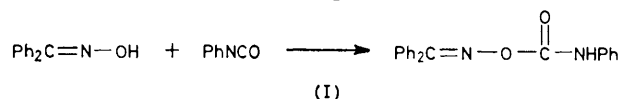# The Reaction of Ketoximes with Isothiocyanates

By **Robert F. Hudson** * and **Hushang Dj-Forudian,**† University Chemical Laboratory, Canterbury, Kent CT2 7NH

Addition intermediates of benzophenone, acetophenone, and fluorenone oximes with phenyl isothiocyanate have been isolated. These are unstable and rapidly dissociate to the starting materials and simultaneously rearrange to the carbamoylated thio-oxime. This product has been isolated from the reaction of benzophenone oxime and phenyl isothiocyanate, but in general is found to be too unstable for isolation in a pure state. In solution the reaction leads to a mixture of O-phenylcarbamoylbenzophenone oxime and 1-diphenylmethylene-3-phenylurea.

ISOCYANATES are very useful intermediates in organic chemistry, mainly because of the ready addition of amines and hydroxylic compounds across the C=N double bond. These reactions are usually exothermic and are regarded as typical acid–base catalysed processes.[1] The addition of oximes to isocyanates proceeds rapidly in nonpolar solvents; thus, for example benzophenone oxime and phenyl isocyanate give O-phenylcarbamoylbenzophenone oxime (I) (formerly called O-diphenylmethyleneamino N-phenylcarbamate). With 0.1M-solutions, we find the reaction to be complete within 1—2 min at room temperature.

$$Ph_2C{=}N{-}OH \ + \ PhNCO \longrightarrow Ph_2C{=}N{-}O{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}NHPh$$

(I)

The corresponding addition to phenyl isothiocyanate is unknown, and small equilibrium constants are usually found for the reaction of other hydroxy-compounds. Oximes do, however, react with aromatic isothiocyanates either at elevated temperatures or at room temperature in the presence of base to give a complex mixture of products,[2] including ureas, thioureas, and in particular
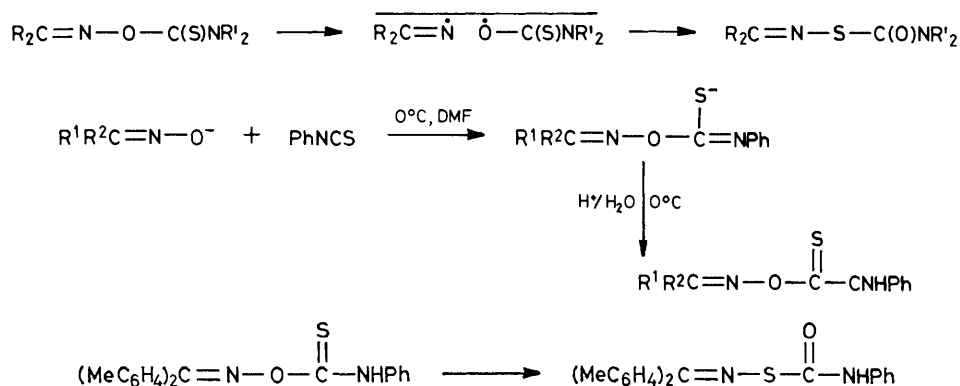
cyanate, react in a different manner. The reaction with aliphatic ketone oximes is exothermic giving the ketone, substituted urea, and sulphur.[3]

The substituted urea is probably formed by hydrolysis of the corresponding cyanamide since cyclohexanone and menthone oximes give the corresponding ketone, cyanamide, and sulphur. Camphor oxime, however, gave diphenylthiourea and carbonyl sulphide.

A remarkable mechanism has been proposed to explain the formation of ketone and cyanamide involving the oxaziridine form of the oxime.[4]

It is clear that in all these reactions one of the main problems is the way in which elemental sulphur is extruded. Most explanations of these reactions [2,3] assume the formation of an adduct analogous to (I), although no compound of this kind has so far been reported. We believe that a key reaction in all the above mentioned reactions is the rearrangement of the initial adduct to its isomer (S-methyleneamino thiocarbamate).

Rearrangements of this kind have recently been shown to occur at low temperatures, through radical cage intermediates.[5]

$$R_2C{=}N{-}O{-}C(S)NR'_2 \longrightarrow R_2C{=}\overset{\displaystyle \cdot}{N} \ \ \overset{\displaystyle \cdot}{O}{-}C(S)NR'_2 \longrightarrow R_2C{=}N{-}S{-}C(O)NR'_2$$

$$R^1R^2C{=}N{-}O^- \ + \ PhNCS \ \xrightarrow{0^{\circ}C, DMF} \ R^1R^2C{=}N{-}O{-}\overset{\displaystyle S^-}{\overset{\displaystyle |}{C}}{=}NPh$$

$$\Big\downarrow H^7H_2O \ \Big|0^{\circ}C$$

$$R^1R^2C{=}N{-}O{-}\overset{\displaystyle S}{\overset{\|}{C}}{-}CNHPh$$

$$(MeC_6H_4)_2C{=}N{-}O{-}\overset{\displaystyle S}{\overset{\|}{C}}{-}NHPh \longrightarrow (MeC_6H_4)_2C{=}N{-}S{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}NHPh$$

carbamates [cf. (I)], i.e. the product formed from the corresponding isocyanate. The nature of the reaction is unknown but the formation of the carbamate was originally attributed to autoxidation or hydrolysis. Elemental sulphur is always produced, and its origin has not been satisfactorily explained.

More reactive isothiocyanates, e.g. benzoyl isothio-

We have isolated the initial addition intermediates in the reactions of benzophenone oxime, acetophenone oxime, and fluorenone oxime, by the reaction of the corresponding sodium salt with phenyl isothiocyanate in dimethylformamide at —10 °C, followed by treatment with a large excess of ice-cold water.

These adducts, characterised by absorption at ca. 1 100

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[1] D. P. N. Satchell, *Chem. Soc. Rev.*, 1975, **4**, 231; J. Burkus, *J. Org. Chem.*, 1961, **26**, 779; J. W. Baker and J. Gaunt, *J. Chem. Soc.*, 1949, 9.

[2] A. Obregia and C. V. Gheorghiu, *J. prakt. Chem.*, 1930, **128**, 239.
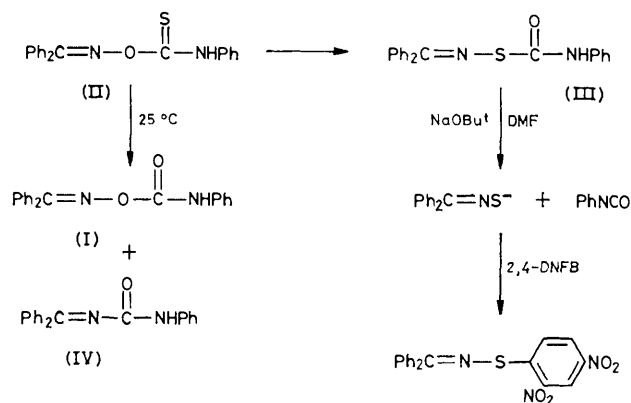
[3] C. Gheorghiu and C. Budeanu, *Bull. sect. sci. acad. roumaine*, 1942, **24**, 15 (*Chem. Zentr.*, 1943, **1**, 1659).

[4] C. V. Gheorghiu and C. Budeanu, *Ann. Sci. Univ. Jassy*, 1948, **31**, 16 (*Chem. Abs.*, **43**, 4232).

[5] R. F. Hudson, A. J. Lawson, and K. A. F. Record, *J. Chem. Soc., Perkin II*, 1974, 869; R. F. Hudson, A. J. Lawson, and E. A. C. Lucken, *Chem. Comm.*, 1971, 807.

(CS) and *ca.* 3 300 cm⁻¹ (NH), are usually unstable, and could not be isolated pure from most oximes. Thus reaction of di-*p*-tolyl ketone oxime with phenyl isothiocyanate gives a product (absorption at 1 080, 955, and 3 280 cm⁻¹), which, when filtered and recrystallised, undergoes isomerisation as shown by the appearance of i.r. absorption at 1 676 cm⁻¹ (CO) and 3 290 cm⁻¹ (NH). Subsequent decomposition to phenyl isocyanate (absorption at 2 240 cm⁻¹) and other products (*vide infra*) is observed.

The rearranged product (III) from the adduct of benzophenone oxide and phenyl isothiocyanate (II) was,
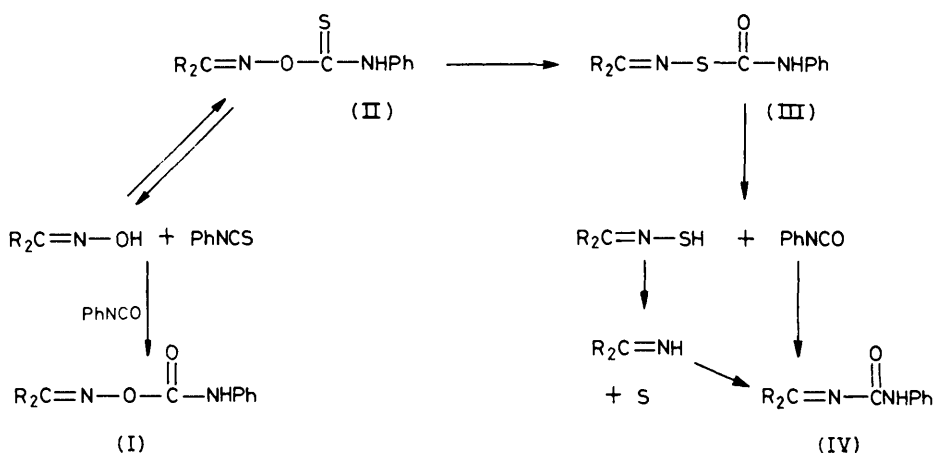
$$Ph_2C{=}N{-}O{-}\overset{\overset{S}{\|}}{C}{-}NHPh \longrightarrow Ph_2C{=}N{-}S{-}\overset{\overset{O}{\|}}{C}{-}NHPh$$

(II) → 25 °C → (III) → NaOBuᵗ / DMF

$$Ph_2C{=}N{-}O{-}\overset{\overset{O}{\|}}{C}{-}NHPh \qquad Ph_2C{=}NS^- \; + \; PhNCO$$

(I) +

$$Ph_2C{=}N{-}\overset{\overset{O}{\|}}{C}{-}NHPh$$

(IV) → 2,4-DNFB

$$Ph_2C{=}N{-}S{-}\langle\!\!\bigcirc\!\!\rangle\substack{NO_2 \\ NO_2}$$

however, isolated from a suspension of (II) in hexane; it is also formed in *ca.* 70% yield over a period of several

$$Ph(Me){-}C{=}N{-}O{-}\overset{\overset{S}{\|}}{C}{-}NHPh \longrightarrow Ph(Me)C{=}N{-}\overset{\overset{O}{\|}}{C}{-}NHPh \xrightarrow{(H_2O)} PhNHCONH_2$$

days in the solid state. This compound may decompose in various ways (*vide infra*).

Strong bases promote elimination, and treatment with sodium t-butoxide rapidly produces phenyl isocyanate and a pink solution probably due to the thio-oximate

In solution, compound (II) decomposes to give a mixture of compound (I) (*i.e.* the product of the reaction of the oxime with phenyl isocyanate) and (IV). The relative proportions of (I) and (IV) depend on the solvent used and on the length of the reaction, (I) being isolated preferentially from chloroform, (IV) from hexane.

The other adducts behave similarly, although the adduct formed from fluorenone oxime appeared to be considerably more stable. It is the only carbamate of this kind so far to remain in the unrearranged form in the solid state. In solution the main product was the carbamate [*cf.* (I)]. On the other hand the intermediate formed from acetophenone oxime is extremely unstable and in solution rapidly rearranges to give the alkylidene-amino-urea [*cf.* (IV)]. This, however, could not be isolated in the pure state, since it hydrolyses rapidly in the atmosphere to phenylurea.

Mono-substituted ureas have frequently been reported in the reactions of oximes with isothiocyanates and these are probably formed in the same way.

These results allow a plausible reaction scheme to be advanced to explain the formation of the various products. The addition of oxime to isothiocyanate is readily reversible, since in solution the adduct (III) rapidly dissociates to oxime and isothiocyanate. At the same time, it rearranges to its isomer (III), probably by a radical process in the same way as the *N*-disubstituted analogues.[5] In support of this conclusion, strong e.s.r. signals are observed for both iminyl and

iminoxy radicals in the early stages of the reaction. Moreover the i.r. spectra show strong absorptions at 2 080 cm⁻¹ corresponding to the isothiocyanate band.

The rearranged product is itself unstable under the conditions of the reaction and dissociates, in the same

$$R_2C{=}N{-}O{-}\overset{\overset{S}{\|}}{C}{-}NHPh \longrightarrow R_2C{=}N{-}S{-}\overset{\overset{O}{\|}}{C}{-}NHPh$$

(II) (III)

$$R_2C{=}N{-}OH \; + \; PhNCS \qquad\qquad R_2C{=}N{-}SH \; + \; PhNCO$$

PhNCO ↓ → R_2C{=}NH ↓ PhNCO

$$R_2C{=}N{-}O{-}\overset{\overset{O}{\|}}{C}{-}NHPh \qquad R_2C{=}NH \; + \; S \searrow \; R_2C{=}N{-}\overset{\overset{O}{\|}}{C}NHPh$$

(I) (IV)

anion. Treatment of this solution with 2,4-dinitrofluorobenzene produces *S*-2,4-dinitrophenylbenzophenone thio-oxime, thus confirming the presence of the thio-oxime.

way as does its isomer, to give isocyanate and thio-oxime. The presence of low concentrations of isocyanate which decrease as the reaction proceeds, is seen in the i.r. spectra.

Thio-oximes have not been isolated in the free state and these rapidly decompose at room temperature with the formation of sulphur.[6]

These considerations lead to the following reaction scheme, which involves the rapid reaction of oxime with phenyl isocyanate to give (I), and the subsequent reaction of imine with the isocyanate (which is known to be an exothermic process [7]), to give the second major product of the reaction (IV).

Further quantitative work is required to substantiate this tentative reaction scheme. It is quite likely that other reactions of hydroxylamine derivatives with iso-thiocyanates, carbon disulphide, and similar cumulenes, which are at the present time not fully understood, may proceed by reactions of the kind shown in the above scheme.

EXPERIMENTAL

O-Phenylthiocarbamoylbenzophenone Oxime (II).—To a cold solution (−10 °C) of phenyl isothiocyanate (5.4 g) in dry dimethylformamide (70 ml) was added in portions sodium benzophenone oximate (8.76 g). The solution was stirred for 1.5 h at −5 °C. The clear yellow liquid was poured into ice–water (1 l) resulting in the precipitation of a white gum-like solid. This was filtered off and dissolved in benzene. On the addition of light petroleum (b.p. 40—60 °C) with cooling, *O*-phenylthiocarbamoylbenzophenone oxime crystallised out of solution (7.7 g, 60%), m.p. 64—66 °C (Found: C, 72.7; H, 4.9; N, 8.2. $C_{20}H_{16}N_2OS$ requires C, 72.3; H, 4.8; N, 8.4%). Absorption in the i.r. spectra were found at 1 100 (CS), 960 (NO), and 3 290 (NH) cm^{-1}.

Rearrangement of O-Phenylthiocarbamoylbenzophenone Oxime (II).—(a) A solution of (II) (1 g) in chloroform was stirred at room temperature for 12 h. Removal of the solvent and treatment of the residue with light petroleum (b.p. 40—60 °C) gave 0.7 g of a mixture of products. The main product *O*-phenylcarbamoylbenzophenone oxime (I), m.p. 174—176 °C (lit.,[2] m.p. 176 °C), was isolated by re-crystallisation from alcohol.

(b) A suspension of compound (II) (2 g) in hexane (50 ml) was stirred for 4 days, to yield 1-diphenylmethylene-3-phenylurea (IV), m.p. 161—162 °C (lit.,[7] m.p. 160—162°), and (I).

(c) A suspension of compound (I) (3 g) in hexane was stirred for 1 day in the presence of strong sunlight to give *S*-phenylcarbamoylbenzophenone thio-oxime (III) (2 g), m.p. 110—120 °C (Found: C, 70.5; H, 4.8; N, 8.5. $C_{20}H_{16}N_2OS$ requires C, 72.3; H, 4.8; N, 8.4%). Absorption in the i.r. region was observed at 3 360 cm^{-1} (NH) and 1 670 cm^{-1} (CO), no absorption was observed at 1 100 cm^{-1} (CS). The compound decomposed when heated in carbon tetra-chloride to give carbonyl sulphide and benzophenone azine.

It was found that compound (II) rearranges to (III) in the solid state over a period of several days.

S-2,4-Dinitrophenylbenzophenone Thio-oxime.—A solution of compound (III) (0.001M) and 2,4-dinitrofluorobenzene (0.001M) in dimethylformamide (10 ml) was treated with sodium t-butoxide (0.001M) and stirred for 2 h at room temperature. The yellow solution was poured into dilute

hydrochloric acid, and the solution extracted with chloro-form. Evaporation of the extract gave *S*-2,4-dinitrophenyl-benzophenone thio-oxime (0.16 g), m.p. 226—228 °C (lit.,[6] m.p. 227—228 °C). Mass spectroscopic analysis gave a parent ion at 379.

O-Phenylthiocarbamoylfluorenone Oxime.—The sodium salt of fluorenone oxime (4.4 g) was added in small portions to a solution of phenyl isocyanate (3 g) in dry dimethyl-formamide (40 ml) at −10 °C. The reaction mixture was stirred for 1 h at this temperature and then added to 2 l of an ice–water mixture. The solid product was filtered off and dissolved in benzene; the solution was cooled to 10 °C, and then the product was precipitated with light petroleum (b.p. 40—60 °C); yield 4.9 g, m.p. 87—88 °C (Found: C, 72.9; H, 4.2; N, 8.4. $C_{20}H_{14}N_2OS$ requires C, 72.7; H, 4.3; N, 8.4%).

Absorptions in the i.r. region were observed at 1 100 (CS), 3 390 (NH), and 955 cm^{-1} (NO).

Rearrangement of O-Phenylthiocarbamoylfluorenone Oxime. —A solution of the oxime (2.2 g) in chloroform (50 ml) was set aside for 1 h at room temperature. The progress of the reaction was monitored by following changes in the i.r. spectrum. The initial peak (CO) at 1 670 cm^{-1} changed to a peak at 1 745 cm^{-1} characteristic of *O*-phenylcarbamoyl-fluorene oxime. Removal of the solvent and recrystallis-ation of the benzene gave 0.4 g of the product, m.p. 124—127 °C (Found: C, 76.4; H, 4.5; N, 9.0. $C_{20}H_{14}N_2O_2$ requires C, 76.4; H, 4.5; N, 8.9%). Absorptions in the i.r. region were observed at 3 360 (NH), 1 740 (CO), and 940 (NO) cm^{-1}.

O-Phenylthiocarbamoylacetophenone Oxime.—The sodium salt of the acetophenone oxime (6.2 g) was added to a solution of phenyl isothiocyanate (6 g) in dimethylform-amide (50 ml) at −10 °C. The mixture was added to 2 l of a mixture of ice–water and acidified with dilute hydrochloric acid. The gum-like product was extracted with ether and the solution treated with light petroleum (b.p. 40—60 °C) to re-precipitate the product; yield 8.1 g, m.p. 66 °C (Found: C, 66.7; H, 5.3; N, 10.3. $C_{16}H_{15}N_2OS$ requires C, 66.7; H, 5.2; N, 10.4%). Absorption in the i.r. region was ob-served at 1 100 (CS) and 3 300 cm^{-1} (NH).

Rearrangement of O-Phenylthiocarbamoylacetophenone Oxime.—(a) A solution of the oxime (1 g) in chloroform (30 ml) was set aside for 12 h at room temperature. The solvent was removed and the remaining solid dissolved in cold benzene. An unstable product (0.4 g) was obtained by treatment of the solution with light petroleum. This could not be purified but was identified as 1-phenylethyl-idene-3-phenylurea by means of the i.r. spectra with absorp-tion at 1 670 (CO) and 3 410 cm^{-1} (NH). This rapidly hydrolysed on attempted purification to phenylurea, m.p. 145—147 °C (lit., m.p. 145—147 °C).

A small quantity of *O*-phenylcarbamoylacetophenone oxime (i.r. absorption at 1 750 and 3 370 cm^{-1}) was also observed.

(b) A suspension of *O*-phenylthiocarbamoylacetophenone oxime (1 g) in hexane (5 ml) at room temperature gave 0.42 g of 1-phenylethylidene-3-phenylurea after 5 h.

Reaction between Sodium Acetone Oxime and Phenyl Isothiocyanate.—The sodium salt of the oxime (2.85 g) was added to a solution of phenyl isothiocyanate (4.1 g) in dimethyl formamide (50 ml) at −10 °C, and the product was extracted with ether. The solution was then dried (MgSO₄)

[6] D. H. R. Barton, P. D. Magnus, and S. I. Pennanen, *J.C.S. Chem. Comm.*, 1974, 1007.

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

and the i.r. spectrum recorded. The rearrangement occurred rapidly and peaks at 2 240 (due to phenyl iso-cyanate) and at 1 680 cm⁻¹ (CO) were observed. After removal of the solvent and recrystallisation of the solid (benzene) the only product isolated was phenylurea (1.9 g), m.p. 145—147 °C.

E.s.r. Spectra.—A solution of compound (II) (0.2 g) in carbon tetrachloride (10 ml) was inserted in the probe of a JEOL-PEIX e.s.r. spectrometer pre-heated to 40 °C.

Strong signals corresponding to the iminyl radical ($g = 2.003$, $a_N = 9.5$ G) and the iminoxy radical ($g = 2.006$, $a_N = 31$G) were immediately observed and these persisted for approximately 2—3 min.