867. *Organic Sulphur Compounds. Part III.*[1] *The Reaction of Sulphenyl Chlorides with Ketones.*

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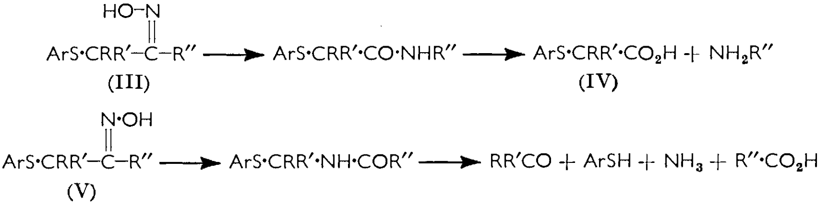
Satisfactory conditions for the condensation of arenesulphenyl chlorides with ketones are established. Derivatives of ketones with *o*-nitro- and 2,4-dinitro-benzenesulphenyl chlorides are prepared and their structures established.

THE formation of α-(arylthio)-ketones (I) by condensation of sulphenyl chlorides and ketones, first noted by Zincke,[2] was subsequently shown [3,4] to be general for aromatic sulphenyl chlorides. Analogous reactions are given by sulphenyl thiocyanates,[5] acetates,[6] and thiolsulphonates [7] but sulphenyl bromides lead only to the bromo-ketones. Aldehydes are oxidised by sulphenyl chlorides. The present work was designed to establish satisfactory conditions for the reaction of sulphenyl chlorides with ketones and to determine the scope of the reaction and the nature of its products.

(I) $\mathrm{ArS{\cdot}CRR'{\cdot}COR''}$ $\qquad$ $o\text{-}\mathrm{NO_2{\cdot}C_6H_4{\cdot}S{\cdot}CH_2{\cdot}COPh}$ (II)

A preliminary investigation of the formation of ω-(o-nitrophenylthio)acetophenone (II) showed that an equimolar mixture of *o*-nitrobenzenesulphenyl chloride and acetophenone gave a yield of 66% after five hours' boiling in ethylene dichloride; longer heating gave no increase in yield and gave a less pure product. Equally high yields were obtained after shorter reaction times by using either an excess of acetophenone or a more polar solvent. Of the solvents employed, acetonitrile proved to be the most effective. The reaction was catalysed by zinc chloride, possibly through the formation of $\mathrm{ArS^+\ ZnCl_3^-}$, or possibly by promoting enolisation of the ketone; other chlorides show a retarding, common-ion effect, and acetates exert strong negative catalysis, probably through the formation of the less reactive sulphenyl acetates.[6]



$$\underset{\text{(III)}}{\mathrm{ArS{\cdot}CRR'{-}\overset{\overset{HO-N}{\|}}{C}{-}R''}} \longrightarrow \mathrm{ArS{\cdot}CRR'{\cdot}CO{\cdot}NHR''} \longrightarrow \underset{\text{(IV)}}{\mathrm{ArS{\cdot}CRR'{\cdot}CO_2H}} + \mathrm{NH_2R''}$$

$$\underset{\text{(V)}}{\mathrm{ArS{\cdot}CRR'{-}\overset{\overset{N{\cdot}OH}{\|}}{C}{-}R''}} \longrightarrow \mathrm{ArS{\cdot}CRR'{\cdot}NH{\cdot}COR''} \longrightarrow \mathrm{RR'CO + ArSH + NH_3 + R''{\cdot}CO_2H}$$

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[1] Part II, Barltrop and Morgan, *J.*, 1957, 3072.

[2] Zincke, *Ber.*, 1911, **44**, 769.

[3] Zincke and Baeumer, *Annalen*, 1918, **416**, 86.

[4] Zincke and Farr, *Annalen*, 1912, **391**, 57; Zincke and Dahm, *Ber.*, 1912, **45**, 3457; Zincke and Kruger, *Ber.*, 1912, **45**, 3468; Zincke and Lenhardt, *Annalen*, 1913, **400**, 2; Zincke and Rose, *ibid.*, 1914, **406**, 103; Zincke and Eismeyer, *Ber.*, 1918, **51**, 751; Ries and Schurman, *Ber.*, 1919, **52**, 2170.

[5] Kharasch, Wehrmeister, and Tigerman, *J. Amer. Chem. Soc.*, 1947, **69**, 1612.

[6] Havlik and Kharasch, *J. Amer. Chem. Soc.*, 1956, **78**, 1207.

[7] Chivers and Smiles, *J.*, 1928, 697.

The reaction of *o*-nitro- and 2,4-dinitro-benzenesulphenyl chloride with a variety of dry ketones, in solution in acetonitrile or in an excess of ketone, gave good yields of the highly crystalline derivatives. 1,3-Dicarbonyl compounds gave quantitative yields of the monosubstitution products, but, unlike Zincke and Baeumer,[3] we found that considerably lower yields were obtained from the cupric complexes of these compounds.

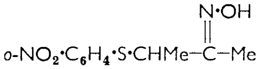
The carbonyl group in the α-(arylthio)-ketones retains its normal characteristics: bands in the infrared spectra due to the carbonyl stretching vibration appear at values close to those of the parent ketones, and oximes and dinitrophenylhydrazones could be prepared by standard methods. Oxidation of ω-(*o*-nitrophenylthio)acetophenone (II) with hydrogen peroxide and acetic acid gave a colourless sulphone, although the closely related compound (4-chloro-2-nitrophenylthio)acetone is reported[3] to be oxidisable only to the sulphoxide under these conditions. The complex action of alkali on the α-(arylthio)-ketone (II) has been described elsewhere.[8]

Zincke and Baeumer[3] showed by synthesis that substitution by the sulphur grouping takes place on the α-carbon atom. In the case of an unsymmetrical ketone two such non-equivalent sites are available and it is necessary to distinguish between the two possible isomers. Since the product is usually homogeneous (but see below), the problem is reduced to the determination of its structure. The α-(arylthio)-ketone was converted into an oxime which was allowed to rearrange under the influence of phosphorus pentachloride (cf. ref. 9). The two possible condensation products from each ketone can each give rise to two geometrically isomeric oximes, each of which on rearrangement leads to a different amide. Hydrolysis of the amide gives a mixture either of an arylthio-carboxylic acid and an amine; or of a carbonyl compound, a carboxylic acid, a thiophenol, and ammonia (see reaction scheme). The assignment of any one of these hydrolysis products to its chemical class gives the geometry of the oxime; their identification leads to the structure of the α-(arylthio)-ketone.

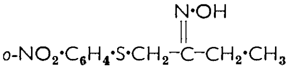
ω-(*o*-Nitrophenylthio)acetophenone (II) was taken as a model. The oxime rearranged to a crystalline amide which was hydrolysed giving aniline and (*o*-nitrophenylthio)acetic acid (IV; $R = R' = H$, $Ar = o\text{-}NO_2\cdot C_6H_4$). The oxime is clearly the *syn*-isomer (III; $R = R' = H$, $R'' = Ph$, $Ar = o\text{-}NO_2\cdot C_6H_4$).

Rearrangement of the oxime from the product of the reaction between isopropyl methyl ketone and *o*-nitrobenzenesulphenyl chloride gave an amide so unstable that all attempts to characterise it led only to di-(*o*-nitrophenyl) disulphide. The crude product was hydrolysed directly, giving a steam-volatile fraction which contained *o*-nitrobenzenethiol and acetone; formaldehyde was not detected. The involatile residue contained ammonia (as ammonium sulphate) and di-(*o*-nitrophenyl) disulphide. The oxime is accordingly the *anti*-isomer (V; $R = R' = R'' = Me$, $Ar = o\text{-}NO_2\cdot C_6H_4$). Similar treatment of the oximes derived from the condensation products of ethyl methyl ketone with both *o*-nitro- and 2,4-dinitro-benzenesulphenyl chlorides and from isopropyl methyl ketone with 2,4-dinitrobenzenesulphenyl chloride showed that they have analogous structures. In each case substitution by the sulphide group has occurred preferentially on the more heavily substituted carbon atom despite the obvious steric restraint; small amounts of the isomeric α-(arylthio)-ketones may well also be formed initially and eliminated during purification of the product (see below). A similar orientation has been demonstrated for the acid-catalysed bromination of ketones[10] but in the absence of more

(VI)



$$o\text{-}NO_2\cdot C_6H_4\cdot S\cdot CHMe\text{-}\overset{\overset{N\cdot OH}{\|}}{C}\text{-}Me$$



$$o\text{-}NO_2\cdot C_6H_4\cdot S\cdot CH_2\text{-}\overset{\overset{N\cdot OH}{\|}}{C}\text{-}CH_2\cdot CH_3$$

(VII)

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[8] Morgan, *J.*, 1959, 3502.

[9] Vinkler and Authereid, *Acta Univ. Szeged, Chem. et Phys.*, 1946, **2**, 50, 105.

[10] Catch, Elliot, Hey, and Jones, *J.*, 1948, 272; Catch, Hey, Jones, and Wilson, *ibid.*, p. 276; Cardwell and Kilner, *J.*, 1951, 2430.

detailed information it is not possible to say whether the sulphenyl chloride reaction conforms to a similar mechanism, *i.e.*, is controlled kinetically by enolisation of the ketone.

During the preparation of 3-(*o*-nitrophenylthio)butan-2-one oxime (VI) there was isolated a small amount of an isomeric substance. The infrared spectra of the isomers (in CS_2) are closely similar except for a band at 756 cm.$^{-1}$ found in the spectrum of the high-melting isomer but not in that of the main fraction. This band may be assigned to a methylene rocking frequency, suggesting that the less abundant isomer has the structure (VII).

EXPERIMENTAL

Reagents.—*o*-Nitrobenzenesulphenyl chloride[11] was prepared from the disulphide;[12] 2,4-dinitrobenzenesulphenyl chloride was prepared similarly.[13] Ketones were dried by fractional distillation.

Formation of ω-(o-*Nitrophenylthio*)*acetophenone.*—(*A*) A solution of acetophenone (0·6 g., 5 mmoles) in ethylene chloride (10 c.c.) was boiled with *o*-nitrobenzenesulphenyl chloride (1·0 g., 1 equiv.) for 2½ hr., giving the α-(arylthio)-ketone (0·8 g., 44%) [2,4-*dinitrophenylhydrazone*, m. p. 203° (Found: C, 52·8; H, 3·2. $C_{20}H_{15}N_5O_6S$ requires C, 53·2; H, 3·3%); *sulphone*, m. p. 132° (Found: C, 54·6; H, 3·4. $C_{14}H_{11}NO_5S$ requires C, 55·1; H, 3·6%)]. The yield was raised to 66% by prolonging the reaction time to 5 hr. Higher yields were obtained after 2½ hr. by use of excess of acetophenone (2 equiv., 66%; 5 equiv., 88%).

(*B*) Similar equimolar solutions of the reagents (5 mmoles) in different solvents (10 c.c.) were boiled for 2½ hr., giving the following yields of sulphide: ether, 22%; tetrahydrofuran, 52%; acetonitrile, 58%. The reaction in acetonitrile was complete (60%) after ½ hr.

(*C*) To an equimolar solution of the reagents (5 mmoles) in ethylene chloride (10 c.c.), an excess of a salt was added and the mixture was boiled for 2½ hr., giving the following yields of sulphide: lithium chloride, 41%; lithium bromide, 49%; potassium chloride, 41%; potassium bromide, 47%; lithium acetate, 25%; sodium acetate, 25%; potassium hydrogen carbonate, 49%; potassium carbonate, 38%; lithium sulphate, 38%; calcium chloride, 25%; calcium sulphate, 30%; calcium phosphate, 22%; triethylamine, 19%; cupric sulphate, 14%. The addition of lithium chloride gave a particularly clean product. A similar solution in ether (10 c.c.) containing zinc chloride (1 g.) gave sulphide (55%) after 1 hr.

Preparation of α-(*Arylthio*)-*ketones.*—Sulphenyl chloride (1 g.) was heated either with an excess of ketone for 5 hr. or with a solution of ketone (2 g.) in acetonitrile (10 c.c.) for 2½ hr. The solution was concentrated *in vacuo* and the residue was crystallised from methanol or acetonitrile. The *derivatives* so prepared are listed in the Table.

Reaction of Ethyl Methyl Ketone with o-*Nitrobenzenesulphenyl Chloride.*—The sulphenyl chloride (5 g.) in the ketone (10 c.c.) was heated for 90 min., giving an oil which, in aqueous ethanol, was converted into the oxime in the usual way. The product crystallised slowly to give 3-(o-*nitrophenylthio*)*butan*-2-*one oxime*, m. p. 87—88° (from aqueous ethanol). Addition of water to the mother-liquors precipitated a sticky solid, from which was isolated a small amount of an isomeric *oxime*, m. p. 135—136° (from methanol) (Found: C, 50·1; H, 5·0; N, 11·7; S, 13·6. $C_{10}H_{12}N_2O_3S$ requires C, 50·0; H, 5·0; N, 11·7; S, 13·3%). A mixture of the two oximes had m. p. 79—98°.

Degradation of the Oximes.—(*A*) Phosphorus pentachloride (500 mg.) was added in small amounts during 30 min. to a solution of ω-(o-*nitrophenylthio*)*acetophenone oxime* (350 mg.) in ethylene chloride (10 c.c.). Evaporation of the solvent left (o-*nitrophenylthio*)*acetanilide*, m. p. 153—154°, golden plates (from acetonitrile) (Found: C, 57·9; H, 4·1. $C_{14}H_{12}N_2O_3S$ requires C, 58·3; H, 4·2%). A solution of the anilide (200 mg.) in methanol (8 c.c.) was boiled under reflux for 2½ hr. with hydrochloric acid (4 c.c.). Addition of water to the cooled solution precipitated (*o*-nitrophenylthio)acetic acid, m. p. 154—155° (Found: C, 45·1; H, 3·1. Calc. for $C_8H_7NO_4S$: C, 45·1; H, 3·3%). The mother-liquor was washed with benzene (3 × 50 c.c.), made alkaline, and distilled. The aqueous distillate was acidified and treated with bromine water, giving a copious precipitate of tribromoaniline, m. p. and mixed m. p. 117·5°.

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[11] *Org. Synth.*, Coll. Vol. I, 1941, p. 220.

[12] *Org. Synth.*, Coll. Vol. II, 1943, p. 453.

[13] Billman, Garrison, Anderson, and Wolnak, *J. Amer. Chem. Soc.*, 1941, **63**, 1920.

Compound	M. p.	Formula	Found (%)		Reqd. (%)	
			C	H	C	H
o-Nitrophenylthiopropan-2-one	81°					
,, ,, *oxime*	94—95	$C_9H_{10}N_2O_3S$	47·4	4·5	47·8	4·4
3-(*o*-Nitrophenylthio)butan-2-one						
,, ,, *oxime*	87—88	$C_{10}H_{12}N_2O_3S$	49·9	4·9	50·0	5·0
3-(2,4-*Dinitrophenylthio*)*butan*-2-*one*	92	$C_{10}H_{10}N_2O_5S$	44·7	3·8	44·4	3·7
,, ,, *oxime*	125	$C_{10}H_{11}N_3O_5S$	42·0	3·9	42·1	3·9
2-(2,4-*Dinitrophenylthio*)*pentan*-3-*one*	88	$C_{11}H_{12}N_2O_5S$	46·8	4·3	46·5	4·3
3-(2,4-*Dinitrophenylthio*)*pentan*-2-*one*	75—76	$C_{11}H_{12}N_2O_5S$	46·7	4·4	46·5	4·3
3-*Methyl*-3-(o-*nitrophenylthio*)*butan*-2-*one*	74—75	$C_{11}H_{13}NO_3S$	55·4	5·4	55·2	5·5
,, ,, ,, *oxime*	154—155	$C_{11}H_{14}N_2O_3S$	51·7	5·4	52·0	5·5
3-(2,4-*Dinitrophenylthio*)-3-*methylbutan*-2-*one*	80—81	$C_{11}H_{12}N_2O_5S$	46·7	4·4	46·5	4·3
,, ,, ,, *oxime*	88	$C_{11}H_{13}N_3O_5S$	43·7	4·4	44·1	4·4
4-*Methyl*-3-(o-*nitrophenylthio*)*pentan*-2-*one*	73—74	$C_{12}H_{15}NO_3S$	57·3	6·0	56·9	6·0
3,3-*Dimethyl*-1-(o-*nitrophenylthio*)*butane*-2-*one*	70	$C_{12}H_{15}NO_3S$	56·9	5·7	56·9	6·0
3,3-*Dimethyl*-1-(2,4-*dinitrophenylthio*)*butan*-2-*one*	135	$C_{12}H_{14}N_2O_5S$	48·8	4·8	48·3	4·7
,, ,, ,, *oxime*	172	$C_{12}H_{15}N_3O_5S$	46·3	4·9	46·0	4·8
2,4-*Dimethyl*-2-(2,4-*dinitrophenylthio*)*pentan*-2-*one*	90	$C_{13}H_{16}N_2O_5S$	50·1	5·1	50·0	5·2
ω-(*o*-Nitrophenylthio)acetophenone	147					
,, ,, ,, *oxime*	171·5	$C_{14}H_{12}N_2O_3S$	58·0	3·9	58·3	4·2
2-(o-*Nitrophenylthio*)-1-*phenylpropan*-1-*one*	80—81	$C_{15}H_{13}NO_3S$	62·5	4·6	62·7	4·6
3-(*o*-Nitrophenylthio)pentane-2,4-dione	136—137	$C_{11}H_{11}NO_4S$	52·2	4·5	52·2	4·4
3-(2,4-*Dinitrophenylthio*)*pentane*-2,4-*dione*	149—150	$C_{11}H_{10}N_2O_6S$	44·2	3·5	44·3	3·4
Me α-(o-*nitrophenylthio*)*acetoacetate*	133—134	$C_{11}H_{11}NO_5S$	49·1	4·1	49·1	4·1
Et α-(o-*nitrophenylthio*)*acetoacetate*	74—75	$C_{12}H_{13}NO_5S$	50·6	4·5	50·9	4·6

(*B*) An ice-cold solution of 3-*methyl*-3-(o-*nitrophenylthio*)*butan*-2-*one oxime* (1 g.) in dry ether (50 c.c.) was treated with phosphorus pentachloride (2·5 g.). After 1 hr. the solution was decanted and washed with ice-water (3 × 50 c.c.). The dried ethereal solution yielded a yellow solid which, on crystallisation from ethanol, acetonitrile, or acetic acid, or by precipitation with methanol from a solution in cold chloroform, was found to be di-(*o*-nitrophenyl) disulphide, m. p. 192°.

(*C*) The same oxime (1 g.) as in (*B*) was rearranged as described in (*B*). The unwashed ethereal solution was evaporated. Dilute sulphuric acid was added to the residual oil and the mixture was distilled. The aqueous distillate carried *o*-nitrobenzenethiol, m. p. 53—54° (Found: C, 46·3; H, 3·2; N, 9·3; S, 20·8. Calc. for $C_6H_5NO_2S$: C, 46·4; H, 3·2; N, 9·0; S, 20·7%). The distillate gave a negative test for formaldehyde with chromotropic acid; with 2,4-dinitrophenylhydrazine, acetone dinitrophenylhydrazone, m. p. 117—120°, was formed. This identity was confirmed chromatographically. The unvolatilised solution was filtered from a quantity of disulphide, made alkaline, and distilled: ammonia was evolved and detected by its action on Nessler's solution and by the formation of ammonium platinichloride (Found: H, 1·7. Calc. for $H_8Cl_2N_2Pt$: H, 1·8%).

(*D*) Similar treatment of 3-(2,4-*dinitrophenylthio*)-3-*methylbutan*-2-*one oxime* (350 mg.) led to the detection of acetone, 2,4-dinitrophenyl disulphide, m. p. 290°, from nitrobenzene–ethanol, and ammonia [as ammonium platinichloride (Found: H, 1·7%)]. Chromotropic acid gave a negative test for formaldehyde.

(*E*) 3-(2,4-*Dinitrophenylthio*)*butan*-2-*one oxime* (1 g.) was treated similarly. The distillate from the acidic solution, which contained no formaldehyde, carried acetaldehyde [dimedone derivative, m. p. and mixed m. p. 137—137·5°; 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 160° (Found: C, 42·8; H, 3·5. Calc. for $C_8H_8N_4O_4$: C, 42·9; H, 3·6%)]. The residue contained bis-2,4-dinitrophenyl disulphide and ammonia [platinichloride (Found: H, 2·0%)].

(*F*) 3-(o-*Nitrophenylthio*)*butan*-2-*one oxime* (1 g., m. p. 87—88°) was decomposed similarly. From the appropriate fractions there were isolated: *o*-nitrobenzenethiol, acetaldehyde, di-(*o*-nitrophenyl) disulphide, and ammonia.

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