Thermal 1,3-Rearrangement of *N*-Benzoyl-*N*-methyl-*O*-thiocarbamoylhydroxylamines (Thiocarbamoyl *N*-Methylbenzohydroxamates)

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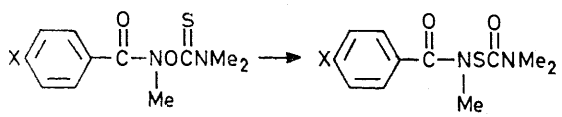
The preparation and thermal rearrangement of several of the title compounds are described. *S*-Carbamoyl *N*-methylbenzothiohydroxamates and the corresponding *N*-methylbenzamide are the principal products. The rate coefficients for rearrangement change only slightly with variations in the aromatic substituent or solvent polarity, suggesting either a concerted or a free radical pair pathway, rather than mechanisms with a polar or an ionic transition state.

THE recently reported [1-3] thermal rearrangement of oxime thiocarbamates (I) to thio-oxime carbamates (II) is the first example of a 1,3-shift which generates a new nitrogen–sulphur σ-bond. The high yields normally obtained

(I) (II)

by this simple reaction under mild conditions suggest that the rearrangement may have wider applications in the preparation of other sulphenamide derivatives difficult to prepare by alternative routes. We have accordingly prepared the thiocarbamoylated hydroxamic acids (III), and now report their thermal rearrangement to the corresponding sulphenamide (IV) at 40—60°.[4]

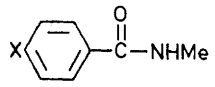
Thiocarbamoylation of *N*-methylbenzohydroxamic acids results in the *O*-thiocarbamoylated products (III). The i.r. absorption spectrum ($CHCl_3$) shows a weak N–O stretch [5] at 977 and a strong band at 1284 cm^{-1}, attributed to the C=S group.[6] These bands are also prominent in the



(IIIa-e) (IVa-e)

+

a; X = H
b; X = MeO
c; X = Me
d; X = CN
e; X = NO_2



(Va-e)

i.r. spectra of the analogues (I) (Table 1). Furthermore, in common with the oxime thiocarbamate (I), the ^1H n.m.r. resonance of the *NN*-dimethylthiocarbamoyl group is a doublet [1] at ambient temperatures.

Solutions of compounds (III), however, are not thermally stable. Rearrangement slowly takes place at room temperature (10 days in $CHCl_3$) to the corresponding sulphenamides (IV), with concomitant loss of the i.r. bands at 977 and 1284 cm^{-1}. Room temperature solution n.m.r. provides the best evidence for the thione–thiol rearrangement. The magnetic non-equivalence of methyl groups of the *NN*-dimethylthiocarbamoyl unit in (III) is replaced by the singlet resonance [also found [1] in the analogues (II)] of the *NN*-dimethylcarbamoyl group (Table 1).

TABLE 1

Spectroscopic data for reactants (III) and products (IV)

	$\nu_{max.}$/cm^{-1} ($CHCl_3$)			δ ($CDCl_3$; 25°)	
	C=S	O=CNMe$_2$	N–O	Me$_2$NCS	Me$_2$NCO
Ph_2C=NOCSNMe$_2$	1288		977	3·33, 2·78	
(IIIa)	1286		977	3·38, 3·14	
(IIIb)	1286		977	3·34, 3·09	
(IIIc)	1283		974	3·29, 3·01	
(IIId)	1285		975	3·25, 3·00	
(IIIe)	1284		977	3·29, 3·05	
Ph_2C=NSCNMe$_2$ (O)		1680			2·91
(IVa)		1682			2·84
(IVb)		1685			2·82
(IVc)		1682			2·80
(IVd)		1680			2·84
(IVe)		1685			2·84

The yields of the sulphenamides (IV), measured by n.m.r. spectroscopy, decrease with increasing temperature, with a corresponding increase in the yield of the principal side products (V), the appropriately substituted *N*-methylbenzamide (identical with authentic samples). Table 2 shows the product ratio (IV) : (V) in chloroform solution at various temperatures.

TABLE 2

Yields (n.m.r.) of (IVc) and (Vc) from thermal rearrangement of (IIIc) in $CDCl_3$ at varying temperatures (sealed tube)

t/h	Temp./°C	(IVc) (±5%)	(Vc) (±5%)
240	20	95	5
15	60	80	20
0·25	120	25	75

The sulphenamide (IVc) is only slowly thermally converted into amide (Vc) in chloroform solution at 120° (sealed tube) over a period of several days, and thus the bulk of amide, observed in the first minutes after complete reaction, is formed in a process, parallel to the re-

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[6] M. S. Newman and H. A. Karnes, *J. Org. Chem.*, 1966, **31**, 3980.

arrangement of (IIIc), which competes more effectively at higher temperatures.

Thus one important factor in maximization of the yield of (IV) is the reaction temperature. Compounds (IIId and e), however, give large (*ca.* 50%) yields of amide even at ambient temperature, and the time needed for complete reaction is nearly one month. To understand this limitation (in an otherwise successful preparative method) requires a knowledge of the reaction mechanism.

The rate of the present rearrangement shows a solvent and substituent dependence virtually identical, however, to that observed in the thermal rearrangement of oxime thiocarbamates.[3] The similarity of the *absolute* rates of rearrangement, *e.g.* $k_{(I)\rightarrow(II)}/k_{(III)\rightarrow(IV)}$ *ca.* 10 further suggests that the reactions have a common mechanism. It has been proposed[3] that the 1,3-shift (I) ⟶ (II) involves a radical pair (as well as possibly proceeding by a concerted process), partly on the evidence of transient

TABLE 3

Rearrangement of (IIIc) in benzene at 59·0° followed by u.v. and i.r. spectroscopy

U.v. (285 nm)				I.r. (1286 cm^{-1})			
t/min	Reaction (%)	10^4[(IIIc)]$_t$/ M	230·3 log $(A_0/A)t^{-1}$/ min^{-1}	*t*/min	Reaction (%)	[(IIIc)]$_t$/ M	230·3 log $(A_0/A)t^{-1}$/ min^{-1}
0	0	2·11		0	0	0·187	
60	14	1·82	0·245	32	7	0·174	0·234
120	27	1·54	0·268	90	19	0·152	0·231
180	39	1·29	0·273	168	34	0·124	0·248
240	49	1·09	0·274	212	39	0·113	0·237
300	57	0·91	0·280	251	45	0·103	0·237
420	70	0·64	0·283	290	47	0·099	0·219
540	80	0·43	0·294	320	55	0·084	0·251
660	85	0·31	0·290				
780	89	0·22	0·289				
900	92	0·17	0·279				
Average			0·28				0·24

The thermal rearrangement (III) ⟶ (IV) follows a first-order rate law as given by equation (1) over a wide range of concentrations. This is demonstrated by the

$$-\mathrm{d}[(\mathrm{III})]/\mathrm{d}t = k_1[\mathrm{III}]_t \qquad (1)$$

data of Table 3 which records the rearrangement of (IIIc) to (IVc) measured in benzene at 59°, in two parallel runs which differ in initial concentration of substrate by a factor of nearly 10^3.

Rate coefficients calculated *via* equation (1) are given in Table 4. Clearly the rate coefficients for the rearrangement (III) ⟶ (IV) are not significantly modified by changes in the aromatic substituent, nor solvent,* and these observations effectively exclude mechanisms involving a large separation of charge in the transition state. Thus nitrenium ion formation[7] (VI) or the Schönberg thione–thiol rearrangement[8] (VII) are both poor analogues for the rearrangement of (III), despite superficial resemblances.

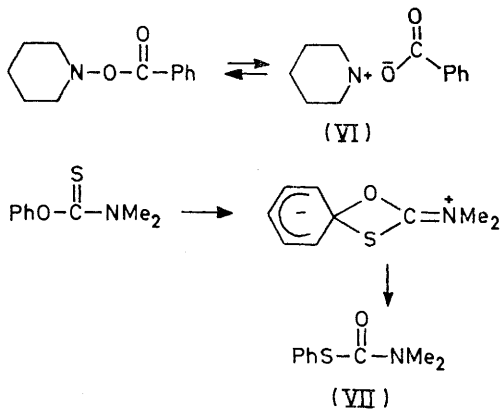
TABLE 4

Substituent and solvent effect on the rate of rearrangement (III) ⟶ (IV) at 60·5°

Substrate	Solvent	10^2k_1/min^{-1}
(IIIa)	Hexane	0·40
(IIIb)	Hexane	0·71
(IIId)	Hexane	0·47
(IIIe)	Hexane	0·58
(IIIc)	Hexane	0·51
(IIIc)	Benzene	0·33
(IIIc)	Acetonitrile	0·29
(IIIc)	Ethanol	0·51

* In chlorinated hydrocarbon solvents the reaction rate did not follow a strict first-order dependence on reactant concentration for (IIIa—c); a short induction period was followed by onset of a rapid conversion into (IV), and this is believed to correspond to an induced chain pathway.

e.s.r. signals attributed to iminyls [*e.g.* (IX)], the postulated intermediate species. In the thermal rearrangement of (III), however, no e.s.r. signals are observed in



either carbon tetrachloride or benzene solvent. This does not invalidate the Scheme, however, when the relative reactivities of acylaminyl (VIII) and iminyl (IX) radicals are considered. Although not isolable, iminyls are moderately stable[9] despite minimal π conjugation to the radical centre,[10] and this may be due to geometry favourable to σ-system delocalization of unpaired spin.[11] In general, therefore, iminyls tend to dimerize, while the unstable[12] acylaminyl radicals are more reactive, and

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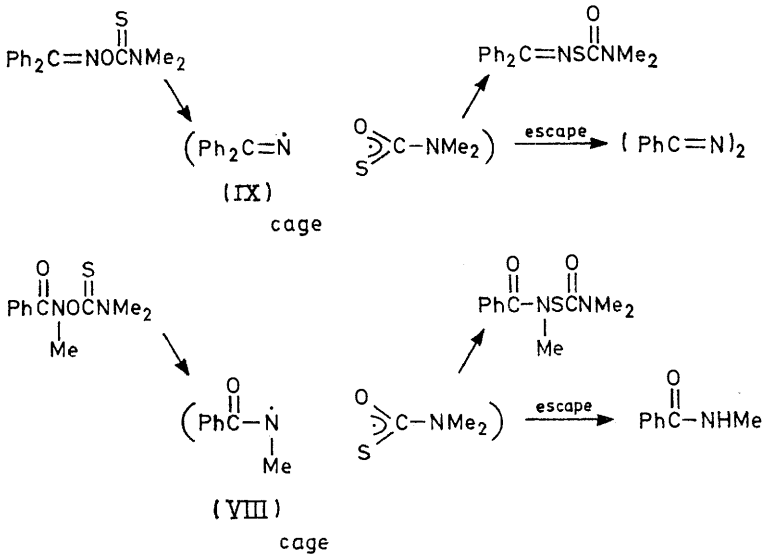
readily abstract hydrogen atoms from a suitable donor,[13] in keeping with the diffusion products detailed in the Scheme. The radical-pair pathways are likewise not inconsistent with the relative rates of conversion (I) ⟶ (II) and (III) ⟶ (IV) discussed above, as a more stable radical intermediate should result in a lessening of transition state energy. The increasing yield of amide with reaction temperature (Table 2) may therefore be the result of a viscosity-dependent cage escape[14] but may equally be attributed to a duality of mechanism, in which



SCHEME

concerted and step-wise paths compete.[15] The problem of the extent of relative contributions of radical-pair and sigmatropic 1,3-shift in these rearrangements is not likely to be simply resolved, however, as stereochemical tests are not available, the products (IV) and (II) quickly losing stereochemical integrity in solution at ambient temperature.[16]

There appears to be a significant chain contribution to the overall yield and reaction rate in both processes discussed in this paper, at least in chlorinated hydrocarbon solvents. This is indicated in particular by the considerable percentage of crossover products produced [3] in the reaction (I) ⟶ (II), and by the fast rate of conversion observed in both series [3] after an initial induction period. This may explain the lower yields and slower rate of conversion described for the products (IVd and e) in the preparative method utilized, involving chloroform solvent. The nitro- and cyano-functions have been shown to act as radical traps in certain circumstances,[17,18] as well as being one-electron acceptors,[19] and it has been shown in this short series that the rearrangement (III) ⟶ (IV) has good preparative value only when aromatic substituents are moderately inert to the presumed chain carrier, as is the case with the methoxy and methyl substituents of (IIIb and c). We will shortly report further studies in the field of 1,3-free radical geminate recombination.

EXPERIMENTAL

Preparation of Substrates.—NN-*Dimethylthiocarbamoyl* N-*methylbenzohydroxamates.* In a typical preparation, a solution of *N*-methylbenzohydroxamic acid (6·8 g, 0·045 mol) in triethylamine (4·55 g, 0·045 mol) and *NN*-dimethylformamide (30 ml) was added over 5 min to a stirred solution of *NN*-dimethylthiocarbamoyl chloride (8·34 g, 0·067 mol) in *NN*-dimethylformamide. The mixture was stirred for a further 1·5 h at room temperature, poured into ice–water (800 ml), and the resulting solid precipitate isolated by filtration. The residue was washed several times with cold water, recrystallized from the minimum amount of warm benzene–light petroleum (b.p. 40—60°) (1 : 2), cooled to −10°. Thus were prepared the *benzohydroxamate* (IIIa) (46%), m.p. 55—56° (Found: C, 55·3; H, 5·9; N, 11·6. $C_{11}H_{14}N_2O_2S$ requires C, 55·5; H, 5·9; N, 11·8%); the 4-*methoxybenzohydroxamate* (IIIb) (43%), m.p. 86·5—87·5° (Found: C, 54·0; H, 6·1; N, 10·4. $C_{12}H_{16}N_2O_3S$ requires C, 53·7; H, 6·0; N, 10·4%); the 4-*toluohydroxamate* (IIIc), (37%), m.p. 99—101° (Found: C, 57·4; H, 6·4; N, 10·8. $C_{12}H_{16}N_2O_2S$ requires C, 57·1; H, 6·4; N, 11·1%); the 4-*cyanobenzohydroxamate* (IIId) (73%), m.p. 134—136° (decomp.) (Found: C, 54·4; H, 4·8; N, 15·9. $C_{12}H_{13}N_3O_2S$ requires C, 54·7; H, 4·9; N, 16·0%); and the 4-*nitrobenzohydroxamate* (IIIe) (71%), m.p. 131—134° (decomp.) (Found: C, 46·2; H, 4·7; N, 14·8. $C_{11}H_{13}N_3O_4S$ requires C, 46·6; H, 4·6; N, 14·8%).

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NN-*Dimethylcarbamoyl N-methylbenzothiohydroxamates*. These were best prepared by allowing a chloroform solution of the appropriate ester (III) (5% w/v) to stand at room temperature. The rearrangement, monitored by t.l.c., was generally complete after 10 days, although the cyano- and nitro-derivatives (IIId and e) may require up to one month. The yield of (IVa—c) determined from the n.m.r. spectra, is usually between 90 and 95%. The other major product is the corresponding *N*-methylbenzamide. Compounds (IIId and e), however, give only *ca.* 50% (IV) (n.m.r.).

Alternatively, the rearrangement of (IIIa—c) may be carried out by maintaining the chloroform solution under reflux for 15 h, which normally results in a lower overall yield of (IVa—c) (*ca.* 60%). The rearrangement product (IV) is isolated by fractional recrystallization [benzene–light petroleum (1 : 2)] of the residue obtained after removal of the chloroform.

Thus were prepared the *thiohydroxamate* (IVa) (33%), m.p. 79—80° (Found: C, 55·8; H, 5·9; N, 11·8%); the *4-methoxybenzothiohydroxamate* (IVb) (26%), m.p. 104—106° (Found: C, 53·9; H, 6·1; N, 10·5%); the *4-toluothiohydroxamate* (IVc) (43%), m.p. 100—103° (Found: C, 57·4; H, 6·4; N, 10·8%); the *4-cyanobenzothiohydroxamate* (IVd) (20%), m.p. 136—138° (decomp.) (Found: C, 54·5; H, 4·6; N, 15·8%); and the *4-nitrobenzothiohydroxamate* (IVe) (10%), m.p. 140—142° (Found: C, 46·6; H, 4·6; N, 14·5%).

Substituted *N*-methylbenzohydroxamic acids and *N*-methylbenzamides were prepared from the appropriate benzoyl chloride by standard methods,[20] and satisfactory agreement with m.p.s given in the literature was obtained in each case. All other materials were of the best available grade, freshly distilled or recrystallized before use.

* With the exception of chlorinated hydrocarbons, already noted above, in which the apparent rate of conversion was increased by the spectrometer beam.

Reaction Kinetics.—(a) The rates of rearrangement of dilute solutions of (III) were determined from decrease in substrate concentration with respect to time. Concentration assays were obtained from u.v. spectrophotometry at a fixed, predetermined wavelength, generally 250 nm, in a manner already described.[3] Analysis by n.m.r., i.r., and u.v. spectroscopy of samples of (III) in parallel reactions in darkened flasks showed that no appreciable rate increase is produced by the light beam of the u.v. spectrometer in kinetic runs followed by monitoring at a fixed wavelength, even with instrument settings of unnecessarily high beam energy and large slit width.* The Beer–Lambert law was obeyed for all substances studied, and excellent isosbestic points were obtained in the time-dependent u.v. spectrum. Monitoring was continued in individual runs until no further change in the spectrum was detected.

(b) In some cases, when higher concentrations were used, the rate of rearrangement was followed by i.r. analysis. In a typical run, a stoppered graduated flask containing a benzene solution of (III) (10 ml; 0·2M) was immersed in a bath at a temperature maintained constant to within 0·1°. At a specific time, a sample (0·25 ml) was rapidly transferred to a graduated flask (1·0 ml) and, after volume adjustment, the i.r. solution spectrum was recorded in cells of 0·5 mm path length. The process was then repeated at noted intervals. First-order rate coefficients were calculated from the concentrations calculated *via* a calibration curve for the absorption at 1286 cm^{-1} (C=S), obtained in turn from successive dilution of a standard solution of (III) in benzene.

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