Thermal Rearrangement of *O*-Methyleneamino Thiocarbamates

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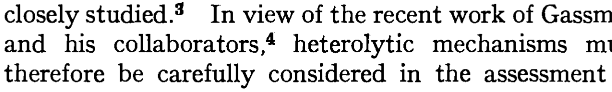
The rate of the thermal, uncatalysed, [1,3] rearrangement of aromatic *O*-methyleneamino thiocarbamates to *S*-methyleneamino thiocarbamates in solution is insensitive to changes in both solvent polarity and substituent on ring and imino-carbon atoms, suggesting a transition state involving little charge separation. The occurrence of rearrangement *via* a radical pair is suggested by the detection by e.s.r. spectroscopy of aromatic iminyls, generated as transients during rearrangement.

THIS paper is concerned with the thermal, uncatalysed [1,3] rearrangement of *O*-methyleneamino thiocarbamates to *S*-methyleneamino thiocarbamates [reaction (1)],[1] which proceeds at ambient temperature in polar and non-polar solvents at a rate convenient for kinetic investigation.



(1)

[1,3] Rearrangements may generally proceed in a variety of ways depending on the substrate structure and reaction conditions. The most extensively studied is the allylic migration of a weakly basic species, particularly in polar solvents, *via* an ion-pair pathway involving an allylic carbonium ion.[2] [1,3] Migration of a carbonium ion *via* ion-pairing with an allylic anion has also been closely studied.[3] In view of the recent work of Gassman and his collaborators,[4] heterolytic mechanisms must therefore be carefully considered in the assessment of reactions (such as the present study) involving nitrogen–oxygen bond cleavage.

The ready nature of the rearrangement of *O*-methyleneamino thiocarbamates in non-polar solvents, however, raises the alternative of a thermal [1,3] sigmatropic process as a possible mode for reaction, which, according to the simple rules of Woodward and Hoffmann,[5] must proceed with inversion of configuration at the migrating centre. The problem of *retention* of configuration in thermal [1,3] shifts (recently demonstrated by Cookson and Kemp [6]) has been considered by Berson, who invokes [7] the role of the ' subjacent orbital ' in sigmatropic rearrangements. This approach approximates to the association of loosely bound free radicals, and thus the formal distinction between concerted and homolysis pathways becomes less clear. [1,3] Shifts occurring, at least in part, *via* a pair of caged radicals have been reported,[8] although no information is currently available on the extent of radical participation in [1,3] sigmatropic processes.

No assignment of mechanism has been made in the thermal rearrangement of *O*-methyleneamino thiocarbamates (I), and we now report our findings, a preliminary report of which has been published.[9]

EXPERIMENTAL

Preparation of Substrates.—O-*Methyleneamino thiocarbamates*. The method of Searle and his co-workers [1] was used to prepare *O*-diphenylmethyleneamino dimethylthiocarbamate (Ia), m.p. 107—108° (lit.,[1] 106—107°), *O*-α-methylbenzylideneamino dimethylthiocarbamate (Ic), m.p. 80—84° (decomp.) (lit.,[1] 91—92°); *O*-α-methyl-4-nitrobenzylideneamino dimethylthiocarbamate (Ie), m.p. 115—117° (decomp.) (lit.,[1] 116—117°), and *O*-diphenylmethyleneamino morpholinothioformate (IIIa), m.p. 92—93° (lit.,[1]

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

[2] *E.g.* B. B. Jarvis, *J. Org. Chem.*, 1968, **33**, 4075.

[3] S. G. Smith, *Tetrahedron Letters*, 1962, 979.

[4] P. G. Gassman and G. D. Hartman, *J.C.S. Chem. Comm.*, 1972, **15**, 853.

[5] R. B. Woodward and R. Hoffmann, *Accounts Chem. Res.*, 1968, **1**, 17.

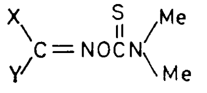
[6] R. C. Cookson and J. E. Kemp, *Chem. Comm.*, 1971, 385.

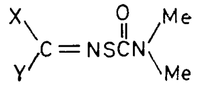
[7] J. A. Berson, *Accounts Chem. Res.*, 1972, **5**, 406.

[8] (*a*) J. E. Baldwin and J. E. Brown, *J. Amer. Chem. Soc.*, 1969, **91**, 3647; (*b*) J. Hollander and W. P. Neumann, *Angew. Chem. Internat. Edn.*, 1970, **9**, 804.

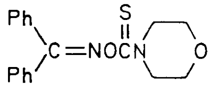
[9] R. F. Hudson, A. J. Lawson, and E. A. C. Lucken, *Chem. Comm.*, 1971, 807.

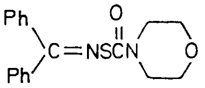
92—93°). In this way were also prepared O-bis-4-*fluorophenylmethyleneamino dimethylthiocarbamate* (Ii) (55%), m.p. 110° (from benzene–light petroleum) (Found: C, 60·2; H, 4·5; N, 8·8. $C_{16}H_{14}F_2N_2OS$ requires C, 60·0; H, 4·4; N, 8·7%), O-α-3-*pyridylbenzylideneamino dimethylthiocarbamate* (Ih) (64%), m.p. 92° (from benzene–light petroleum) (Found: C, 63·3; H, 5·3; N, 14·6. $C_{15}H_{15}N_3OS$ requires C, 63·2; H, 5·3; N, 14·7%), O-α-*methyl*-4-*methoxybenzylideneamino dimethylthiocarbamate* (Id) (35%), m.p. 101° (from benzene–light petroleum) (Found: C, 57·2; H, 6·2; N, 11·0. $C_{12}H_{16}N_2O_2S$ requires C, 57·1; H, 6·3; N, 11·1%), O-*bis*-4-*methylphenylmethyleneamino dimethylthiocarbamate* (Ij) (65%), m.p. 108—110° (decomp.) (from benzene–light petroleum) (Found: C, 69·2; H, 6·2; N, 8·8. $C_{18}H_{20}N_2OS$ requires C, 69·2; H, 6·4; N, 9·0%), O-α-*methyl*-4-*chlorobenzylideneamino dimethylthiocarbamate* (If) (44%), m.p. 91—92° (decomp.) (from benzene–light petroleum) (Found: C, 51·7; H, 5·2; N, 10·7. $C_{11}H_{13}N_2ClOS$ requires C, 51·5; H, 5·1; N, 10·9%), and O-α,4-*dimethylbenzylideneamino dimethylthiocarbamate* (Ig) (52%), m.p. 95—96° (decomp.) (from benzene–light petroleum) (Found: C, 61·2; H, 6·8; N, 11·8. $C_{12}H_{16}N_2OS$ requires C, 61·0; H, 6·8; N, 11·9%).

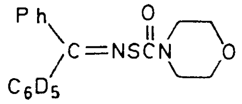

(I)


(II)

a; X = Y = Ph
b; X = Ph, Y = C_6D_5
c; X = Ph, Y = Me
d; X = 4-$MeOC_6H_4$, Y = Me
e; X = 4-$NO_2C_6H_4$, Y = Me
f; X = 4-ClC_6H_4, Y = Me
g; X = 4-MeC_6H_4, Y = Me
h; X = Ph, Y = 3-C_5H_4N
i; X = Y = 4-FC_6H_4
j; X = Y = 4-MeC_6H_4


(IIIa)


(IIIb)


(IIIc)

$Ph_2C=NH$

(IV)

S-*Methyleneamino thiocarbamates*. These were prepared by brief heating of a carbon tetrachloride solution of the appropriate O-ester in the manner described.[1] Thus were prepared the S-esters (IIa), m.p. 144—145° (lit.,[1] 145—146°); (IIc), m.p. 84—86° (lit.,[1] 84—86°), (IIe) m.p. 133° (lit.,[1] 130—132°), and (IIIb), m.p. 111° (lit.,[1] 76—77°). The new S-*esters* (IIi), (75%), m.p. 147° (from benzene–light petroleum) (Found: C, 60·0; H, 4·6; N, 8·5%), (IIh) (81%), m.p. 114° (from benzene–light petroleum) (Found: C, 63·0; H, 5·2; N, 14·7%), (IId) (63%), m.p. 107° (from benzene–light petroleum) (Found: C, 57·4; H, 6·4; N, 11·1%), (IIj) (65%), m.p. 147° (from benzene–light petroleum) (Found: C, 69·4; H, 6·2; N, 8·9%), (IIf) (70%), m.p. 142—143° (from benzene–light petroleum) (Found: C, 51·7; H, 5·1; N, 10·7%), and (IIg) (68%), m.p. 123° (from benzene–light petroleum) (Found: C, 60·9; H, 6·8; N, 11·8%) were also prepared in this way.

Reagents and Solvents.—2′,3′,4′,5′,6′-Pentadeuteriobenzophenone, m.p. 47—48° (lit., 50°) was prepared by an established procedure.[10] Diphenylmethyleneamine, prepared and purified by the method of Pickard and Tolbert,[11] was kindly donated by Dr. B. T. Grayson, and reagent grade sulpholan was purified by successive distillation from permanganate and sodium hydride. Other solvents were of AnalaR grade, distilled before use.

Reaction Kinetics.—Rates of rearrangement of thiocarbamates (I) (*ca.* 10^{-4}M) in solution were determined from the decrease in substrate concentration with time. Concentration assays were obtained from u.v. spectrophotometry at a fixed, predetermined wavelength, generally 255 nm. The reactions were initiated by transference *via* a graduated syringe of the appropriate quantity (*ca.* 0·1 ml) of the substrate solutions to a pre-heated 1 cm cell containing 3·0 ml of solvent in the cell-housing of a Unicam SP 800 spectrophotometer. The cell and contents, after mixing, were maintained at the required temperature in a temperature-controlled bath. The reactions were followed until no further change occurred. All compounds displayed excellent isosbestic points in the time-dependent u.v. spectrum, and the final spectrum obtained in the kinetic runs was identical with that of the pure thiocarbamates (II) (>90% conversion). The Beer–Lambert law was obeyed in all cases. A control reaction in a darkened flask showed no appreciable variation in the rate of rearrangement at a specified temperature. The data of Table 1 display these features for a typical kinetic run.

E.s.r. spectra.—Spectra were recorded on a JEOL MEIX X-band spectrometer fitted with the VT3 temperature control unit. A dilute solution (*ca.* 10^{-2}M) of the appropriate thiocarbamate (I) in oxygen-free carbon tetrachloride was inserted in the pre-heated cavity of the spectrometer. An approximately steady concentration of free radical could then be detected after an initial period of several minutes; the signal persisted for a time critically dependent on the temperature at which the sample was subsequently maintained. Ultimately the signal intensity decayed, and independent checks demonstrated that the onset of decay corresponded to the approach of completion of the rearrangement process (I) ⟶ (II). *g* Values were measured relative to that of diphenylpicrylhydrazyl.

Crossover Experiments.—(a) A mixture of compounds (Ib) (0·040 g, 7·2 × 10^{-4} mol) and (IIIa) (0·043 g, 7·2 × 10^{-4} mol) was dissolved in carbon tetrachloride (10·0 ml) at room temperature. The solution was heated to boiling and maintained at this temperature for 10 min. The solvent was then removed by evaporation. The resulting oil, subjected to preparative t.l.c. [alumina; light petroleum–ether (30 : 70)] yielded two S-ester fractions. The procedure was then repeated exactly for a mixture of compounds (Ib) (0·040 g) and (IIIb) (0·043 g). The analysis of the products by mass spectrometry is discussed below.

(b) The deuteriated thiocarbamate (Ib) (0·040 g) was dissolved in diphenylmethyleneamine (1·0 g), the solution heated to 80°, and maintained at this temperature for 10 min. On cooling, and after the addition of light petroleum–benzene (1 : 1; 4·0 ml), a white solid slowly precipitated.

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[10] N. P. Buu-Hoï and N. Dat Xuong, *Compt. rend.*, 1958, **247**, 654.

[11] P. L. Pickard and T. L. Tolbert, *J. Org. Chem.*, 1961, **26**, 4886.

TABLE 1

Rearrangement of compound (Ia) in hexane at 52·8° in the dark

$[\text{(Ia)}]_{\text{initial}}$ 6·0 × 10^{-5}M; ε_{260} 2·7 × 10^4, ε_{300} 5·5 × 10^3 $[\text{(IIa)}]_{\text{initial}}$ 0·0M; ε_{260} 1·0 × 10^3, ε_{300} 1·2 × 10^3

		260 nm		300 nm	
t/min	Reaction (%)	A_t	$2{\cdot}303\log[(A_0 - A_\infty)/(A_t - A_\infty)] \times 10^2 t^{-1}$	A_t	$2{\cdot}303\log[(A_\infty - A_0)/(A_\infty - A_t)] \times 10^2 t^{-1}$
15	17	1·515	1·32	0·360	1·07
30	30	1·390	1·19	0·415	1·19
45	41	1·275	1·17	0·455	1·17
60	50	1·185	1·15	0·490	1·17
75	57	1·105	1·14	0·520	1·18
90	64	1·040	1·12	0·545	1·19
105	69	0·980	1·13	0·565	1·14
120	74	0·930	1·13	0·580	1·16
135	78	0·890	1·13	0·595	1·17
150	82	0·850	1·15	0·610	1·21
165	85	0·820	1·15	0·615	1·14
180	88	0·790	1·17	0·625	1·16
195	90	0·770	1·17	0·630	1·13
210	92	0·750	1·18	0·640	1·19
225	93	0·735	1·19		
285	97	0·700	1·19		
∞		0·665		0·670	
		k_1	1·16 × 10^{-2} min^{-1}		1·16 × 10^{-2} min^{-1}

Yield of (IIa), based on measured values of ε, *ca.* 92% (k_1, measured by continuous u.v. monitoring, 1·25 min^{-1}).

The mixture was filtered and the residue recrystallized. An identical procedure was then followed for a sample of compound (IIb). Mass spectral analyses of the *S*-esters so obtained are presented below.

DISCUSSION

The aromatic thiocarbamates (I) rearrange thermally in high yield to the isomers (II) upon a short period of reflux in carbon tetrachloride or benzene.[1] The reaction is not purely intramolecular. The simultaneous rearrangement of equimolar quantities of (Ib) and (IIIa) in solution results in the predominant retention of molecular integrity (Scheme 1; Table 2) with a considerable percentage of crossed products also formed. Mixtures of (Ib) and (IIIb), as a control, produce no detectable scrambling, however, on reflux in solution and subsequent analysis by mass spectrometry.

TABLE 2

Mass spectral analyses of products from crossover studies

Reaction precursors	m/e	Fragment	Relative intensity
(Ib) + (IIIa)	284	(IIa)	37
	289	(IIb)	63
(Ib) + (IIIa)	326	(IIIb)	57
	331	(IIIc)	43
(Ib) + (IIIb)	284	(IIa)	(IIa) : (IIb) <0·02
	289	(IIb)	
	326	(IIIb)	(IIIc) : (IIIb) <0·02
	331	(IIIc)	
(Ib) + (IV)	289	(IIb)	85
	284	(IIa)	15
(IIb) + (IV)	289	(IIb)	(IIa) : (IIb) <0·02
	284	(IIa)	

(IIIa) + (Ib)

$\downarrow$

(IIIc) + (IIb) + (IIIb) + (IIa)

(IIIc) : (IIIb) = 0·7; (IIa) : (IIb) = 0·6

(IIIb) + (Ib)

$\downarrow$

(IIIb) + (IIb)

SCHEME 1 Reactions carried out by refluxing in CCl_4 for 10 min.

Consideration of the rearrangement of thiocarbamate (Ib) in 1,1-diphenylmethyleneamine (IV) also suggests that the reaction has intramolecular and intermolecular aspects: the *S*-ester (IIb) predominantly retains the deuterium label, although *ca.* 15% of the unlabelled derivative (IIa) is also formed, demonstrating the incorporation of a solvent molecule at some stage (Table 2; Scheme 2). (IIb) Undergoes no appreciable isotopic exchange in the solvent (IV) under the same conditions.

(Ib) + (IV)

$\downarrow$

(IIb) + (IIa)

(IIa) : (IIb) = 0·18

$\text{(IIb)} \underset{\text{(IV)}}{\not\longrightarrow} \text{(IIa)}$

SCHEME 2 Reactions carried out by heating at 80° for 10 min.

The analogous thermal rearrangement of *O*-phenyl dimethylthiocarbamates (V) to the *S*-phenyl isomers has been shown [12] to proceed *via* intramolecular nucleophilic attack of sulphur on the aromatic ring, involving a σ bonded intermediate (VI). The superficial resemblance of this thiono–thiolo rearrangement to the present study leads to a consideration of a similar nucleophilic attack on the oximino π system to yield the σ bonded intermediate (VII). Clearly, electron-withdrawing substituents attached to the ring or imino-carbon atoms should greatly accelerate the rate of conversion in this case. Variation of the substituent Z in (V), for example, results [12] in a ρ value of +1·92 based on σ^0 values.

The thermal uncatalysed conversion (I) ⟶ (II) in

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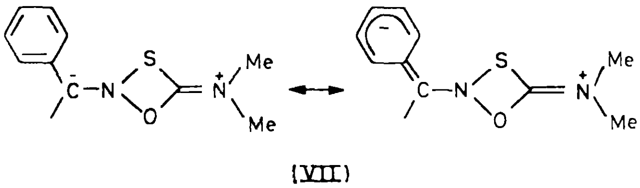
[12] K. Miyazaki, *Tetrahedron Letters*, 1968, 2793.

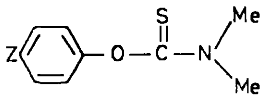
dilute solution (hexane) follows a first-order kinetic expression according to equation (2) (Table 1). Values

$$-\mathrm{d(I)}/\mathrm{d}t = k_1[\mathrm{(I)}]_t \qquad (2)$$

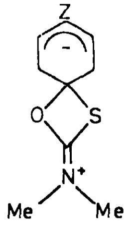
of k_1 for a range of thiocarbamates (I), in hexane solvent at 54°, are listed in Table 3.



(VII)

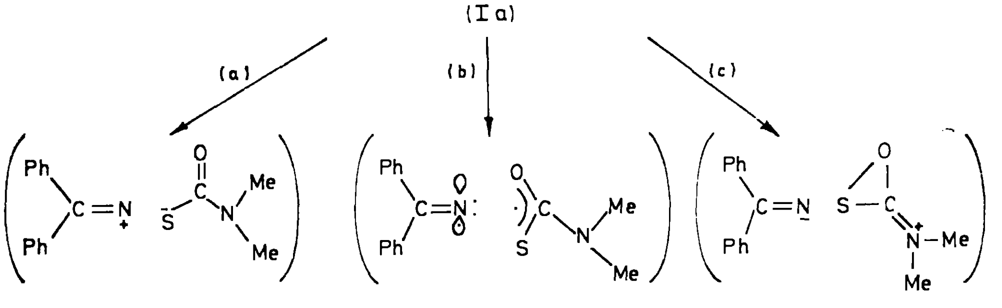


(V)



(VI)

Variation of substituents in the *para*-position of the aromatic ring results in an insignificant rate variation, while replacement of a methyl group at the imino-carbon atom with a phenyl or pyridyl group also results in no significant change in the observed rate. These results are inconsistent with any appreciable excess charge delocalization in the imino π system in the transition state of the reaction, thus excluding nucleophilic attack of sulphur on the imino-nitrogen atom as a major pathway in hexane solvent.



SCHEME 3

The observation of cross products (Scheme 2) suggests some contribution from a step-wise mechanism. Since a nitrogen–oxygen σ bond must be broken during the reaction, ions and radicals generated respectively by heterolysis and homolysis of this bond must now be considered (Scheme 3) as possible reactive intermediates, in line with the incorporation of solvent previously described in Scheme 2. The ion (X) has recently been postulated as a reactive intermediate in an oxidation of thiones.[13]

A reaction pathway which leads to heterolysis [(a) or (c)] must involve considerable charge separation in the transition state, and consequently a large rate enhancement on appreciable increase in solvent polarity. The first-order rate coefficients for rearrangements of thiocarbamates (Ia and c) in solvents of widely varying polarity are recorded in Table 4.*

TABLE 3

Substituent effects on the rate of the rearrangement (I) ⟶ (II) in hexane

Substrate	Aromatic substituent	T/°C	10^2k_1/min^{-1}
(Id)	4-MeO	54·0	4·6
(Ig)	4-Me	54·0	4·8
(Ic)	4-H	54·0	6·0
(If)	4-Cl	54·0	4·2
(Ie)	4-NO_2	54·0	3·0
(Ia)	4,4′-H_2	66·0	5·4
(Ii)	4,4′-F_2	66·0	10·2
(Ij)	4,4′-Me_2	66·0	5·3
(Ia)		54·0	1·5
(Ih)		54·0	1·3

The influence of solvent polarity on the rate is clearly small, and thus the transition state for reaction involves little charge separation. This is consistent with the homolysis pathway (c) (Scheme 3). Moreover an electron-deficient nitrogen atom normally leads to the Beckmann rearrangement, and this is not observed.[1] Homolytic bond fission is supported by the direct detection by e.s.r. spectroscopy of a transient radical[9] maintained at an approximately steady state concentration during the conversion of (Ia) into (IIa) in carbon tetrachloride or benzene. Significantly, an identical spectrum was observed during the thermal rearrangement of (IIIa), although each of the thiocarbamates (Ib—h) produced a spectrum differing substantially in the proton

TABLE 4

Solvent effects on 10^2k_1/min^{-1} at 54°

	Hexane	Sulpholan	Acetonitrile	Ethanol
(Ia)	1·5	0·97	0·78	4·5
(Ic)	6·0	2·2	0·8	11·5

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* In chlorinated hydrocarbons the rate of reaction often did not follow a strict first-order dependence, showing a short induction period followed by fast ' zero-order ' rearrangement.

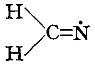
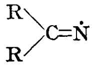
[13] N. H. Nilsson and A. Senning, *Angew. Chem. Internat. Edn.* 1972, **11**, 295.

hyperfine splitting pattern. Iminyl radicals have not been fully characterized by e.s.r. in solution at ambient temperature, although a recent report by Ingold and Mendenhall suggests [14] that a transient radical (a_N 2·89 mT) is an iminyl precursor of di-t-butyliminoxyl. The spectral characteristics of the radicals observed in the present rearrangement are however in agreement with those more commonly attributed to iminyls [15] (a_N *ca.* 1·0—1·5 mT) and not to those corresponding to aromatic iminoxyl radicals [16] (a_N 3·1 mT).

The data of Table 5, therefore, are consistent with the assignment of structure (VIII) (Scheme **3**) to the transient paramagnetic species, in agreement with the above observation on the variations of spectral structure with substrate. The complementary radical (IX) was not detected spectrally, and this therefore provides a novel method of generation of aromatic iminyls in solution for e.s.r. study.[17]

TABLE 5

Spectral parameters of iminyls, and the radical (VIII)

Radical	Medium	a_N/mT	g_{iso}
 [15]	KCl	0·95	
 [16]	Adamantane	0·95—0·97	2·0028
(VIII)	CCl_4	1·02	2·0033

As well as being consistent with radical processes, the exclusion of reaction pathways involving appreciable charge separation also suggests a concerted [1,3] sigmatropic shift as a likely mode for rearrangement. Concerted processes are subject to considerations of orbital symmetry conservation, although the simple predictions of Woodward and Hoffmann [5] have recently been revised [7] for [1,3] sigmatropic processes. Thio-oximes, however, rapidly lose their configurational integrity in solution at ambient temperature,[18] in sharp contrast to oximes.[19] Mechanistic arguments based on the configuration of the isolated products (II) are therefore of no value.

The detection of free radicals by e.s.r. spectroscopy does not of itself necessitate rearrangement occurring *via* a radical pair, but the occurrence of cross-products obviously cannot be explained by a unimolecular concerted process. Further studies on this and related reactions will therefore be reported elsewhere in an attempt to resolve the general problem of competition between concerted and radical pathways in [1,3] sigmatropic shifts, a problem of great difficulty.

One of us (A. J. L.) is grateful to Professor E. A. C. Lucken for the opportunity to work in his laboratories, and also thanks Dr. J. Searle for discussions.

[3/2617 *Received*, 28*th December*, 1973]

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[14] G. D. Mendenhall and K. U. Ingold, *J. Amer. Chem. Soc.*, 1973, **95**, 2963.

[15] M. C. R. Symons, *Tetrahedron*, 1973, **29**, 615; D. E. Wood, R. V. Lloyd, and D. W. Pratt, *J. Amer. Chem. Soc.*, 1970, **92**, 4115.

[16] B. C. Gilbert and R. O. C. Norman, *J. Chem. Soc.* (*B*), 1966, 86.

[17] R. F. Hudson, A. J. Lawson, and E. A. C. Lucken, *J.C.S. Chem. Comm.*, 1972, 721.

[18] C. Brown, B. T. Grayson, and R. F. Hudson, *Tetrahedron Letters*, 1970, **56**, 4925.

[19] O. L. Brady and L. Klein, *J. Chem. Soc.*, 1927, 874.