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MANNICH-TYPE CONDENSATION PRODUCTS OF SULFINIC ACIDS WITH ALDEHYDES AND HYDROXYLAMINES OR HYDROXAMIC ACIDS

AN ESR STUDY OF DERIVED NITROXIDES

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Abstract—Hydroxylamine and some of its derivatives, including hydroxamic acids, have been used as the amine component in Mannich-type condensation reactions with aldehydes and sulfinic acids or thiols. The condensation products have been oxidized to the corresponding nitroxides. The ESR spectra of these nitroxides are reported and interpreted in terms of the structure of these radicals. In several cases the ESR spectra showed alternating line-widths and varied with temperature and solvent.

INTRODUCTION

SULFINIC acids can be used as the acidic component in Mannich-type condensation reactions with aldehydes and primary or secondary amines,[1] (thio)carbamates,[2] carboxamides,[3] sulfonamides[3] or lactams.[3]

$$RSO_2H + R'CHO + HNXY \rightarrow RSO_2\overset{R'}{\overset{|}{C}}HNXY + H_2O \qquad (1)$$

The nature of the amine component is important in determining the possible variation in the aldehyde structure. In the cases of amines, the reaction is restricted to formaldehyde as the carbonyl component but with less nucleophilic bases a variety of aliphatic or aromatic aldehydes may be used successfully. A number of the condensation products have found application as initiators of polymerization reactions[4] and show other interesting chemical[5] and stereochemical[6] properties.

In the present investigation the scope of the reaction (1) has been extended to hydroxylamine and several derivatives, including hydroxamic acid as the amine component. The use of these nitrogen bases as the amine component in Mannich-type reactions finds only limited precedent in the literature.[7]

The condensation products, which are new classes of hydroxylamines, offered the possibility of oxidation to the corresponding nitroxide radicals. Since ESR spectral data provide detailed information on the electronic structure and conformational properties of free radicals, the ESR hyperfine splitting constants of these new classes of nitroxides have been measured and compared.

SYNTHESIS

Hydroxylamine and several derivatives successfully underwent condensation with sulfinic acids and aldehydes. A few reactions with arenethiols, instead of arenesulfinic acids, have also been investigated. The new compounds are recorded in Table 1.

Use of hydroxylamines. Hydroxylamine has been used as the acidic reactant[8,9] in the Mannich-type condensation with formaldehyde and secondary amines, and as the amine component[9–11] only in the reaction with formaldehyde and some CH acidic components.

We found that with an arenesulfinic acid as the active hydrogen reactant and hydroxylamine as the amine component, the condensation reactions with formaldehyde were easily performed in acidic aqueous solutions using formic acid as the catalyst. A rapid reaction occurred at room temperature and crystallization of the condensation product started immediately after mixing the reactants. In all cases the IR spectra of the products (OH stretching at 3450–3510 cm^{-1}; SO_2 stretching at ~1140 and 1320 cm^{-1}) and the PMR spectra (characteristic singlet at ~δ 4·5 ppm for the $SO_2C\underline{H}_2N$ group) showed unequivocally that both H atoms at the N atom of hydroxylamine are replaced to give bis-N-(sulfonylmethyl)hydroxylamines (**1a–1d**).

$$2RSO_2H + 2CH_2O + NH_2OH \rightarrow (RSO_2CH_2)_2NOH + 2H_2O \qquad (2)$$

1a–1d

No reaction products could be obtained by replacing formaldehyde with other aliphatic or aromatic aldehydes. In both respects the behaviour of hydroxylamine resembles aliphatic primary amines.[12,13]

Using N-phenylhydroxylamine with *p*-toluenesulfinic acid and formaldehyde resulted in condensation to give N-phenyl-N-(*p*-tolylsulfonylmethyl)hydroxylamine(**2**) (yield 75%). N-Phenylhydroxylamine resembles aniline[14] in its ability to condense with arenesulfinic acids and formaldehyde. This may be compared with ethyl N-phenylcarbamate[2b] which failed to react with *p*-toluenesulfinic acid and formaldehyde, probably being the result of the further decreased nuleophilicity of the nitrogen atom due to the electronic effect of the ester function.

By replacing hydroxylamine with N-alkylhydroxylamines (e.g. cyclohexyl, isopropyl, t-butyl) no reaction products could be obtained.

Use of benzohydroxamic acid. Benzohydroxamic acid is known[9] to be an active hydrogen component which reacts with formaldehyde and secondary amines to give the N-aminomethylation products.

However, benzohydroxamic acid can also behave as the amine component in a Mannich-type condensation which is illustrated by its reaction with arenesulfinic acids, and formaldehyde at room temperature, with formic acid as catalyst, to give the corresponding N-hydroxy-N-(sulfonylmethyl)benzamides (**4a–4d**).

$$RSO_2H + R'CHO + C_6H_5CONHOH \rightarrow RSO_2\underset{\displaystyle R'}{\underset{|}{C}}HN(OH)COC_6H_5 + H_2O \qquad (3)$$

4a–4d

The condensation products separated as oils after about 12 hr and upon work up became solid products (Experimental).

With *p*-toluenesulfinic acid and benzohydroxamic acid the condensation products with some higher aliphatic aldehydes (R′ = Et, iso-Pr) were isolated (**4e**, 30%; **4f**, 53%). Crystallization of the products started after about 12 hr. Due to their instability no pure reaction products could be isolated from aromatic aldehydes.

Benzohydroxamic acid condensed appreciably more slowly than hydroxylamine, presumably due to the less nucleophilic N atom. In this reaction the hydroxamic acid behaves similarly to the carboxamides[3] in their reaction with sulfinic acids and aldehydes.

The products, **4a–4f**, showed characteristic IR absorption bands at 1600–1640 cm^{-1} (CO str) and ~1140 and 1320 cm^{-1} (SO_2 str) while the OH stretching frequencies (3300–3400 cm^{-1}) were found at a lower value as compared with **1a–1d**.

Use of N-*hydroxybenzenesulfonamide.* Hellmann and Teichmann[9] have reported the use of N-hydroxybenzenesulfonamide as the acidic component in a Mannich-type reaction with formaldehyde and secondary amines.

We found that N-hydroxybenzenesulfonamide can also be used as the basic component as is shown by the condensation with *p*-toluenesulfinic acid and formaldehyde to give **6a** (yield 68%) or with propionaldehyde to give **6b** (yield 80%). The reaction could be carried out at room temperature and crystallization of the products started after several hours. Benzaldehyde failed to give the corresponding product.

$$RSO_2H + R'CHO + C_6H_5SO_2NHOH \rightarrow RSO_2\underset{\displaystyle R'}{\underset{|}{C}}HN(OH)SO_2C_6H_5 + H_2O \quad (4)$$

6a–6d

N-Hydroxybenzenesulfonamide also reacted smoothly with ethanesulfinic acid to give **6c** (yield 46%) and 1-adamantanesulfinic acid to give **6d** (yield 64%).

This reaction can be compared[3] favourably with the condensation of benzenesulfonamide with sulfinic acids and aldehydes.

IR and PMR spectral data were in accordance with the proposed structures and showed characteristic absorptions due to the groups introduced into the N-hydroxybenzenesulfonamide.

Use of arenthiols. An investigation[15, 16] of the reactions of arenethiols with secondary amines and formaldehyde indicates that in general, N-(arylthiomethyl)-N,N-dialkylamines are formed.

With arenethiols, formaldehyde and hydroxylamine using formic acid as catalyst, at 50–70° for several hours, condensation occurs to yield bis-N-(arylthiomethyl)-hydroxylamines (**3a**, 52%; **3b**, 68%).

Benzohydroxamic acid reacts with *p*-toluenethiol and formaldehyde, at 50°, to give N-hydroxy-N-(*p*-tolylthiomethyl)benzamide **5** (yield 68%). Similarly N-hydroxybenzenesulfonamide also reacts with *p*-toluenethiol and formaldehyde, at 50°, but attempts to obtain the analytically pure product were unsuccessful.

Stability and mechanism. Several of the compounds, particularly **2** and the benzohydroxamic acid derivatives (**4a–4f**, **5**) are unstable and slowly decompose at room temperature. When heated in some solvents, e.g. benzene or ethanol, they decompose. Therefore crystallization was carried out at low temperature (Experimental). This type of behaviour in solution may be compared to the instability of N,N-disubstituted aminomethylsulfones which has been attributed[14] to the low nucleophilicity of the sulfinate ions and inductive effects of the N-substituents.

The details of the mechanism of this Mannich-type reaction with hydroxylamine derivatives, aldehydes and sulfinic acids are not known but it is very likely that the first step will be a condensation reaction of the aldehyde with the hydroxylamine

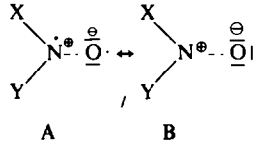
rather than with the sulfinic acid. The reaction rate will depend on such factors[17] as pH, nucleophilicity of the nitrogen atom, nature of aldehyde and ease of crystallization of the condensation products.

NITROXIDE RADICALS DERIVED FROM THE HYDROXYLAMINE CONDENSATION PRODUCTS

The new hydroxylamine derivatives (Table 1) obtained by the Mannich-type reaction described in the preceding section were all converted into the corresponding nitroxide radicals by oxidation with PbO_2 in CH_2Cl_2. ESR hyperfine splitting (hfs) constants and g-values are given in Table 2. The structural assignment of the nitroxides is based on the following evidence: (i) the hyperfine splitting patterns are those expected for the proposed structures (*vide infra*); (ii) a series of hydroxylamines gives, upon oxidation, the expected related ESR spectra and (iii) the preparation of **7b** by using an independent route, i.e. peracid oxidation[18] of bis-(*p*-tolylsulfonylmethyl)amine.

$$(p\text{-}CH_3C_6H_4SO_2CH_2)_2NH \xrightarrow{p\text{-}NO_2C_6H_4CO_3H} (p\text{-}CH_3C_6H_4SO_2CH_2)_2NO^{\cdot} \qquad (5)$$

The relation between the electronic structure of the nitroxide function and the observed ESR spectral data has been the subject of a number of investigations.[19] Generally the unpaired electron delocalization may be described in terms of two resonance structures A and B. It has been shown[20] that the nitrogen hfs constant is dependent on the configuration around the N atom, deviation from planarity of the N-O moiety resulting in a larger a_N value. For nitroxides which have a planar



A B

or approximately planar configuration a_N values were shown[21] to correlate with the spin density at the N atom and are dependent on the inductive and resonance effects of the substituents X and Y. Changes of the spin distribution in the NO group will also be accompanied by variations of the g-values. Since spin-orbit coupling is somewhat larger for oxygen than for nitrogen, an increase of the a_N value will result in a decrease of the g-value.

The results given in Table 2 clearly demonstrate significant effects of the various substituents at the NO group on the ESR spectra of the nitroxides.

The bis-(arylsulfonylmethyl)nitroxides **7a–7d** show smaller a_N values (10·9 gauss) than usually found for dialkylnitroxides (15–16 gauss).[22] This can be attributed to the electron withdrawing effect of the two $ArSO_2CH_2$ groups (polar substituent constant $\sigma^* \sim 1{\cdot}3$)[23] which will favour resonance structure A relative to B.

The four magnetically equivalent β-H atoms of **7a–7d** form a 1:4:6:4:1 quintet with a_{H_β} about 6 gauss (see Fig 1). All the nitroxides described in this paper which possess a CH_2 or CH group attached to the nitroxide function exhibit a_{H_β} values smaller than those expected (on the basis of the McConnell equation[24]) for free rotation about the N–CH_2 or N–CH bond respectively. The occurrence of preferred con-

formations around the N--CH_2 or N--CH bond has been previously observed[25] for a number of nitroxides.

In nitroxide 8, the unpaired electron is delocalized into the phenyl ring. Due to the inductive effect of the arenesulfonyl group the a_N value is 1·1 gauss smaller than that found for ethyl phenylnitroxide.[26] Replacement of the arenesulfonyl groups in

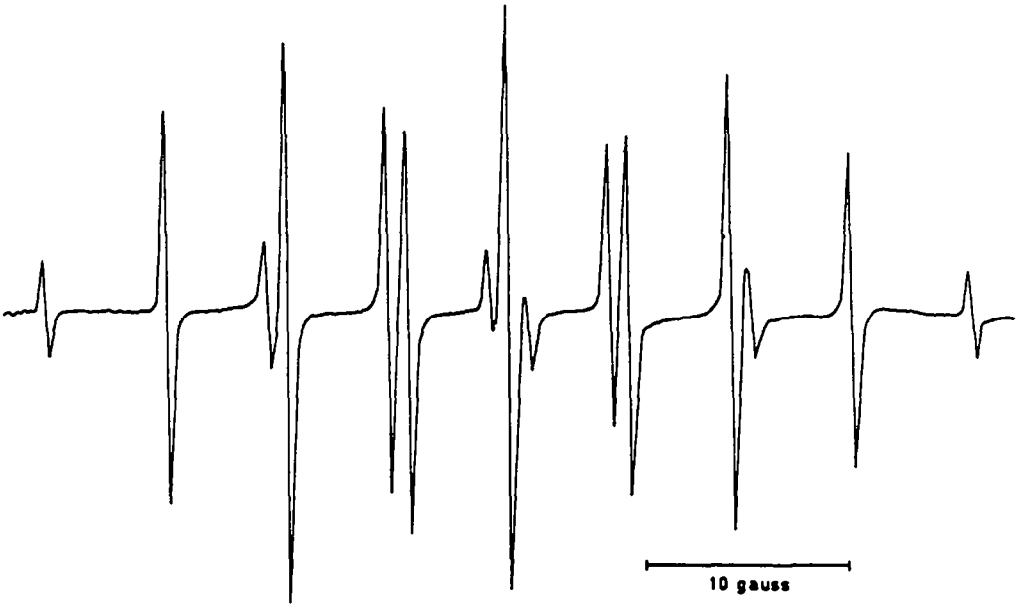
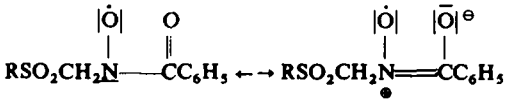


FIG 1. ESR spectrum of bis-(*p*-tolylsulfonylmethyl)nitroxide (**7b**).

7a–7d by arenethio groups (**9a–9b**) results in larger nitrogen hfs constants (a_N = 13·5 gauss) in accordance with the decrease in electron withdrawing ability of the substituents.

The ESR spectra of the benzoylnitroxides **10a–10f** and **11** are characterised by small nitrogen hfs constants ($a_N \sim$ 7·0–7·25 gauss)* indicating a lower spin density on the N atom than is found for **7a–7d** and **9a–9b**. This is supported by a concommitent increase in the *g*-values compared with **7a–7d** or **9a–9b** (*g* = 2·0066–69 and 2·0061 resp). The reduced nitrogen hfs constants can be best reconciled with electron pair delocalization such as C ↔ D which will be favoured over unpaired electron delocalization.[28]



C D

* These a_N values may be compared with those of benzoyl benzylnitroxide (a_N = 7·5 gauss)[27] and benzoyl 1-phenylethylnitroxide (a_N = 7·6 gauss).[27]

This explains why in **10a–10f** the β-sulfonylmethyl moiety is not particularly effective in further lowering the a_N values since the inductive effect of the RSO_2CH_2 group will destabilize resonance structure D.

As is also found for the nitroxides **7a–7d**, very little change in spin density on the N atom is observed as a function of the *p*-substituent in the arenesulfonyl group of **10a–10d**.

The very small β-hydrogen hfs constants for **10e** (a_{H_β} = 1·25 gauss, Fig 2) and **10f** (a_{H_β} = 0·3 gauss) indicates that in the favoured conformation the β-H atom is situated close to the nodal plane of the nitrogen *p*-orbital.[29] These conformational effects may be readily seen from molecular models.

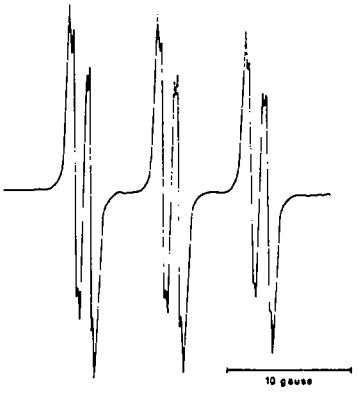


FIG 2. ESR spectrum of benzoyl (1-*p*-tolylsulfonylpropyl)nitroxide (**10e**).

The aryl- and alkylsulfonylmethyl benzenesulfonylnitroxides (**12a–12d**) show appreciably larger nitrogen hfs constants (a_N ~ 10·1–10·4 gauss) than the corresponding benzoylnitroxides (compare **12a** and **10b**; **12b** and **10e**). This is in accordance with a recent study of alkyl and aryl benzenesulfonylnitroxides (**13**) and bis-(benzenesulfonyl)nitroxide (**14**) by De Boer *et al.*[30] The relatively high nitrogen hfs constants (a_N ~ 10–12 gauss) found by them are explained by assuming that the unpaired electron occupies an orbital with increased s-character as compared with acyl- and alkylnitroxides. Our results support this theory. The almost equal a_N values of **7a** and **14** are completely unexpected in view of the sensitivity of the nitrogen hfs constants to electrostatic effects of substituents at the NO function but can be reasonably accounted for in terms of a more pyramidal structure of the nitroxide group in **14** and hence an increase in orbital s-character.

Line-width alternation. Since all nitroxides **7–12** show hindered rotation around the N—CH_β bond, as indicated by the low a_{H_β} values, an alternating line-width effect[31] might be observed. Indeed, at room temperature significant line-width alternation is apparent in the triplet from the β-H atoms of **10a–10d**, **12a**, **12c** and **12d**, due to slow exchange (on the ESR time scale) between two favoured conformations having magnetically nonequivalent β-H atoms. The ESR spectra of **10a** and

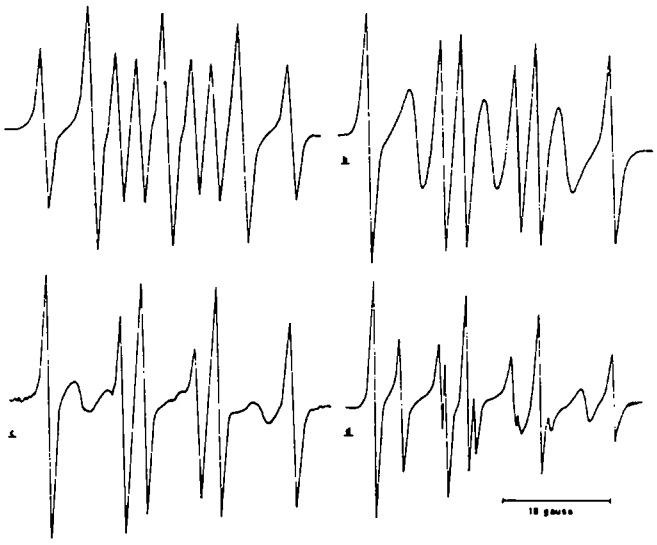


FIG 3. ESR spectra of benzoyl (phenylsulfonylmethyl)nitroxide (**10a**) at (a) +25°, (b) −21°, (c) −81° and (d) −110°.

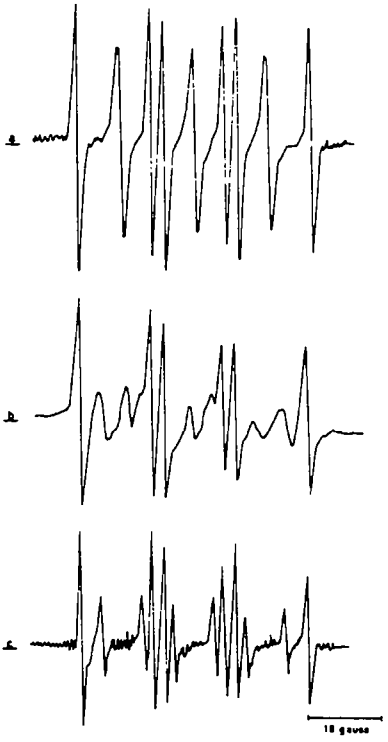


FIG 4. ESR spectra of phenylsulfonyl (*p*-tolylsulfonylmethyl)nitroxide (**12a**) at (a) +25°, (b) −34° and (c) −58°.

TABLE 1

No.	Hydroxylamine	Yield (%)	m.p. °C[a]	C		H		N		S		δ-$SO_2C\underline{H}_2N$[c] or -- $SO_2C\underline{H}N$ (ppm)	IR absorption bands (cm^{-1})
				calc.	found	calc.	found	calc.	found	calc.	found		
1a	$(C_6H_5SO_2CH_2)_2NOH$	42	102–104	49·24	49·00	4·43	4·41	4·11	3·92	18·78	18·81	4·63	3520, 1320, 1145[d]
1b	$(p\text{-}CH_3C_6H_4SO_2CH_2)_2NOH$	38	106–107	52·01	51·91	5·19	5·23	3·80	3·92	17·36	17·45	4·55	3510, 1320, 1145[d]
1c	$(p\text{-}CH_3OC_6H_4SO_2CH_2)_2NOH$	56	95–96	47·86	47·71	4·77	4·91	3·49	3·36	15·90	15·85	4·45	3510, 1345, 1147[d]
1d	$(p\text{-}NO_2C_6H_4SO_2CH_2)_2NOH$	64	108–110	38·97	39·17	3·05	3·27	9·74	9·63	14·88	14·92	4·06	3450, 1350, 1140
2	$C_6H_5(p\text{-}CH_3C_6H_4SO_2CH_2)NOH$	75	79–82	60·63	60·21	5·45	5·46	5·05	4·98	11·56	11·57	4·87	3450, 1310, 1140
3a	$(p\text{-}CH_3C_6H_4SCH_2)_2NOH$	52	45–46	62·91	62·95	6·27	6·36	4·59	4·62	21·00	20·94	4·47	3550[d]
3b	$(p\text{-}BrC_6H_4SCH_2)_2NOH$	68	72–73	38·64	38·37	3·01	2·89	3·22	3·23	14·74	15·01	4·51	3540[d]
4a	$C_6H_5SO_2CH_2N(OH)COC_6H_5$	28	148–149	57·72	57·70	4·50	4·59	4·81	4·81	11·00	10·95	5·25	3310, 1630, 1320, 1150
4b	$p\text{-}CH_3C_6H_4SO_2CH_2N(OH)COC_6H_5$	26	141–141·5	59·01	59·24	4·96	5·24	4·59	4·56	10·50	10·56	5·20	3340, 1635, 1330, 1145[d]
4c	$p\text{-}CH_3OC_6H_4SO_2CH_2N(OH)COC_6H_5$[b]	21	143–143·5	56·07	55·23	4·71	4·75	4·36	4·00	9·98	9·42	5·16	3320, 1635, 1320, 1145
4d	$p\text{-}NO_2C_6H_4SO_2CH_2N(OH)COC_6H_5$	42	148–148·5	50·00	49·82	3·60	3·84	8·33	8·38	9·53	9·24	5·38	3400, 1620, 1330, 1150
4e	$p\text{-}CH_3C_6H_4SO_2CH(C_2H_5)N(OH)COC_6H_5$	30	110·5–111·5	61·24	61·19	5·74	5·67	4·20	4·05	9·62	9·78	5·33–5·78(m)	3400, 1640, 1310, 1138[d]
4f	$p\text{-}CH_3C_6H_4SO_2CH[CH(CH_3)_2]N(OH)COC_6H_5$[b]	53	134·5–135	62·22	61·00	6·09	6·10	4·03	3·97	9·22	9·25	5·35–5·65(m)	3300, 1635, 1315, 1140
5	$p\text{-}CH_3C_6H_4SCH_2N(OH)COC_6H_5$	68	94–95	65·92	65·89	5·53	5·57	5·13	5·02	11·73	11·61	5·12	3200, 1600
6a	$p\text{-}CH_3C_6H_4SO_2CH_2N(OH)SO_2C_6H_5$	50	158–158·5	49·25	49·08	4·43	4·41	4·10	3·93	18·78	18·74	4·53	3370, 1350, 1320, 1168, 1140
6b	$p\text{-}CH_3C_6H_4SO_2CH(C_2H_5)N(OH)SO_2C_6H_5$	80	91·7–92·7	52·01	52·06	5·19	5·18	3·80	3·63	17·35	17·48	4·88–5·16(m)	3310, 1365, 1308, 1170, 1130
6c	$C_2H_5SO_2CH_2N(OH)SO_2C_6H_5$[b]	46	155–155·5	39·84	38·91	4·83	4·84	5·16	4·99	23·63	22·96	4·38	3505, 1365, 1325, 1170, 1135[d]
6d	1-Adamantyl $SO_2CH_2N(OH)SO_2C_6H_5$	64	162–162·5	52·97	52·96	6·01	6·08	3·63	3·60	16·63	16·60	4·39	3400, 1355, 1310, 1175, 1135

[a] Decomposition points. [b] Unstable, difficulties with purifications. [c] PMR spectra recorded in acetone-d_6; **4f** in DMSO-d_6.
[d] IR spectra recorded in CH_2Cl_2 (30 mg/ml) otherwise in Nujol Mulls.

12a have been recorded in CH_2Cl_2 at lowered temperature and are shown in Figs 3 and 4. From the spectra observed in the slow exchange region, the two β-hydrogen h.f.c's could be obtained (**10a**, $-110°$, $a_{H_{\beta_1}} = 2{\cdot}5$, $a_{H_{\beta_2}} = 6{\cdot}0$ gauss; **12a**, $-58°$, $a_{H_{\beta_1}} = 3{\cdot}0$, $a_{H_{\beta_2}} = 8{\cdot}5$ gauss). Since the two forms will be equally populated the equation $a_{H_\beta} = \frac{1}{2}(a_{H_{\beta_1}} + a_{H_{\beta_2}})$ should hold, a condition which is reasonably fulfilled.

Very recently, Jonkman and Kommandeur[32] have presented evidence that the conformational energy barrier may be a property of the solvent rather than of the molecule in those cases where a large "free volume" is associated with the conformational change. Although more extensive studies are required, including the determination of activation parameters, some of our observations may be accounted for by this theory of solvent induced conformational kinetics. Firstly, in the case of **12a** the line-width alternation effect becomes stronger upon increasing viscosity of the solvent ($CS_2 < CH_2Cl_2 <$ mesitylene). Secondly, the observation of line-width alternation for **10b** and the absence of this effect for **11** (both at 20°) is in accordance with the larger "free volume" for conformational change for **10b** as compared with **11**.

TABLE 2. ESR SPECIAL DATA[a] OF NITROXIDE RADICALS OBTAINED FROM HYDROXYLAMINE DERIVATIVES

	Nitroxide	a_N	a_{H_β}	other coupling constants	g-value
7a	$(C_6H_5SO_2CH_2)_2N\text{-}O$	10·9	5·9 (4H)		2·0061
7b	$(p\text{-}CH_3C_6H_4SO_2CH_2)_2N\text{-}O$	10·9	5·8 (4H)		
7c	$(p\text{-}CH_3OC_6H_4SO_2CH_2)_2N\text{-}O$	10·9	6·0 (4H)		
7d	$(p\text{-}NO_2C_6H_4SO_2CH_2)_2N\text{-}O$	10·9	5·9 (4H)		
8	$p\text{-}CH_3C_6H_4SO_2CH_2N(O\cdot)C_6H_5$	10·0	5·38 (2H)	$a_{o,p-H} = 2{\cdot}92$; $a_{m-H} = 0{\cdot}81$	
9a	$(p\text{-}CH_3C_6H_4SCH_2)_2N\text{-}O$	13·5	7·0 (4H)		2·0066
9b	$(p\text{-}BrC_6H_4SCH_2)_2N\text{-}O$	13·5	7·0 (4H)		
10a	$C_6H_5SO_2CH_2N(O\cdot)COC_6H_5$	7·0	4·5 (2H)		2·0066
10b	$p\text{-}CH_3C_6H_4SO_2CH_2N(O\cdot)COC_6H_5$	7·0	4·5 (2H)		
10c	$p\text{-}CH_3OC_6H_4SO_2CH_2N(O\cdot)COC_6H_5$	7·0	4·5 (2H)		
10d	$p\text{-}NO_2C_6H_4SO_2CH_2N(O\cdot)COC_6H_5$	7·0	4·5 (2H)		
10e	$p\text{-}CH_3C_6H_4SO_2CH(C_2H_5)N(O\cdot)COC_6H_5$	7·1	1·25 (1H)	$a_{H'_\beta} = 0{\cdot}25$ (2H)	
10f	$p\text{-}CH_3C_6H_4SO_2CH(HC(CH_3)_2)N(O\cdot)COC_6H_5$	7·1	0·3 (1H)	*b*	2·0069

TABLE 2—*continued*

	Nitroxide	a_N	a_{H_β}	other coupling constants	g-value
11	$p\text{-}CH_3C_6H_4SCH_2N(O\cdot)COC_6H_5$	7·25	4·25 (2H)		2·0071
12a	$p\text{-}CH_3C_6H_4SO_2CH_2N(O\cdot)SO_2C_6H_5$	10·1	6·0 (2H)		2·0064
12b	$p\text{-}CH_3C_6H_4SO_2CH(C_2H_5)N(O\cdot)SO_2C_6H_5$	10·25	1·45 (1H)	$a_{H_\gamma} \approx 0{\cdot}45$ (1H)[c]	
12c	$C_2H_5SO_2CH_2N(O\cdot)SO_2C_6H_5$	10·4	6·2 (2H)		
12d	1-Adamantyl $SO_2CH_2N(O\cdot)SO_2C_6H_5$	10·4	6·0 (2H)		
13	$C_6H_5SO_2N(O\cdot)$-Alkyl[d]	11–12[d]			2·0060
14	$(C_6H_5SO_2)_2N\cdot\leftarrow O$[d]	10·5, 10[d]			

[a] All ESR spectra were obtained in CH_2Cl_2 at 25°. H.f.c's are given in gauss.
[b] a_{H_γ} was not resolved.
[c] H.f.s. of only one of the two magnetically different γ-hydrogen atoms could be resolved.
[d] See Ref 30.

EXPERIMENTAL

The m.ps (to be considered as decomposition points) were determined on a Mettler FP2 apparatus with microscope attachment. Microanalyses were carried out in the Analytical Section of the Department under the direction of Mr. W. M. Hazenberg. PMR spectra were taken on a Varian A-60 spectrometer using TMS ($\delta = 0$) as an internal standard. IR spectra were determined by the normal Nujoll Mull or solution techniques on a Unicam SP200 or Perkin–Elmer Model 125 Grating Infrared Spectrophotometer. The ESR spectra were measured on a Varian E3 apparatus. g-Values were determined using solid 1,1-diphenyl-2-picrylhydrazyl ($g = 2{\cdot}0036$) as an external standard with an accuracy of $\pm 0{\cdot}0002$. The nitroxides were prepared *in situ* by PbO_2 oxidation, at room temp, of diluted (4 mg/ml) solns of the hydroxylamines in CH_2Cl_2. All the nitroxides (except **12c** and **12d**) were stable in solution for at least 2 hr, while the benzoylnitroxides (**10a–10f**) showed unfaded ESR spectra for more than 5 hr.

Commercial sodium benzenesulfinate and sodium p-toluenesulfinate were used. The sodium sulfinates RSO_2Na with R = $p\text{-}CH_3OC_6H_4$,[33] $p\text{-}NO_2C_6H_4$,[34] 1-adamantane,[35] Et[36]; N-phenylhydroxylamine,[37] benzohydroxamic acid[38] and N-hydroxybenzenesulfonamide[39] were prepared by standard procedures.

The condensation products were recrystallized by dissolution in methylene chloride at 25° and subsequent cooling of the soln to −20°. Most of the condensation products tended to decompose slowly at room temp and were stored at −20°. No attempts were made to optimise yields.

Bis-N-(arylsulfonylmethyl)hydroxylamines (**1a–d**)

Hydroxylamine hydrochloride (0·35 g, 0·005 mole) was added to a soln of the appropriate sodium arenesulfinate (0·01 mole) in 10 ml water under an atmosphere of N_2. After the addition of 36% aqueous formaldehyde soln (0·011 mole) the soln was acidified with 4 ml formic acid. Precipitation of the product occurred immediately. After stirring for a further 30 mins the solid was filtered off, washed successively with water and n-hexane, dried and then recrystallized from methylene chloride at −20°.

N-Phenyl-N-(p-tolylsulfonylmethyl)hydroxylamine (**2**)

N-Phenylhydroxylamine (1·1 g, 0·01 mole) was added to a rapidly stirred soln of 1·8 g (0·01 mole) sodium *p*-toluenesulfinate in 20 ml water under an atmosphere of N_2. After the addition of 36% aqueous formaldehyde soln (0·011 mole) the soln was acidified with 5 ml formic acid. An oily product was formed after several min which solidified over a period of about 45 min. Work up of the yellowish solid, as described above for **1a–d**, gave 2·1 g (75%) of the desired product.

Bis-N-(arylthiomethyl)hydroxylamines (**3a, b**)

A mixture of the appropriate arenethiol (0·01 mole), hydroxylamine hydrochloride (0·35 g, 0·005 mole), 36% aqueous formaldehyde soln (0·011 mole) and 3 ml formic acid in 20 ml water, was prepared as described above for **1a–d**, and heated at 70° for 2 hr. The mixture was then cooled to room temp and the solid products worked up as described above for **1a–d**.

N-Hydroxy-N-(alkyl- or aryl-sulfonylmethyl)benzamides (**4a–f**)

Potassium benzohydroxamic acid (1·5 g, 0·01 mole) was added to a stirred soln of the appropriate sodium sulfinate (0·01 mole) in 10 ml water under an atmosphere of N_2. After the addition of 36% aqueous formaldehyde soln (0·011 mole) and 4 ml formic acid the mixture was set aside at room temp for 15 hr. An oily product was obtained which on trituration with n-hexane resulted in the formation of a white solid which was worked up in the usual way.

With compounds **4e** and **4f**, in which propionaldehyde (0·01 mole) and iso-butyraldehyde (0·01 mole) were used respectively, the required products crystallized from the solution after about 12 hr.

N-Hydroxy-N-(p-tolylthiomethyl)benzamide (**5**)

A mixture of *p*-toluenethiol (1·24 g, 0·01 mole), potassium benzohydroxamic acid (1·5 g, 0·01 mole), 36% aqueous formaldehyde soln (0·01 mole) and 5 ml formic acid in 15 ml water was heated at 55° for 1 hr under an atmosphere of N_2; then set aside at room temp for 24 hr. The oily product was extracted with methylene chloride (2 × 15 ml), the combined extracts washed with water, dried over Na_2SO_4, and the solvent evaporated *in vacuo*. The remaining oil was dissolved in the minimum amount of methylene chloride and cooled in a Dry-Ice-acetone bath. Upon the addition of n-hexane to this cold soln a white solid precipitated; this was filtered off and recrystallized from methylene chloride at low temp to give 1·6 g (68%) of **5**.

N-Hydroxy-N-(p-tolylsulfonylmethyl)benzenesulfonamide (**6a**)

N-Hydroxybenzenesulfonamide (1·73 g, 0·01 mole), sodium *p*-toluenesulfinate (1·8 g, 0·01 mole), 36% aqueous formaldehyde soln (0·011 mole), 5 ml formic acid and 10 ml water were mixed under N_2 and the soln set aside at room temp. The first crystals were observed after several hr and crystallization was complete after 12 hrs. Work up as above gave 1·7 g (50%) of the desired product.

With propionaldehyde (0·01 mole) the product **6b** crystallized from the solution after 30 min (yield 80%).

N-Hydroxy-N-(ethylsulfonylmethyl)benzenesulfonamide (**6c**)

From sodium ethanesulfinate (0·01 mole) as described above for **6a**. An oil was produced after several days which was triturated with n-hexane to give a white solid; this was filtered off and recrystallized from methylene chloride to give 1·3 g (46%) of **6c**.

N-Hydroxy-N-(1-adamantylsulfonylmethyl)benzenesulfonamide (**6d**)

To a suspension of 0·225 g (0·0011 mole) of 1-adamantanesulfinic acid in 15 ml of water was added 1·9 ml of 5·8 N NaOH aq to convert the acid into its soluble Na salt. N-Hydroxybenzenesulfonamide (0·19 g, 0·0011 mole), 36% aqueous formaldehyde soln (0·0011 mole) and 3 ml formic acid were added to the soln which was set aside at room temp. Crystallization started after about 4 hr and after 16 hr the yield of **6d** amounted to 0·28 g (69%).

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