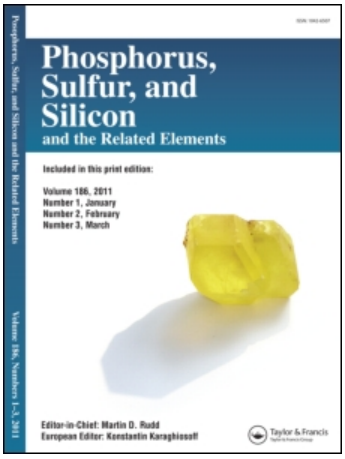

Phosphorus, Sulfur, and Silicon and the Related Elements
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STUDIES IN THE HETEROCYCLIC COMPOUNDS IV[1]. THE REACTIONS OF SULFURYL AZIDE AND CHLOROSULFONYL AZIDE WITH INDOLE AND N-METHYLINDOLE

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STUDIES IN THE HETEROCYCLIC COMPOUNDS IV[1]. THE REACTIONS OF SULFURYL AZIDE AND CHLOROSULFONYL AZIDE WITH INDOLE AND N-METHYLINDOLE.

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Treatment of indole or 1-methylindole with chlorosulfonyl azide gave the 2-chlorosulfonyliminoindoline (**1**) or 2-chlorosulfonylimino-1-methylindoline (**3**). Similar reaction of sulfuryl azide with indole or 1-methylindole gave the 2-azidosulfonyliminoindoline (**2**) or 2-azidosulfonylimino-1-methylindoline (**4**). Catalytic hydrogenation of the iminosulfonyl azides, (**2**) and (**4**), gave the corresponding iminosulfonamides, (**5**) and (**6**). The chlorosulfonyliminoindoline (**3**) reacted with sodium azide, hydrazine hydrate and aniline giving the iminosulfonyl azide (**4**), iminosulfonyl hydrazide (**12**) and iminosulfonyl-N-phenylamide (**13**), respectively. Similar treatment of iminosulfonyl chloride (**1**) with sodium azide and aniline gave, respectively, the iminosulfonyl azide (**2**) and iminosulfonyl-N-phenylamide (**11**). Structural assignments rested on correct elemental analysis, spectroscopic (ir, nmr and ms) as well as chemical evidences.

INTRODUCTION

It is well known that sulfonyl compounds show marked biological activity.[2] In particular, heteroarylsulfonyl derivatives have been shown to have some antifungal and antibacterial activities.[3] Certain sulfonyl- and sufamoyl ureas have been found to be effective oral hypoglycemic agents[4–6] and a number of sulfamoyl azides have been synthesized and their hypotensive activity studied.[7]

Although there have been reported many studies on the reactions of arylsulfonyl azides with indole and 1-methylindole, to give the corresponding 2-arylsulfonyliminoindolines and 2-arylsulfonylimino-1-methylindolines as major products,[8–10] the halogeno- amino- and pseudohalogenosulfonyliminoindolines, which belong to a new type of sulfonyl derivatives, have not been reported in the literature. Thus, the present investigation deals with the reaction of solutions of chlorosulfonyl azide and sulfuryl azide with indole and 1-methylindole, and some reactions of the products, in order to obtain new compounds of potential biological activity.

RESULTS AND DISCUSSION

The following sequence of reactions produces the desired compounds (Scheme 1).

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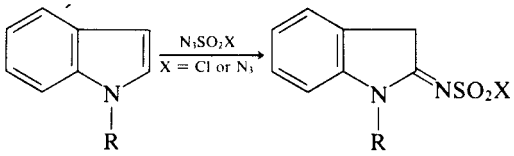
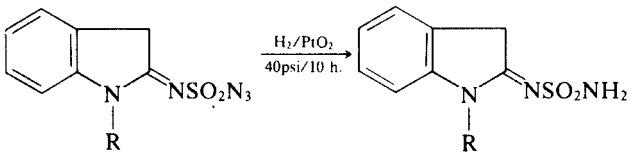
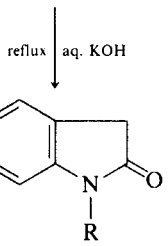


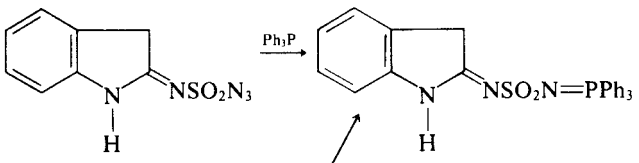
(**1**): R = H, X = Cl
(**2**): R = H, X = N_3
(**3**): R = CH_3, X = Cl
(**4**): R = CH_3, X = N_3



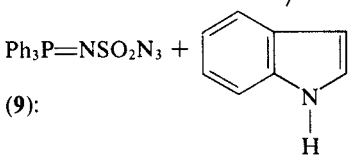
(**5**): R = H
(**6**): R = CH_3



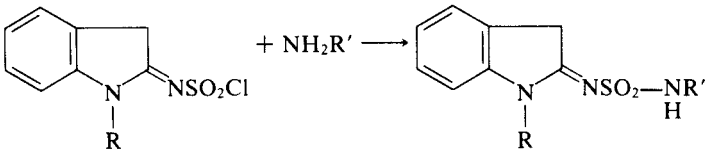
(**7**): R = H
(**8**): R = CH_3



(**10**):



(**9**):



(**11**): R = H, R′ = Ph
(**12**): R = CH_3, R′ = NH_2
(**13**): R = CH_3, R′ = Ph

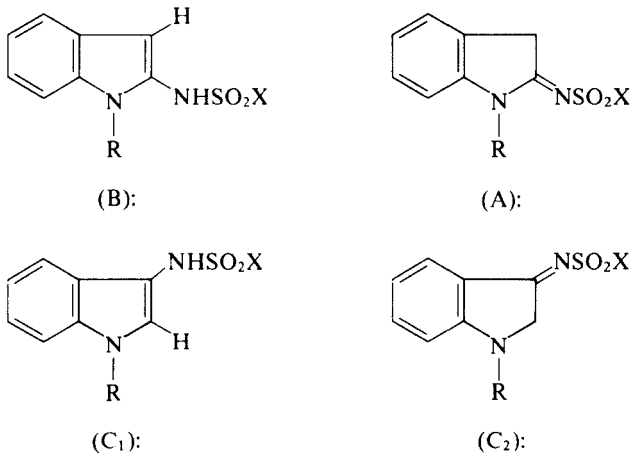
SCHEME 1 Sequence of reactions.

The reaction of chlorosulfonyl azide with indole or 1-methylindole gave the 2-chlorosulfonyliminoindoline (**1**) or 2-chlorosulfonylimino-1-methylindoline (**3**). Similarly, treatment of indole or 1-methylindole with sulfuryl azide gave the 2-azidosulfonyliminoindoline (**2**) or 2-azidosulfonylimino-1-methylindoline (**4**). The reaction of chlorosulfonyl azide with indole and 1-methylindole and of sulfuryl azide with indole were found to proceed smoothly, at 10°C to room temperature, to give compounds (**1**), (**3**) and (**2**), respectively. On the other hand, the reaction of sulfuryl azide with 1-methylindole required heating to about 60°C to give compound (**4**). Platinum oxide catalysed hydrogenation of the azidosulfonyliminoindolines (**2**) and (**4**) afforded the corresponding aminosulfonyliminoindolines (**5**) and (**6**) in high yields.

The chlorosulfonyliminoindoline (**3**) was reacted with sodium azide, hydrazine hydrate and aniline to give the iminosulfonyl azide (**4**), iminosulfono-hydrazide (**12**)[11] and iminosulfonyl-N-phenylamide (**13**), respectively. Similarly, the chlorosulfonyliminoindoline (**1**) reacted with sodium azide and aniline to give, respectively, the iminosulfonyl azide (**2**) and iminosulfonyl-N-phenylamide (**11**). The iminosulfonyl azide (**2**) reacted with triphenyl-phosphine to give the iminophosphorane (**10**). The same compound was obtained from the reaction of azidosulfonylimino-(triphenyl)phosphorane (**9**) (obtained by treating a solution of sulfuryl azide with an equimolar amount of triphenyphosphine in 10% yield) with equimolar amount of indole in *p*-xylene (ir, ms, mp and elemental analysis evidence).

The structures of the compounds are based on correct elemental analysis, comparison with the structures of compounds obtained when indole and 1-methylindole were treated with arenesulfonyl azides[8–10] and spectroscopic data. If we represent these compounds by a general structure such as A, the alternative structures to A could be in the forms B (the tautomeric structure of A), or C_1 or C_2 (Figure 1).

The proton nmr spectra of the compounds exhibited a methylene resonance at δ 4.0–4.20 attributable to the two C-3 protons of structure A. Structures of type C_1 are thus ruled out because the C-2 proton signal, expected to appear at around δ



R = H or CH_3
X = Cl, N_3, NH_2, NHR', N = PPh_3.

FIGURE 1 Possible structural assignments.

7.0[9] for such structures, was absent in all the nmr spectra of the compounds. Also, the contribution of the indole structure of type B is negligible because the signal for the C-3 proton for such structures expected at around δ 5.70[9], was not observed in any of the compounds. In particular, the infra-red spectra of the compounds confirmed the presence of the C=NSO_2 functional group, with strong and broad absorptions at 1545–1590 cm^{-1}.[12] The mass spectra of most of the compounds exhibit parent peaks of varying intensities and fragments at M^+—X and M^+—SO_2X. Specifically, typical fragments were observed at m/e 145, 118 and 91 for the 1-methylsulfonyliminoindolines and at m/e 131, 104 and 77 for the 1-unsubstituted sulfonyliminoindolines[9] (with the appropriate metastable peaks).

Furthermore, the assigned structures were confirmed by aqueous KOH hydrolysis of the compounds giving the oxindoles 7 and 8 in about 40% yields thus ruling out the other structures such as C_1 and C_2. Detailed spectroscopic data are given in the experimental section.

EXPERIMENTAL

All melting points were taken on a Gallenkamp melting point apparatus and are uncorrected. (The mps are taken as the temperature at which the compounds decomposed to black residues). Ir absorption spectra were determined with a Perkin-Elmer 727B spectrometer, using KBr discs. Nmr spectra were determined with a Varian T60 spectrometer in DMSO-d_6[13] using tetramethylsilane as the internal standard. The mass spectra were determined with an AEI MS12 spectrometer at 70 ev. Reagent grade solvents were dried by standard methods and sulfuryl chloride was freshly distilled through an efficient fractionating column (bp 69.0–69.5°C).

Chlorosulfonyl azide.[14]

Finely powdered sodium azide (6.5 g, 100 mmole) was added to acetonitrile (200 ml) in a 500 ml flask and stirred for 1 h. Freshly distilled sulfuryl chloride (13.5 g, 100 mmole) was then added and the flask stoppered and stirring continued for further 20 h. Methylene chloride (200 ml) was added and stirring was continued for 4 h. The precipitated sodium chloride was filtered off and the solution used for the subsequent reactions.

Sulfuryl azide.

This was prepared as described above for chlorosulfonyl azide from 1 mole of sulfuryl chloride and 3 moles of sodium azide.

2-Chlorosulfonyliminoindoline (**1**).

A solution of chlorosulfonyl azide in acetonitrile-methylene chloride (1:1 by volume) (from 100 mmole of sulfuryl chloride) was kept at 10°C. To this solution was added indole (11.7 g, 100 mmole) with stirring and the solution allowed to warm up to room temperature during 2 h. and during which the 2-chlorosulfonyliminoindoline (**1**) separated. Recrystallisation from chloroform-light petroleum (4:1) gave the pure compound (**1**), (13.8 g, 60%),[15] mp 170–172°C (decomp.). Found: C, 41.7; H, 3.2; N, 12.3. $C_8H_7ClN_2O_2S$ requires: C, 41.7; H, 3.1; N, 12.1. IR (KBr): 3180 (NH), 1570 (s, br, C=NSO_2),[12] 1340, 1150 (SO_2) cm^{-1}. Ms showed the molecular ion (M^+, 230, <1%).

2-Azidosulfonyliminoindoline (**2**).

(a) Indole (15.0 g, 128 mmole) was added to a solution of sulfuryl azide in acetonitrile-methylene chloride (1:1 by volume) (from 128 mmole of sulfuryl chloride and 384 mmole of sodium azide) at room temperature. The reaction started within 2 min. with rapid evolution of nitrogen. The reaction mixture was stirred for 8 h. during which some of the azidosulfonyliminoindoline (**2**) separated. More of the compound (**2**) was recovered by concentration of the solution followed by addition of petroleum-ether (bp 40–60°C). The total yield of compound (**2**) was 11.8 g (39%).[15] Recrystallisation from ethanol-light petroleum gave the pure azidosulfonyl derivative (**2**), mp 140–142°C (decomp.). Found: C, 40.6; H, 2.9;

N, 29.8. $C_8H_7N_5O_2S$ requires: C, 40.5; H, 3.0; N, 29.5. ^1H nmr (DMSO-d_6)[13] δ 12.19 (NH, removed by D_2O treatment),[16] 6.91–7.52 (m, 4H, Ar) and 4.23 (s, C-3 (H_2)). MS m/e 237 (M^+, 9.3%), 195 (M^+—N_3, 16.3%) and 131 (M^+—SO_2—N_3, 35.0%). IR (KBr): 3100 (NH), 2140 (N_3), 1585 (s, br, C=NSO_2),[12] 1350, 1145 (SO_2) cm^{-1}.

(b) Compound (**1**) (5.0 g, 22 mmole) and sodium azide (2.1 g, 33 mmole) were added to a dry flask (250 ml), equipped with a reflux condenser and a magnetic stirrer. Acetonitrile (100 ml) was added and the mixture was stirred vigorously and heated at 40–50°C for about 24 h. The mixture was allowed to cool and then poured into water (100 ml) and the precipitate filtered off, washed with water and dried in vacuo. Recrystallisation from ethanol-light petroleum gave the azide (**2**) (85% yield),[15] mp 145–147°C (decomp.), identical (ir, nmr, ms) with the compound prepared in (a).

2-Chlorosulfonylimino-1-methylindoline (**3**).

This compound was prepared as described for compound (**1**), from equimolar amounts of chlorosulfonyl azide and 1-methylindole, yield 35%,[15] mp 160–163°C (decomp.). Found: C, 44.0; H, 3.7; N, 11.6. $C_9H_9ClN_2O_2S$ requires: C, 44.2; H, 3.7; N, 11.4. IR (KBr): 1545 (s, br, C=NSO_2)[12], 1345, 1150 (SO_2) cm^{-1}. Ms m/e 244 (M^+, 5.0%), 209 (M^+—Cl, 4.0%), 180 (M^+—SO_2, 3.6%), 145 (M^+—SO_2—CL, 20.0%).

2-Azidosulfonylimino-1-methylindoline (**4**).

(a) 1-methylindole (13.1 g, 100 mmole) was added to a solution of sulfuryl azide in acetonitrile-methylene chloride (1:1) (prepared from 100 mmole of sulfuryl chloride and 300 mmole of sodium azide) at room temperature. After stirring for 1 h., no reaction occured. It was therefore heated to about 60°C with stirring for 12 h. during which some of the azidosulfonyliminoindoline (**4**) separated. The mixture was cooled and petroleum-ether (bp 40–60°C) added. The precipitate was filtered and recrystallised from chloroform-light petroleum or ethanol-light petroleum to give compound (**4**), (14.6 g, 58%),[15] mp 125–127°C (decomp.). Found: C, 42.9; H, 3.7; N, 28.0. $C_9H_9N_5O_2S$ requires: C, 43.0; H, 3.6; N, 27.9. ^1H nmr (DMSO-d_6)[13] δ 3.41 (s, NCH_3), 4.19 (s, C-3(H_2)), 7.12–7.73 (m, 4H, Ar). IR (KBr): 2142 (N_3), 1565 (C=NSO_2, s, br),[12] 1355, 1160 (SO_2)cm^{-1}. Ms m/e 251 (M^+, 6%), 209 (M^+—N_3, 19%), 145 (M^+—SO_2—N_3, 12%).

(b) Compound (**3**) (5.0 g, 20 mmole) and sodium azide (4.0 g, 60 mmole) in acetonitrile (100 ml) were heated with vigorous stirring at 60°C for 24 h. and worked-up as described for compound (**2**) above. The product was identical (ir, ms, nmr) to compound (**4**) obtained in procedure (a) (90% yield, mp 124–127°C).

2-Aminosulfonyliminoindoline (**5**).

2-Azidosulfonylimioindoline (1.0 g, 4.2 mmole) was dissolved in ethyl acetate (100 ml)) and hydrogenated catalytically (ptO_2) under 40 psi pressure for 15 h., after which the solvent was removed under reduced pressure. The crude 2-aminosulfonyliminoindoline (**5**) was recrystallised from methanol to give the pure compound (0.76 g, 85%),[17] mp 195–197°C (decomp.). Found: C, 45.3; H, 4.3; N, 19.9. $C_8H_9N_3O_2S$ requires: C, 45.5; H, 4.3; N, 19.9. ^1H nmr (DMSO-d_6)[13] δ 11.11(NH), 7.48–6.80 (m, 4H, Ar), 6.53, 6.13 (br, SO_2NH_2, SO_2NH?) 4.0 (s, C-3(H_2)). The three signals at δ 11.11, 6.53 and 6.13 were removed by D_2O treatment.[16] IR (KBr): 3360, 3280 (NH_2), 3100 (br, NH), 1590 (s, br, C=NSO_2),[12] 1360, 1130 (SO_2) cm^{-1}. Ms m/e 211 (M^+, 29.5%), 131 (M^+—SO_2NH_2, 100%).

2-Aminosulfonylimino-1-methylindoline (**6**).

2-Azidosulfonylimino-1-methylindoline (**4**) was catalytically hydrogenated, as described for the preparation of 2-aminosulfonyliminoindoline (**5**), to give compound (**6**), (yield, 88%),[17] mp, 184–185°C (decomp.). Found: C, 47.9; H, 4.7; N, 18.5. $C_9H_{11}N_3O_2S$ requires: C, 48.0; H, 4.9; N, 18.7. ^1H nmr (DMSO-d_6),[13] δ 7.61–6.90 (m, 4H, Ar), 6.62 (s, SO_2NH_2, removed by D_2O treatment),[16] 4.22 (s, C-3(H_2)), 3.33 (s, NCH_3). IR (KBr): 3340, 3270 (NH_2), 1565 (s, br, C=NSO_2),[12] 1375, 1130 (SO_2) cm^{-1}. Ms m/e 225 (M^+, 8.0%), 145 (M^+—SO_2—NH_2, 20%).

2-Phenylaminosulfonyliminoindoline (**11**).

Aniline (1.2 g, 13 mmole) was addeded to a mixture of 2-chlorosulfonyliminoindoline (1.0 g, 4.3 mmole) and chloroform (30 ml) and the mixture refluxed for 2 h. The solvent was evaporated off and the residue washed with water three times and the product recrystallised from methanol to give compound (**11**) (1.1 g, 85%), mp 177–179°C. Found: C, 58.7; H, 4.5; N, 14.5. $C_{14}H_{13}N_3O_2S$ requires; C, 58.5; H, 4.5; N, 14.6. ^{1}H nmr (DMSO-d_6)[13]: δ 9.54 (NH), 7.40–6.80 (m, 9H, Ar), 4.07 (s, C-3(H_2)), 3.40 (br, NH). The signals at δ 9.54 and 3.40 were removed upon treatment with D_2O[16]. IR (KBr): 3390 (w), 3260 (NH), 1585 (s, C=NSO_2)[12], 1370, 1130 (SO_2) cm^{-1}. Ms showed the molecular ion at m/e 287.

2-Phenylaminosulfonylimino-1-methylindoline (**13**).

This compound was prepared as described for compound (**10**) from 2-chlorosulfonylimino-1-methylindoline and aniline in 80% yield. Mp 155–156°C. found: C, 59.7; H, 4.9; N, 14.0. $C_{15}H_{15}N_3O_2S$ requires C, 59.8; H, 5.0; N, 13.9. ^{1}H nmr (DMSO-d_6)[13]: δ 9.34 (NH), 7.43–6.83 (m, 9H, Ar), 4.17 (s, C-3(H_2)), 3.30 (s, NCH_3). IR (KBr): 3280 (NH), 1565 (s, C=NSO_2),[12] 1375, 1130 (SO_2) cm^{-1}. Ms showed the molecular ion at m/e 301.

2-Hydrazinosulfonylimino-1-methylindoline (**12**).

A mixture of 2-chlorosulfonylimino-1-methylindoline (1.0 g, 4.1 mmole) and chloroform (30 ml) was cooled to 0°C and with stirring hydrazine hydrate (0.72 g, 12 mmole) was added dropwise, after which it was stirred for a further 1 h. at 0°C. The mixture was then allowed to warm to room temperature with continuous stirring (1 h.). The precipitate was filtered off, washed with water and dried in vacuo to give the iminosulfonyl hydrazide (**12**). Mp 150°C (eff.). Found: C, 45.0; H, 5.2; N, 23.5. $C_9H_{12}N_4O_2S$ requires: C, 45.0; H, 5.0; N, 23.3. IR(KBr): 3360, 3240 ($NHNH_2$), 1560 (s, br, C=NSO_2),[12] 1375, 1140 (SO_2) cm^{-1}.

2-(Triphenylphosphoranylidene)sulfonyliminoindoline (**10**).

(a) A mixture of 2-azidosulfonyliminoindoline (**2**) (5.0 g, 21 mmole) and triphenylphosphine (5.5 g, 21 mmole) in *p*-xylene (100 ml) was heated at 80–100°C for 24 h. during which a black solid separated. The *p*-xylene was removed and the solid dissolved in methylene chloride and treated with activated charcoal and the solvent removed. The resulting solid was recrystallised from dichloromethane-light petroleum to give compound (**10**), mp 196–198°C (decomp.). Found: C, 66.2; H, 4.6; N, 8.7. $C_{26}H_{22}N_3O_2PS$ requires: C, 66.2; H, 4.7; N, 8.9. IR (KBr): 1610 (br, C=NSO_2),[12] 1440, 1380 (SO_2), 1160, 1120 (SO_2, P=NSO_2) cm^{-1}.

(b) Azidosulfonylimino(triphenyl)phosphorane (**9**) (10.0 g, 26 mmole, prepared from equimolar amounts of triphenylphosphine and sulfuryl azide in 10% yield, mp 149–150°C, lit.[18] mp 145°C) and indole (3.0 g, 26 mmole) in *p*-xylene (40 ml) was heated under reflux for 30 h. to give a brown solid. Work-up as in (a) gave compound (**10**), mp 191–192°C (decomp.) (Found: C, 66.1; H, 4.9; N, 8.8) and was identical with the product obtained in (a) (ir and mass spectra).

REFERENCES AND NOTES

1. Part III: C. A. Obafemi, *J. Organometal. Chem.*, in press.
2. For a review on the sulfones and sulfonamides, see N. Anand in M. E. Wolff (Ed.), "Burger's Medicinal Chemistry", Wiley-Interscience, New York, 1979, Part II, Ch. 13.
3. G. A. Carter, G. W. Dawson and J. L. Garraway, *Pestic. Sci.* **6**, 43 (1975).
4. C. F. Gerber, J. W. McFarland and W. M. McLamore, *J. Med. Chem.*, **8**, 781 (1965).
5. F. J. Marshall and M. V. Sigal Jr., *J. Org. Chem.* **23**, 927 (1958).
6. J. M. McManus, J. W. McFarland, C. F. Gerber, W. M. McLamore and G. D. Laubach; *J. Med. Chem.* **8**, 766 (1965).
7. W. L. Matier, W. T. Comer and D. Deitchman, *J. Med. Chem.* **15**, 538 (1972).
8. A. S. Bailey, M. C. Churn and J. J. Wedgwood, *Tetrahedron Letters*, 5953 (1968).
9. A. S. Bailey, A. J. Buckley, W. A. Warr and J. J. Wedgwood, *J. Chem. Soc.* Perkin I, 2411 (1972). Of course, the C-2 proton absorption at around δ 7.0 could be obscured in the aromatic region which appeared as a multiplet, however, integration showed the C-2 proton signal to be absent.

10. J. M. Peach and A. S. Bailey, in R. B. Mitra, N. R. Ayyangar, V. N. Gogte, M. Acheson and N. Cromwell (Eds.), "New Trends in Heterocyclic Chemistry", Elsevier Scientific Publishing Company, 1979, p. 56.
11. In another experiment, when the reaction of chlorosulfonyl azide with 1-methylindole was carried out for 24 h. and the solid product that separated was treated directly with hydrated hydrazine, a good yield of 1-methyloxindole hydrazone was obtained. IR (nujol): 3320, 3200, 3070 (NH_2, NH), 1600 (C=N). Ms m/e 161 (M^+, 100%), 145 (M^+—NH_2, 14.0%), 131 (M^+—NNH_2, 68.0%). The oxindole hydrazone is probably formed by hydrolysis of the 2-chlorosulfonylimino-1-methylindoline, initially formed, to 1-methyloxindole which then reacts with the hydrazine, or the hydrazine is reacting directly with the 2-chlorosulfonyliminoindoline.
12. G. L'abbe and J-P Dekerk, Tetrahedron Letters, 3213 (1979).
13. The DMSO-d_6 contains about 20% $CDCl_3$ as 100% DMSO-d_6 reacted and decomposed some of the compounds.
14. J. Griffiths, *J. Chem. Soc.* (*C*), 3191 (1971).
15. The yields of the compounds were not optimized.
16. Shaking with D_2O for a long time also led to exchange of protons at C-3 and disappearance of the signals at around δ 4.15.
17. The yield is based on the starting iminosulfonyl azide.
18. D. E. Arrington, J. Chem. Soc. (Dalton Trans.), 1221 (1975).