ANTITUBERCULOSIS AGENTS

PART VII.* 4,4′-DIPYRIDYL SULPHONE AND RELATED COMPOUNDS

BY A. M. COMRIE AND J. B. STENLAKE

From The School of Pharmacy, The Royal College of Science and Technology, Glasgow

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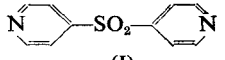
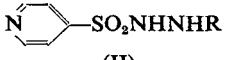
Pyridine-4-sulphinic acid, 4,4′-dipyridyl sulphone and other related 4-pyridyl sulphides and 4-pyridyl sulphones have been prepared.

BOTH 2,2′-dipyridyl sulphone (Dewing, Gray, Platt and Stevenson, 1952) and 3,4′-dipyridyl sulphone (Goldberg and Teitel, 1954) are known, but 4,4′-dipyridyl sulphone (I), the analogue of dapsone (4,4′-diaminodiphenyl sulphone), has not been investigated. Although, Ochai, Itai, and Yoshino (1944) prepared 4,4′-dipyridyl sulphide 1,1′-dioxide and 4,4′-dipyridyl sulphone 1,1′-dioxide, no attempt was made to convert the latter to 4,4′-dipyridyl sulphone. The synthesis of this and other related sulphones is now reported.

In a recent investigation of sulphonyl analogues of isoniazid and cognate compounds attempts to prepare *N*-alkyl derivatives (II, R = alkyl) were unsuccessful (Comrie and Stenlake, 1958b). Condensation of the sodio derivative of pyridine 4-sulphonhydrazide (II, R = H) with benzyl chloride gave benzyl 4-pyridyl sulphone (III, R = H) in some 10 per cent yield instead of the required 1-benzyl-2-pyridine-4′-sulphonylhydrazine (II, R = $C_6H_5CH_2$). Sulphone formation could be readily explained



(I)



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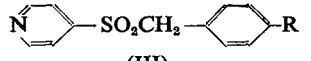


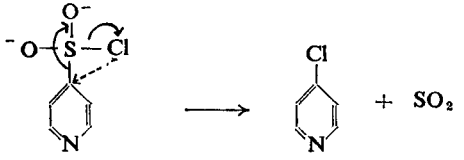
(III)

assuming decomposition of the pyridine-4-sulphonhydrazide to sodium pyridine-4-sulphinate (McFadyen and Stevens, 1936), and condensation of the latter with the alkyl halide. Since a similar condensation of sodium pyridine-3-sulphinate with 4-bromopyridine had already been reported in the preparation of 3,4′-dipyridyl sulphone (Goldberg and Teitel, 1954), the isolation of pyridine-4-sulphinic acid was attempted.

Pyridine-4-sulphonhydrazide is unstable even in cold aqueous solution (Comrie and Stenlake, 1958b), but at 40° decomposition was accompanied by a brisk evolution of gas, and on pouring the resulting acidic solution into acetone pyridine-4-sulphinic acid was obtained as yellow needles. It was characterised by analysis, by formation of a sodium salt and by oxidation to pyridine-4-sulphonic acid (Comrie and Stenlake, 1958a). Condensation of the sodium sulphinate and benzyl chloride gave the same benzyl sulphone still in poor yield. Attempted condensations with 4-chloropyridine to obtain 4,4′-dipyridyl sulphone (I), however, gave only a dark blue non-crystalline product either with the reactants alone or in the presence of a trace of iodine and copper as catalyst (Burton and Davy, 1947).

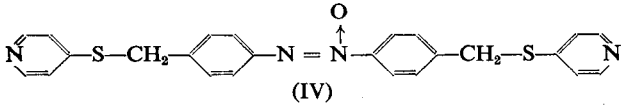
* Part VI, Comrie, Mital and Stenlake, *J. med. pharm. Chem.*, 1960, **2**, 171–177.

Oxidation of 4,4′-dipyridyl sulphide was next considered. This substance had been obtained by King and Ware (1939) as a by-product in the chlorination of pyrid-4-thione during an attempt to prepare pyridine-4-sulphonamide *via* pyridine-4-sulphonyl chloride. The latter is thermolabile (King and Ware, 1939; Comrie and Stenlake, unpublished work) decomposing to give sulphur dioxide and 4-chloropyridine, with cleavage of the C–S bond as depicted by Kwart and Miller (1958).



4,4′-Dipyridyl sulphide is therefore almost certainly formed from unreacted pyrid-4-thione and 4-chloropyridine formed by the above desulphonation, a general method for sulphide formation. Direct condensation of pyrid-4-thione and 4-chloropyridine gave 4,4′-dipyridyl sulphide in good yield (71 per cent). Oxidation of the sulphide with hydrogen peroxide in glacial acetic acid gave only starting material, and a viscous liquid from which no crystalline product could be isolated. Potassium dichromate, as used in the oxidation of 2,2′-dipyridyl sulphide (Dewing, Gray, Platt and Stephenson, 1942), was also unsuccessful, but with cold potassium permanganate in dilute acetic acid oxidation proceeded smoothly to give 4,4′-dipyridyl sulphone in 72 per cent yield, the manganese dioxide formed during the reaction being removed by the addition of 30 per cent hydrogen peroxide (Takahashi, Shibasaki and Uchibayashi, 1954). Removal of manganese dioxide with sulphur dioxide (King and Ware, 1939) proved unsatisfactory probably due to overheating during evaporation of the solution to dryness (Burton and Davy, 1947).

Condensation of benzyl chloride and pyrid-4-thione, followed by oxidation of the resulting benzyl 4-pyridyl sulphide with potassium permanganate gave benzyl 4-pyridyl sulphone in greatly improved yield (60 per cent). Pyrid-4-thione and *p*-nitrobenzyl bromide gave the expected sulphide which was readily oxidised to 4-nitrobenzyl-4′-pyridyl sulphone (III, R = NO_2). Reductions of both 4-nitrobenzyl-4′-pyridyl sulphide and sulphone at a platinum catalyst were anomalous, and gave products possessing none of the properties of primary aromatic amines. The nitro-sulphide gave 4,4″-azoxybenzyl-4′-pyridyl sulphide (IV), characterised by analysis, formation of a dipicrate, and ultra-violet absorption spectrum, whilst the nitro-sulphone gave 4-hydroxylaminobenzyl-4′-pyridyl sulphone (III, R = NHOH). The latter structure was



(IV)

assigned on the basis of the hydrogen uptake (2 moles), analysis, and its ability to reduce ammoniacal silver nitrate in the cold. Similar incomplete

catalytic hydrogenations of aromatic nitro compounds are known, as for example that of 2-nitrofluorene to 2,2′-azoxyfluorene (Campbell and Temple, 1957), and 4-nitroquinoline-1-oxide to 4-hydroxylaminoquinoline-1-oxide (Ochiai, Ohta and Nomura, 1957). As with this latter compound, the insolubility of 4-hydroxylaminobenzyl 4′-pyridyl sulphone made a molecular weight determination impracticable. The partial hydrogenations described above probably follows from the low solubility of the isolated products, which are deposited from solution as the reaction proceeds. 4-Aminobenzyl-4′-pyridyl sulphide and 4-aminobenzyl-4′-pyridyl sulphone (III, R = NH_2) were obtained by reduction of the corresponding nitro compounds using iron powder and hydrochloric acid in boiling ethanol (Campbell and Temple, 1957). Both compounds were pale yellow when freshly prepared but on standing the colour intensified. Toxicity associated with the NH_2 group can often be decreased by acylation and Schiff base formation, without seriously reducing antibacterial activity (Buttle, Dewing, Foster, Gray and Stephenson, 1938), hence the acetyl derivatives (which are more stable) and several Schiff bases of the amino sulphide and amino sulphone were prepared.

Biological Results

We are indebted to Dr. S. R. M. Bushby of the Wellcome Research Laboratories for the *in vitro* examination of 4,4′-dipyridyl sulphide and sulphone, 4-acetylaminobenzyl-4′-pyridyl sulphide and sulphone, 4-aminobenzyl-4′-pyridyl sulphide, 4,4″-azoxybenzyl 4′-pyridyl sulphide against *Myco. tuberculosis* var. *hominis* H37Rv in Peizer and Schecter medium, and in presence of 33 per cent lysed blood. None of the compounds showed significant tuberculostatic activity compared with isoniazid.

The chemical similarity of pyridine-4-sulphinic acid and *p*-aminobenzoic acid prompted an examination of the former as an antimetabolite. We wish to express our thanks to Dr. E. O. Morris of the Microbiology Department of this College for screening this compound against a selection of Gram-positive and Gram-negative organisms. Antibacterial activity was negligible at concentrations below 1 in 1,000.

Experimental

Melting points, which are uncorrected, were determined on a hot-stage microscope. We wish to thank Mr. W. McCorkindale, Dr. A. C. Syme and Miss M. Buchanan for the micro-analyses.

Pyridine-4-sulphinic acid. A solution of pyridine-4-sulphonhydrazide (0·865 g.) in water (5 ml.) was heated on a water bath at 40° to 50° until effervescence ceased (*ca.* 10 min.). The yellow acidic solution was slowly added to acetone (100 ml.) and left at room temperature for several hr. *Pyridine-4-sulphinic acid* (0·45 g., 63 per cent) separated as yellow needles, m.p. 140–141° after washing with acetone and drying *in vacuo*. Found: C, 42·6; H, 3·7; N, 9·6; S, 21·9 per cent. Equiv. (titration) 145. $C_5H_5NO_2S$ requires C, 42·0; H, 3·5; N, 9·8; S, 22·4 per cent. Equiv. 143.

Sodium pyridine-4-sulphinate. Pyridine-4-sulphinic acid (0·72 g.) was suspended in ethanol (10 ml.) and a solution containing sodium (0·12 g.) dissolved in ethanol (10 ml.) added. The mixture was gently warmed till homogeneous and the alcohol removed under reduced pressure. The residue was washed with ethanol (2 ml.) and crystallised from ethanol to give sodium pyridine-4-sulphinate (0·58 g., 68 per cent) as small white needles. Found: Na, 13·7 per cent. $C_5H_4NO_2S$ Na requires Na, 13·9 per cent.

Pyridine-4-sulphonic acid. An aqueous solution of pyridine-4-sulphinic acid was treated dropwise with 30 per cent hydrogen peroxide until the yellow colour was discharged. The solution was concentrated and diluted with ethanol to give pyridine-4-sulphonic acid m.p. 330° (decomp.) on standing. (Comrie and Stenlake (1958a) give pyridine-4-sulphonic acid m.p. 333°, decomp.).

Benzyl 4-pyridyl sulphone (method a). Pyridine-4-sulphinic acid (0·72 g.) in ethanol (10 ml.) was converted into a solution of the sodium salt as before and benzyl chloride (0·63 g.) in ethanol (10 ml.) added. The mixture was refluxed on a water bath for 3 hr., concentrated progressively, and sodium chloride removed by filtration until the product (0·12 g., 10 per cent) m.p. 169–170° crystallised (Comrie and Stenlake (1958b) give m.p. 169–170°). *Picrate*, needles m.p. 190–191° (from methanol). Found: C, 46·6; H, 3·3; N, 11·6 per cent. $C_{18}H_{14}N_4O_9S\frac{1}{2}CH_3OH$ requires C, 46·4; H, 3·4; N, 11·7 per cent.

4,4′-Dipyridyl sulphide. Pyrid-4-thione (5·55 g.) in hot ethanol (40 ml.) was allowed to react with 4-chloropyridine (prepared by the method of Wibaut and Brockman, 1939) (5·7 g.) in ethanol (15 ml.). The deep-orange coloured solution was heated on a water bath till pale-yellow (*ca.* 15 min.), cooled and left overnight at 0°. The yellow crystals were separated and a further yield of crude product obtained by concentrating the filtrate. The crude solid was dissolved in water (10 ml.) basified with 20 per cent sodium hydroxide and extracted with ether (3 × 50 ml.) each extract being washed with water (5 ml.). The combined ether solution was dried ($CaCl_2$) and filtered, and the ether removed leaving a red oil which quickly set to a crystalline mass in a vacuum desiccator. Recrystallisation from light petroleum (b.p. 40–60°) gave 4,4′-dipyridyl sulphide (6·7 g., 71 per cent) as colourless needles m.p. 72°. Found: C, 63·6; H, 4·3; N, 14·9 per cent. Calc. for $C_{10}H_8N_2S$, C, 63·8; H, 4·3; N, 15·0 per cent. *Dipicrate* needles m.p. 228° (from methanol). Found: C, 40·9; H, 2·5; N, 18·0 per cent. Calc. for $C_{22}H_{14}N_8O_{14}S$, C, 40·9; H, 2·2; N, 17·3 per cent. (King and Ware (1939) give 4,4′-dipyridyl sulphide m.p. 72° and dipicrate m.p. 229°).

4,4′-Dipyridyl sulphone. 4,4′-Dipyridyl sulphide (1·88 g.) was dissolved in cold 20 per cent acetic acid (20 ml.) and 5 per cent potassium permanganate slowly added shaking after each addition, until an excess of reagent was considered to be present (*ca.* 35 ml. of reagent was added over a period of 45 min.). The mixture was left for a few hr. at room temperature and the precipitated manganese dioxide removed by the careful addition of 30 per cent hydrogen peroxide. The white solid

remaining suspended in the solution was removed by filtration and washed with water. The filtrate was neutralised with dilute ammonia, extracted with ether (4 × 50 ml.) filtered, and the ether solution dried (KOH). The volume was reduced to 10 to 15 ml. and the ether decanted from more solid which had separated. The solids were combined and crystallised from water to give 4,4′-*dipyridyl sulphone* (1·42 g.) as beautiful long lustrous needles m.p. 145°. Found: C, 54·5; H, 3·7; N, 12·4; S, 15·1 per cent. $C_{10}H_8N_2O_2S$ requires C, 54·6; H, 3·7; N, 12·7; S, 14·5 per cent. The ether was taken down to dryness leaving a pale-yellow oil (0·2 g.) which solidified on standing. Recrystallisation from light petroleum (b.p. 40–60°) gave 4,4′-dipyridyl sulphide m.p. 72° (mixed m.p. with starting material undepressed). The yield of 4,4′-dipyridyl sulphone allowing for recovery of unchanged starting material, 72 per cent.

4,4′-*Dipyridyl sulphone dihydrochloride.* Mixing cold ethanolic solutions of 4,4′-dipyridyl sulphone and hydrogen chloride, and washing the white crystalline solid with ethanol gave the *dihydrochloride* m.p. 138° (decomp.). Found: C, 41·4; H, 3·9; N, 9·5 per cent. $C_{10}H_{10}Cl_2N_2O_2S$ requires C, 41·0; H, 3·4; N, 9·6 per cent. The *monopicrate* separated in needles m.p. 175–176° on mixing methanolic soutions of 4,4′-dipyridyl sulphone and picric acid. Found: C, 42·7; H, 2·6; N, 15·6 per cent. $C_{16}H_{11}N_5O_9S$ requires C, 42·8; H, 2·5; N, 15·6 per cent.

Benzyl 4-*pyridyl sulphide hydrochloride.* A mixture of pyrid-4-thione (0·555 g.) and benzyl chloride (0·63 g.) in ethanol (15 ml.) was refluxed for 10 min. and the solution concentrated till crystallisation commenced. On standing *benzyl* 4-*pyridyl sulphide hydrochloride* (0·76 g., 64 per cent) separated. It was washed with ether and crystallised from ethanol in needles m.p. 196–198°. Found: C, 59·8; H, 4·6 per cent. $C_{12}H_{12}ClNS$ requires C, 60·6; H, 5·1 per cent. *Benzyl* 4-*pyridyl sulphide* was liberated from the hydrochloride by addition of dilute ammonia and extracted into ether (50 ml.). The ether was removed and the residue crystallised from aqueous ethanol to give the *product* (0·55 g., 54 per cent) as needles or prisms m.p. 70–71°. Found: C, 71·8; H, 5·8; N, 6·9 per cent. Calc. for $C_{12}H_{11}NS$, C, 71·6; H, 5·5, N, 7·0 per cent. (Stevenson, Cranham Cummings and Brookes (1956) give m.p. 69–71°). *Picrate* needles m.p. 170° (from methanol). Found: C, 50·4; H, 3·3; N, 12·8 per cent. $C_{18}H_{14}N_4O_7S$ requires C, 50·2; H, 3·3; N, 13·0 per cent.

Benzyl 4-*pyridyl sulphone* (*method b*). Benzyl 4-pyridyl sulphide (0·201 g.) in 20 per cent acetic acid (10 ml.) was oxidised with 5 per cent potassium permanganate as described under 4,4′-dipyridyl sulphone. The brown solid remaining suspended in solution after removal of manganese dioxide, was filtered washed with water and crystallised from ethanol (charcoal) giving glistening plates of *benzyl* 4-*pyridyl sulphone* (0·14 g., 60 per cent) m.p. 169–170°. Melting point when mixed with the product obtained in *method a*, undepressed. Picrate m.p. 190–191°.

4-*Nitrobenzyl* 4′-*pyridyl sulphide hydrobromide.* Pyrid-4-thione (1·11 g.) and *p*-nitrobenzyl bromide (2·16 g.) in ethanol (50 ml.) was refluxed on a water bath for 10 min. and the solution concentrated till crystallisation commenced. Recrystallisation of the solid which had separated

on standing for several hr., gave *4-nitrobenzyl 4′-pyridyl sulphide hydrobromide* (2·8 g., 85 per cent) as pale-yellow needles m.p. 220–221°. Found: C, 44·7; H, 3·8; N, 8·0 per cent. $C_{12}H_{11}BrN_2O_2S\frac{1}{2}C_2H_5OH$ requires C, 44·6; H, 4·0; N, 8·0 per cent.

4-Nitrobenzyl 4′-pyridyl sulphide. The hydrobromide obtained in the previous experiment was dissolved in warm water (50 ml.) and the solution made alkaline with dilute ammonia. The solid separating was filtered, washed with water and the filtrate extracted with ether (4 × 50 ml.). The ether was removed and the residue combined with the solid obtained on basifying with ammonia. Recrystallisation from methanol gave 4-nitrobenzyl 4′-pyridyl sulphide (2·0 g.) as pale yellow needles or prisms m.p. 98°. Found: C, 58·6; H, 4·3; N, 11·3 per cent. Calc. for $C_{12}H_{10}N_2O_2S$, C, 58·6; H, N, 4·1; 11·4 per cent. (Stevenson and others (1956) give m.p. 97–98·5°). Yield (calculated on pyrid-4-thione) 81 per cent. *Picrate*, needles m.p. 198–199° (from methanol). Found: C, 45·7; H, 2·8; N, 14·3 per cent. $C_{18}H_{13}N_5O_9S$ requires C, 45·5; H, 2·8; N, 14·7 per cent.

4-Nitrobenzyl 4′-pyridyl sulphone. 4-Nitrobenzyl 4′-pyridyl sulphide (1·23 g.) was dissolved in 33 per cent acetic acid (30 ml.) and oxidised with potassium permanganate as before. Addition of 30 per cent hydrogen peroxide gave a light brown precipitate which recrystallised from ethanol (charcoal) giving long pale-yellow needles of *4-nitrobenzyl 4′-pyridyl sulphone* (0·82 g., 59 per cent) m.p. 185–186°. Found: C, 52·0; H, 3·7; N, 10·0 per cent. $C_{12}H_{10}N_2O_4S$ requires C, 51·8; H, 3·6; N, 10·1 per cent. *Picrate*, needles m.p. 191° (from methanol). Found: C, 42·8; H, 2·6; N, 13·4 per cent. $C_{18}H_{13}N_5O_{11}S$ requires C, 42·7; H, 2·6; N, 13·8 per cent.

4,4″-Azoxybenzyl 4′-pyridyl sulphide. 4-Nitrobenzyl 4′-pyridyl sulphide (0·82 g.) in ethanol (100 ml.) was hydrogenated at room temperature and atmospheric pressure using Adams' platinum oxide catalyst (50 mg.) till no further uptake of gas occurred. The solid which had crystallised from solution was redissolved by boiling and the catalyst removed by filtration. The solvent was removed under reduced pressure and the residue recrystallised from a large volume of ethanol to give *4,4″-azoxybenzyl 4′-pyridyl sulphide* (0·5 g., 68 per cent) as orange needles m.p. 206–208°. Found: C, 65·1; H, 4·9; N, 12·5 per cent. $C_{24}H_{20}N_4OS_2$ requires C, 64·9; H, 4·5; N, 12·6 per cent. *Dipicrate* m.p. 210–212° (from ethanol). Found: C, 47·8; H, 3·2; N, 15·2 per cent. $C_{36}H_{26}N_{10}O_{15}S_2$ requires C, 47·9; H, 2·9; N, 15·5 per cent.

4-Aminobenzyl 4′-pyridyl sulphide. Finely divided iron powder (1·0 g.) was added to a boiling solution of 4-nitrobenzyl 4′-pyridyl sulphide(1·23g.) in ethanol (80 ml.). Concentrated hydrochloric acid (10 ml.) was added dropwise over a period of *ca.* 30 min. and the mixture refluxed for a further 1½ hr. before taking down to dryness under reduced pressure. The residue was dissolved in water (10 ml.), made alkaline with dilute ammonia and extracted with ether (4 × 50 ml.). The ethereal solution was filtered and concentrated till crystallisation commenced. On standing *4-aminobenzyl 4′-pyridyl sulphide* (0·51 g., 48 per cent) separated as pale-yellow glistening plates, m.p. 167–168° when dried *in vacuo*. Found:

C, 66·6; H, 5·4; N, 12·9 per cent. $C_{12}H_{12}N_2S$ requires C, 66·7; H, 5·6; N, 13·0 per cent. *Monopicrate* rosettes m.p. 170° (dried at 100°) (from ethanol). Found: C, 48·8; H, 3·8; N, 15·5 per cent. $C_{18}H_{15}N_5O_7S$ requires C, 48·5; H, 3·4; N, 15·7 per cent.

4-*Acetylaminobenzyl 4′-pyridyl sulphide.* 4-Aminobenzyl 4′-pyridyl sulphide (0·216 g.) was dissolved in acetic anhydride (2 ml.) and heated on a water bath for 5 min. The solvent was removed under reduced pressure and the solid residue recrystallised from methanol (charcoal) to give 4-*acetylaminobenzyl 4′-pyridyl sulphide* (0·165 g., 64 per cent) as long needles m.p. 157°. Found: C, 64·8; H, 5·6; N, 10·7 per cent. $C_{14}H_{14}N_2OS$ requires C, 65·1; H, 5·5; N, 10·85 per cent. *Picrate* needles m.p. 179° resolidifying in spikes and remelting at 199° (from ethanol). Found: C, 49·7; H, 4·2; N, 14·2 per cent. $C_{20}H_{17}N_5O_8S\frac{1}{2}C_2H_5OH$ requires 49·4; H, 4·0; N, 13·7 per cent.

4-*Hydroxylaminobenzyl 4′-pyridyl sulphone.* 4-Nitrobenzyl 4′-pyridyl sulphone (0·93 g.) was dissolved in ethanol (150 ml.) by the aid of heat. The solution was cooled and hydrogenation carried out as described under 4,4″-azoxybenzyl 4′-pyridyl sulphide. The catalyst was removed as before and on concentrating the filtrate the *product* separated as a yellow micro-crystalline solid (0·51 g., 58 per cent) which did not melt below 330°. Found: C, 54·9; H, 4·5; N, 10·5 per cent. $C_{12}H_{12}N_2O_3S$ requires C, 54·5; H, 4·6; N, 10·6 per cent.

4-*Aminobenzyl 4′-pyridyl sulphone.* 4-Nitrobenzyl 4′-pyridyl sulphone (0·93 g.) was reduced with iron powder and concentrated hydrochloric acid in boiling ethanol as described under 4-aminobenzyl 4′-pyridyl sulphide and the reaction mixture concentrated till solid started to separate. After standing for several hr. the solid was removed and washed liberally with ethanol. It was suspended in water (10 ml.) made alkaline with dilute ammonia and extracted with ether (4 × 50 ml.). The ether solution was filtered and the volume reduced to *ca.* 100 ml. On standing the *product* separated as the hemihydrate in pale-yellow shining needles m.p. 159–160°. Yield, 0·39 g., 42 per cent. Found: C, 56·25; H, 5·4; N, 11·2 per cent. $C_{12}H_{12}N_2O_2S\frac{1}{2}H_2O$ requires C, 56·0; H, 5·1; N, 10·9 per cent. The *dipicrate* separated in sheaves m.p. 174–175° (decomp.) (from ethanol). Found: C, 41·3; H, 3·1; N, 14·2 per cent. $C_{24}H_{18}N_8O_{16}SC_2H_5OH$ requires C, 41·5; H, 3·2; N, 14·9 per cent.

4-*Acetylaminobenzyl 4′-pyridyl sulphone.* 4-Acetylaminobenzyl 4′-pyridyl sulphide (0·258 g.) was dissolved in 33 per cent acetic acid (35 ml.) and oxidised with potassium permanganate as described under 4-nitrobenzyl 4′-pyridyl sulphone, giving 4-*acetylaminobenzyl 4′-pyridyl sulphone* (0·14 g., 48 per cent) as shining needles of the hemihydrate m.p. 210–211°. Found: 56·6; H, 5·1; N, 9·4 per cent. $C_{14}H_{14}N_2O_3S\frac{1}{2}H_2O$ requires C, 56·2; H, 5·05; N, 9·4 per cent. The same product was obtained in 42 per cent yield by acetylating 4-aminobenzyl 4′-pyridyl sulphone by the method described under 4-acetylaminobenzyl 4′-pyridyl sulphide. *Picrate* prisms m.p. 200–201° (from methanol). Found: C, 45·8; H, 3·3; N, 13·4 per cent. $C_{20}H_{17}N_5O_{10}S$ requires C, 46·2; H, 3·3; N, 13·5 per cent.

The following Schiff bases were prepared by mixing methanolic solutions containing equimolecular proportions of 4-aminobenzyl 4′-pyridyl sulphide and the appropriate carbonyl compound, and recrystallising the product from methanol.

Yields are given in parenthesis.

4-*Benzylideneaminobenzyl 4′-pyridyl sulphide*, aggregates of pale-yellow prisms m.p. 158–159° (89 per cent). Found: C, 75·7; H, 5·4; N, 9·25 per cent. $C_{19}H_{16}N_2S$ requires C, 75·0; H, 5·3; N, 9·2 per cent.

4-(o-*Hydroxybenzylideneamino*)*benzyl 4′-pyridyl sulphide*, orange-yellow needles m.p. 197–198° (washed with methanol) (69 per cent). Found: C, 71·7; H, 5·4; N, 8·6 per cent. $C_{19}H_{16}N_2OS$ requires C, 71·25; H, 5·0; N, 8·75 per cent.

4-(p-*Hydroxybenzylideneamino*)*benzyl 4′-pyridyl sulphide* (commences to char *ca.* 240° but does not melt below 340°) small pale-yellow prisms (75 per cent). Found: C, 71·45; H, 5·2; N, 9·1 per cent. $C_{19}H_{16}N_2OS$ requires C, 71·25; H, 5·0; N, 8·75 per cent.

Schiff bases of 4-aminobenzyl 4′-pyridyl sulphone were similarly prepared.

4-*Benzylideneaminobenzyl 4′-pyridyl sulphone*, glistening pale-yellow plates m.p. 208–209° (85 per cent). Found: C, 67·75; H, 4·9; N, 8·6 per cent. $C_{19}H_{16}N_2O_2S$ requires C, 67·8; H, 4·8; N, 8·3 per cent.

4-(o-*Hydroxybenzylideneamino*)*benzyl 4′-pyridyl sulphone*, pale-yellow shining plates m.p. 206–207° (77 per cent). Found: C, 65·3; H, 4·6; N, 8·4 per cent. $C_{19}H_{16}N_2O_3S$ requires C, 64·8; H, 4·6; N, 8·0 per cent.

4-(p-*Hydroxybenzylideneamino*)*benzyl 4′-pyridyl sulphone hemihydrate*, bright-yellow prisms m.p. 182–183° (80 per cent). Found: C, 63·1; H, 5·15; N, 8·6 per cent. $C_{19}H_{16}N_2O_3S\frac{1}{2}H_2O$ requires C, 63·2; H, 4·7; N, 7·8 per cent.

4-*Cinnamylideneaminobenzyl 4′-pyridyl sulphone hemihydrate* yellow shining plates m.p. 193° (75 per cent). Found: C, 67·9; H, 5·2; N, 7·7 per cent. $C_{21}H_{18}N_2O_2S\frac{1}{2}H_2O$ requires C, 67·9; H, 5·15; N, 7·5 per cent.

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