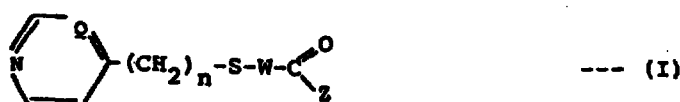


SPECIFICATION Pyridine and Pyrimidine Intermediates

This invention relates to certain pyridines and pyrimidines substituted at the 4-position with a thio-ether-containing sidechain. It is a divisional from our copending application No. 8032971.

- 5 These pyridines and pyrimidines are useful intermediates in the preparation of certain pyridine and pyrimidine anti-inflammatory and immunoregulatory agents as described and claimed in the said copending application.

According to the invention there are provided compounds of the formula:—



- 10 wherein

n is 1 or 2;

W is methylene or methylene substituted with either a methyl or phenyl group;

Z is hydroxy, (C₁—C₄) alkoxy, hydrogen, methyl, phenyl or —O[⊖] (alkali metal)[⊕];

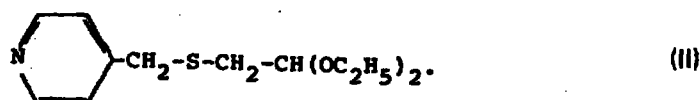
Q is CH or N;

- 15 with the provisos that (a) when Z is phenyl, W is other than methylene substituted by phenyl and (b) when Q is CH and n is 1, Z is other than hydroxy, (C₁—C₄) alkoxy and —O[⊖] (alkali metal)[⊕].

The compounds within proviso (b) are described in British Patent Specification No. 1,434,271 (E. R. Squibb & Sons) as intermediates in the preparation of certain cephalosporin end products.

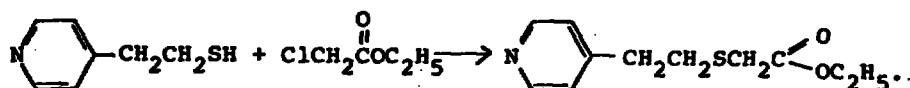
- 20 In the preferred compounds of the formula (I), either:— Q is CH, n is 1 and W is methylene (Z is preferably hydrogen in this case); or Q is N, n is 1, W is methylene and Z is methyl or phenyl; or Q is N, n is 1, W is phenyl-substituted methylene and Z is (C₁—C₄) alkoxy.

The invention also includes the acetal of the formula:—

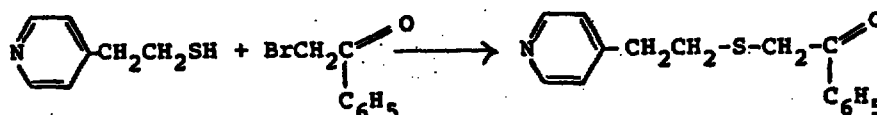
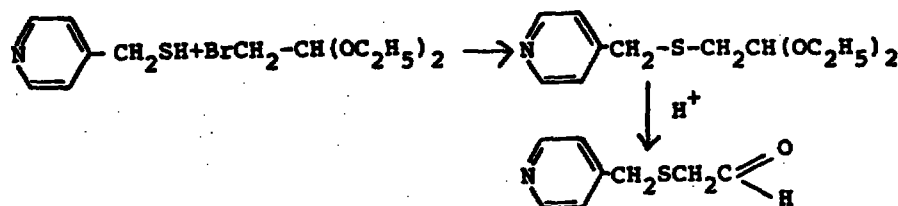
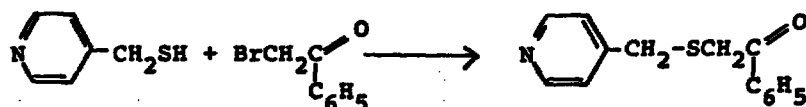


- 25 A variety of convenient methods are available for the preparation of the pyridines of the present invention. The methods are enumerated as follows:

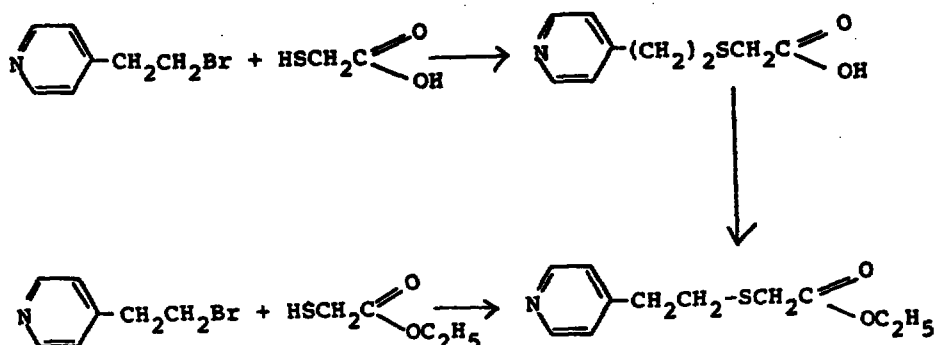
(1) Reaction of 2-(4-pyridyl)ethyl mercaptan with an alphahaloacid or ester. For example:



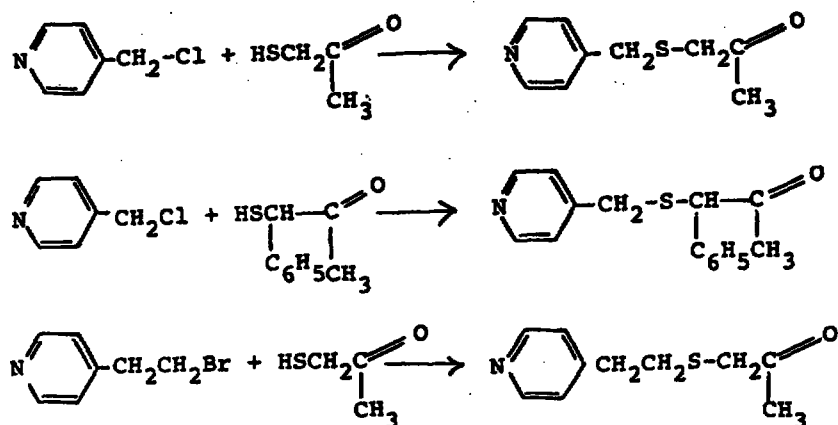
- 30 (2) Reaction of 4-picolyl mercaptan or 2-(4-pyridyl)ethyl mercaptan with an alpha-haloketone or alpha-haloaldehyde (preferably protected as the acetal), followed by deprotection if necessary. For example:



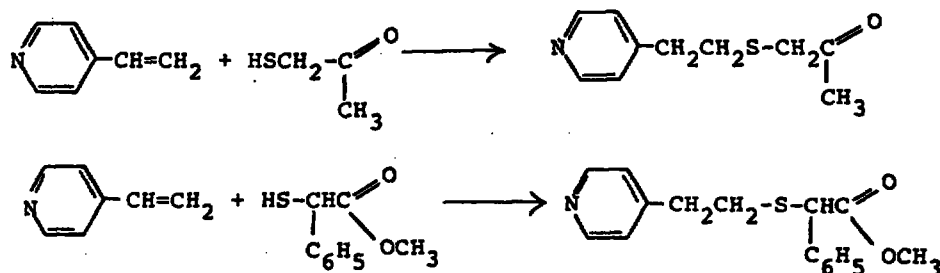
(3) The reaction of 2-(4-pyridyl)-ethyl halide with an alpha-mercapto acid or alpha-mercapto ester. For example:



(4) The reaction of 4-picolyl halide or 2-(4-pyridyl) ethyl halide with an alpha-mercapto ketone. For example:



(5) Addition of mercaptoesters or mercaptoketones to 4-vinylpyridine. For example:



Preparation methods (1) to (4) in all cases involve a reaction in which the halogen of an organic halide is replaced by an organic thio residue. The reaction is facilitated by using an equivalent of strong base to convert the mercaptan to anionic salt, which is much more efficient in converting the organic halogen to the thio ether. When an acid salt of the pyridine moiety (e.g. 4-picolyl chloride hydrochloride) or an acid (e.g. alpha-mercapto propionic acid) is employed as one of the reactants, a compensating amount of base is added. A wide variety of solvents are suitable for this reaction, including alcohols, acetonitrile, dimethylformamide, etc., the only requirement being that the solvent be inert towards reactants and product, and that the reactants have some degree of solubility.

Preferably, the solvent should be less acidic than the mercaptan, so as to facilitate formation of the thio anion. The temperature employed for this reaction is not critical (e.g. 0—120°C.). It should be high enough to provide a reasonable rate, but not so high as to lead to undue decomposition. As is well known in the art, rate will vary with the nature of the organic halide (rate: I>Br>Cl), the structure of both the halide and the mercaptan, and the solvent. The reaction time should be such that the reaction is nearly complete (e.g. >95% conversion when equivalent amounts of halide and mercaptan are employed) to maximize yields (e.g. 1 hour to several days). These reactions are readily monitored by thin layer chromatography, employing one of a variety of commercially available silica gel plates containing an ultraviolet indicator. Suitable eluants are chloroform/methanol mixtures with the

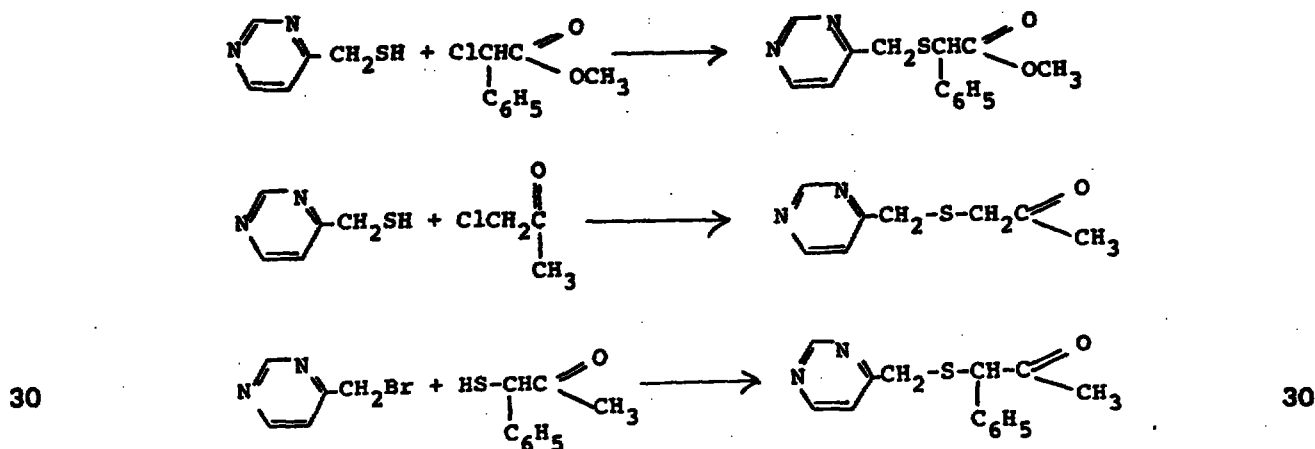
proportion of these solvents varied with the polarity of the reaction product, a practice well-known in the art. For most of the reactions of this type, an eluant consisting of 9 parts of chloroform and 1 part of methanol is well suited. For the more polar compounds the proportion of methanol is increased (e.g. 4 chloroform/1 methanol). It is sometimes advantageous to add up to 5% acetic acid to the eluant,

5 particularly when dealing with acid addition salts. Ethyl acetate and other alcohols (e.g. butanol) as well as a proportion of water can also be employed in the eluant. As the reaction proceeds, an equivalent of strong acid is produced, neutralizing the mole of base used in the reaction. For this reason pH can also be used as an aid in monitoring this reaction.

10 The method (5), addition of mercaptans to 4-vinylpyridine is carried out under conditions of temperature and solvent which correspond to those for the replacement of organic halogen by organic thio radical as discussed above. In this case also, suitable reaction times can be determined by use of the same thin layer chromatography systems.

The starting materials required for methods (1)–(5) are quite generally available from the literature or commercially. Aliphatic mercaptans can be prepared from the corresponding halides by reaction of the halide with thiourea to form the isothiuronium salt followed by basic hydrolysis (see 15 Preparations 1 and 2 below), by reaction of organic halides with hydrogen sulfide or alkali metal hydrosulfide [e.g. mercaptoacetone, Hromatka *et al.*, Monatsh. 78, 32 (1948)], or by hydrolysis of thiol esters [e.g. 2-methoxyethylmercaptan, 2-mercapto-1-propanol, alpha-mercapto-alpha-phenylacetone [Chapman *et al.*, J. Chem. Soc., 579 (1950); Sjöberg, Ber. 75, 13 (1942); von Wacek *et al.*, Ber 75, 20 1353 (1942)], while the only aromatic mercaptan required as a starting material for this invention, 2-mercaptophenol, is available commercially. Organic halides required as starting materials are also generally available commercially or in the literature. Typical methods for making the required halides are direct halogenation, action of hydrogen or phosphorous halides on an alcohol, or addition of hydrogen halides to epoxides. The requisite reagents, including hydride reducing agents and Grignard 25 reagents, are available commercially.

The same convenient methods are available for the preparation of the pyrimidine alcohols, ethers and esters of the present invention. For example:



The present invention is illustrated by the following Examples.

Example 1

By following the methodology of Examples 1–4, of our copending application No. 8032971 4-picolyl chloride hydrochloride is reacted with 1-phenyl-1-mercaptoacetone [von Wacek *et al.*, Ber. 75, 1353 (1942)] to yield 1-(4-picolylthio-1-phenylacetone, and with mercaptoacetone to yield 4-picolylthioacetone.

Furthermore 4-picolyl chloride hydrochloride or 4-picolyl bromide hydrobromide is converted to the free base by rendering the salt basic in ethanol, and then reacting with sodium or potassium cyanide (1.05 equivalents) to form the corresponding nitrile. The nitrile is solvolyzed in ethanol with aqueous hydrochloric acid to form ethyl 4-picolylacetate [cf. Rising *et al.*, J. Am. Chem. Soc. 50, 1211 (1928)]. 40 The latter is reduced with Red-al in benzene-tetrahydrofuran and isolated by the method of Examples 9 and 10 of the said copending application, yielding 2-(4-pyridyl)ethanol. The alcohol is converted to corresponding chloride by reaction with thionyl chloride in refluxing methylene chloride [cf. Gilman *et al.*, Rec. trav. chim. 51, 93 (1932)]. The 2-(4-pyridyl)ethyl chloride hydrochloride which forms is 45 isolated by evaporation.

Using the procedures of Examples 1 to 4 of the said copending application, 2-(4-pyridyl)ethyl chloride is reacted with methyl mercaptoacetate (preferably in methanol rather than ethanol solution) to yield methyl 2-[2-(4-pyridyl)ethylthio]acetate and with mercaptoacetone to yield 2-(4-pyridyl)ethylthioacetone.

Example 2**Sodium 2-(4-Picolylthio)propionate**

Sodium methoxide (5.1 g., 94 mmoles) was dissolved in 50 ml. of absolute ethanol and cooled in an ice bath. A slurry of 4-picolyl chloride hydrochloride (5.0 g., 30.4 mmoles) in 45 ml. of ethanol was added and the chilled reaction mixture stirred for approximately 10 minutes. Finally, 2-mercaptopropionic acid (3.23 g., 30.4 mmoles) dissolved in 5 ml. of ethanol was added over a 10 minute period. The mixture was allowed to warm to room temperature and stirred overnight (approximately 16 hours). The reaction was filtered through filter aid to remove salts, carbon treated and concentrated to crude sodium 2-(4-picolylthio)propionate (approximately 7 g. of oil used directly in the next step).

Example 3**Sodium Phenyl(4-picolylthio)acetate**

Sodium methoxide (6.8 g., 0.124 mole) was dissolved in 150 ml. of ethanol and cooled to 0°C. A solution of alpha-mercatophenylacetic acid (7.0 g., 0.042 moles) in 50 ml. of ethanol was added over a period of 5 minutes to the cold methoxide solution. After 5 minutes, a slurry of 4-picolyl chloride hydrochloride (6.83 g., 0.042 moles) slurried in 50 ml. of ethanol was then added over 5 minutes. The reaction was removed from the ice bath and left to stir for approximately 60 hours. The reaction mixture was filtered and evaporated to yield sodium phenyl(4-picolylthio)-acetate (11.8 g.); waxy solid; ir: 3.0, 6.1, 6.25, 7.3, 13.6 μ used directly in the next step.

By the method of Examples 2 and 3, 4-picolyl chloride hydrochloride is reacted with mercaptoacetic acid to yield sodium 2-(4-pyridylmethylthio)acetate.

Example 4**4-Picolylthioacetone**

Under a nitrogen atmosphere, sodium methoxide (2.6 g., 48 mmoles) was dissolved in 40 ml. of ethanol and cooled in an ice bath. 4-Picolyl mercaptan (6.0 g., 48 mmoles) in 40 ml. of ethanol was added over 5 minutes, followed by the addition of chloroacetone (4.5 g., 48 mmoles) in 25 ml. of ethanol over 5 minutes. After stirring for an additional 15 minutes to 0—5°C., the reaction mixture was allowed to warm to room temperature and stirred for approximately 65 hours. To isolate the product, the reaction was filtered through diatomaceous earth and the mother liquor evaporated to yield crude product as an oil (8.3 g.). The entire crude was chromatographed on 480 g. of silica gel with chloroform as eluant. Once the desired product began to come off the column, 2% methanol was added to the chloroform eluant. Product fractions were combined and concentrated to an oil. Finally dissolution in ethyl acetate, drying over anhydrous magnesium sulfate and reconcentrating gave purified 4-picolylthioacetone (4.91 g., m/e calcd.: 181, found: 181, 138, 124, 92, 65, 43; ir (KBr): 5.8, 6.2, 7.05, 12.25 μ).

Example 5**Alpha-(4-picolylthio)acetophenone**

Under a nitrogen atmosphere, sodium methoxide (0.81 g., 15 mmoles) was dissolved in 17.9 ml. of stirring absolute ethanol, and cooled in an ice bath. 4-Picolyl mercaptan (1.88 g., 15 mmoles) in 3 ml. of absolute ethanol was added dropwise over approximately 5 minutes, followed by alpha-bromoacetophenone (3.05 g., 15 mmoles) in 10 ml. of warm absolute ethanol added over approximately 10 minutes. The stirring reaction mixture was warmed to room temperature and left to stir for 17 hours. Salts were removed by filtration through diatomaceous earth, and the solids repulped for 0.5 hour with additional ethanol and refiltered. The ethanol filtrates were combined and concentrated to yield a waxy solid. The waxy solid was taken up in approximately 11 volumes of diethyl ether, treated with activated carbon, filtered and the mother liquor concentrated to a solid (1.90 g.). Recrystallization from diethyl ether/hexane gave purified alpha-(4-picolylthio)acetophenone (1.25 g. in two crops, m.p. 55—59°C., ir (KBr): 5.92, 6.18, 7.00, 7.76, 9.78, 12.38, 13.70 μ).

Analysis: Calcd.: C₁₄H₁₃ONS:

Found: C, 69.11 H, 5.39; N, 5.76; m/e 243.
C, 69.07; H, 5.47; N, 5.70; m/e 243.

Yields are improved by combining the ether dissolution-carbon treatment-concentration step with the ether-hexane recrystallization step.

Example 6**Alpha-(4-picolylthio)propiophenone**

Under a nitrogen atmosphere, sodium methoxide (0.80 g., 11 moles) was dissolved in approximately 15 ml. of stirring ethanol and cooled in an ice bath. 4-Picolyl mercaptan (1.4 g., 11

mmoles) in approximately 3 ml. of absolute ethanol was added over 5 minutes and the mixture stirred for 15 minutes. Alpha-bromopropiophenone (2.4 g., 11 mmoles) in approximately 15 ml. of absolute ethanol was then added over 5 minutes. The reaction mixture was warmed to room temperature and stirred for approximately 16 hours. The reaction mixture was filtered and the filtrate evaporated to an oil, which was chromatographed on 100 g. of silica gel, with chloroform as eluant, to yield purified alpha-(4-picolylthio)-propiophenone [2.17 g.; oil; ir (CHCl₃): 3.5, 6.0, 6.25, 6.95, 7.05, 10.55; mass spectra: m/e calcd.: 257, found: 251, 197, 152, 134, 105; pnmr/CHCl₃/TMS)τ: 8.5 (d, 3H), 6.4 (s, 2H), 5.7 (q, 1H), 2.8, 2.6, 2.1, 1.5 (all multiplets, 9H)].

By following the method of Examples 4—6, 4-picolyl mercaptan is reacted with bromoacetaldehyde diethyl acetal (followed by acid catalyzed hydrolysis) to yield 4-picolylthioacetaldehyde.

Furthermore, by following this method 2-(4-pyridyl)ethyl mercaptan is reacted with ethyl 2-chloropropionate to yield ethyl 2-[2-(4-pyridyl)ethylthio]propionate, with methyl 2-phenyl-2-bromoacetate to yield methyl 2-phenyl-2-[2-(4-pyridyl)ethylthio]acetate, with alpha-bromoacetophenone to yield alpha-[2-(4-pyridyl)ethylthio]acetophenone, and with chloroacetone to yield 2-(4-pyridyl)-ethylthioacetone.

Example 7

By the method of Example 26 of the said copending application, 4-vinylpyridine is reacted with mercaptoacetone to yield 2-(4-pyridyl)ethylthioacetone, and with methyl 2-mercaptoacetate (preferably in methanol rather than ethanol solution) to yield methyl 2-[2-(4-pyridyl)ethylthio]acetate.

Example 8

By the method of Example 27 of our copending application No. 8032971, 4-pyrimidylmethyl bromide is reacted with ethyl 2-mercaptoacetate to yield ethyl 2-(4-pyrimidylmethylthio)acetate, with ethyl 2-mercaptoacetate to yield ethyl 2-(4-pyrimidylmethylthio)acetate, with ethyl 2-phenyl-2-mercaptoacetate to yield ethyl 2-phenyl-2-(4-pyrimidylmethylthio)acetate (when ethyl esters are prepared, it is preferable to substitute an equivalent of sodium ethoxide for sodium methoxide), with mercaptoacetone to yield 4-pyrimidylmethylthio-acetone, and with 1-phenyl-1-mercaptoacetone to yield 1-(4-pyrimidylmethylthio)-1-phenylacetone.

Example 9

2-(4-Pyrimidyl)ethylthio Derivatives

Employing the methodology of Examples 1 to 4 of the said copending application, 2-(4-pyrimidyl)ethyl chloride hydrochloride is reacted with ethyl 2-mercaptoacetate to yield ethyl 2-[2-(4-pyrimidyl)ethylthio]acetate, with ethyl 2-mercaptoacetate to yield ethyl 2-[2-(4-pyrimidyl)ethylthio]acetate, with ethyl 2-phenyl-2-mercaptoacetate to yield ethyl 2-phenyl-2-[2-(4-pyrimidyl)ethylthio]acetate (when ethyl esters are prepared, it is preferable to substitute an equivalent amount of sodium ethoxide for sodium methoxide), with mercaptoacetone to yield 1-[2-(4-pyrimidyl)ethylthio]-acetone and with 1-phenyl-1-mercaptoacetone to yield 1-[2-(4-pyrimidyl)ethylthio]-1-phenylacetone.

Example 10

4-Pyrimidylmethylthio Derivatives

According to the methodology of Examples 4 to 6, 4-pyrimidylmethyl mercaptan is reacted with chloroacetone to yield 4-pyrimidylmethylthioacetone, with alpha-bromoacetophenone to yield alpha-(4-pyrimidylmethylthio)acetophenone, with alpha-bromopropiophenone to yield alpha-(4-pyrimidylmethylthio)propiophenone, with ethyl 2-bromoacetate to yield 2-(4-pyrimidylmethylthio)acetate, with ethyl 2-chloropropionate to yield 2-(4-pyrimidylmethylthio)propionate and with ethyl 2-phenyl-2-bromoacetate to yield 2-phenyl-2-(4-pyrimidylmethylthio)acetate (when ethyl esters are prepared, it is preferable to substitute an equivalent of sodium ethoxide for sodium methoxide; when the corresponding methyl esters are prepared, it is preferable to substitute methanol for ethanol).

The following Preparations illustrate the preparation of certain starting materials used in the previous Examples:—

Preparation 1

4-Picolylisothiuronium Chloride Hydrochloride

Thiourea (11.42 g., 0.15 moles) was suspended with stirring in 45 ml. of absolute ethanol. The suspension was heated to reflux under nitrogen and a suspension of finely divided 4-picolyl chloride hydrochloride (25.37 g., 0.15 moles) in approximately 100 ml. of absolute ethanol was added over 15 minutes, with external heating removed as necessary to avoid overly vigorous reflux. After 6 hours additional reflux, the reaction mixture was cooled to room temperature and filtered, with cold ethanol wash, to yield 4-picolylisothiuronium chloride hydrochloride (35.8 g.; m.p. 226—227°C); ir (KBr): 3.40, 6.05, 6.14, 6.27, 6.71 and 12.34 μ.

Analysis: Calcd. for $C_7H_9N_3S \cdot 2HCl$:

Found: C, 35.01; H, 4.62; N, 17.50
C, 35.04; H, 4.61; N, 17.55

The same method is used to convert 2-(4-pyridyl)ethyl chloride to 2-(4-pyridyl)ethylisothiuronium chloride.

Preparation 2 4-Picolyl Mercaptan

4-Picolylisothiuronium chloride hydrochloride (32.4 g., 0.135 moles) was dissolved in 45 ml. of water with stirring, a warm solution of sodium hydroxide (11.02 g., 0.27 mole) in 18 ml. of water was added dropwise over approximately 10 minutes during which oil droplets began to form. The mildly exothermic reaction was allowed to stir for approximately 30 minutes, at which time the pH was increased from 7 to 8 by the addition of sodium. The pH was then reduced to 6 by the slow addition of 6N hydrochloric acid. The oily product was extracted into ether (three 125 ml. portions). The combined ether extracts were dried over anhydrous sodium sulfate, and evaporated to an oil containing solids, with a potent mercaptan odor (11.18 g.). Fractional distillation gave purified 4-picolyl mercaptan (4.47 g.; b.p. 109—104°C./15 mm.; thin layer chromatography on silica gel: Rf 0.65—0.7 when eluted with $4CHCl_3/ICH_3OH$). This mercaptan readily forms a solid disulfide when contacted with air.

The same method is used to convert 2-(4-pyridyl)-ethylisothiuronium chloride to 2-(4-pyridyl)ethyl mercaptan.

Preparation 3 4-Picolyl Acetate

4-Picoline N-oxide (250 g.) was dissolved in a mixture of 2.5 l. of acetic acid and 425 ml. of acetic anhydride. The solution was slowly heated to reflux and refluxed for about 22 hours. The reaction mixture was then stripped of acetic acid and acetic anhydride and the residual oil vacuum distilled, using a 6 inch fractionation column. Material boiling at a pot temperature of 100°C. and a head temperature of 82°C. at 1.2 mm. was combined, yielding 305.9 g. of an 87:13 mixture of 4-picolyl acetate and 3-acetoxy-4-picoline.

Preparation 4 4-Picolyl Bromide Hydrobromide

4-Picolylacetate (300 g., 87% pure) was combined with 3.0 l. of 48% hydrobromic acid. A spontaneous exotherm occurred, the temperature rising from 26° to 42°C. The mixture was heated to reflux and refluxed for about 1 hour (pot temperature 124°C.). The reaction mixture was then concentrated *in vacuo* to yield a gummy solid which was dissolved in 1500 ml. of absolute alcohol. Crude hydrobromide salt (379 g.) crystallized on chilling and was recovered by filtration. Purified 4-picolylbromide hydrobromide (33.1 g., m.p. 187.5—189°C.) was obtained by recrystallization of 50 g. of crude from absolute alcohol.

Preparation 5 4-Pyrimidylmethyl Bromide

Under a nitrogen atmosphere, finely divided N-bromosuccinimide (4.45 g., 25 mmoles) was suspended in 75 ml. of dry carbon tetrachloride (distilled from P_2O_5). The stirred suspension was added 4-methyl-pyrimidine (97% pure, 1.94 g., 20 mmoles). Benzoyl peroxide (0.44 g., 1.8 mmoles) was then added cautiously. The stirred reaction was heated to reflux and irradiated with a 300 watt flood light for 6 hours. The reaction mixture was then cooled in an ice bath and crude 4-pyrimidylmethyl bromide (3.74 g.) recovered by filtration and used directly in the next step.

4-Pyrimidylmethyl bromide is further purified by dissolution in dilute hydrobromic acid, extraction of the aqueous phase with methylene chloride, basification of the aqueous phase with sodium hydroxide and extraction of the product into methylene chloride. The methylene chloride solution is dried and evaporated to recover purified product.

Preparation 6 2-(4-Pyrimidyl)ethyl Chloride Hydrochloride

4-Pyrimidylmethyl bromide is converted to the nitrile, then to ethyl 4-pyrimidylacetate, then to 2-(4-pyrimidyl)ethanol and finally to 2-(4-pyrimidyl)ethyl chloride hydrochloride according to the methods detailed in Example 4 of the said copending application no. 8032971.

Preparation 7

55 4-Pyrimidylmethyl Mercaptan

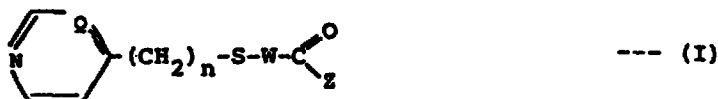
The methods of Preparations 1 and 2 are employed to convert 4-pyrimidylmethyl bromide to 4-

pyrimidyl mercaptan via 4-pyrimidylmethylisothiuronium bromide. Half as much base is employed in the first stage of the synthesis as compared to Preparation 1, since the free base of the starting material is employed for this preparation.

Claims

- 5 1. A compound of the formula:

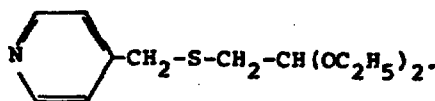
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wherein:—

- n is 1 or 2;
W is methylene or methylene substituted with either a methyl or a phenyl group;
10 Z is hydroxy, (C₁—C₄) alkoxy, hydrogen, methyl, phenyl, or —O[⊖] (alkali metal)[⊕] Q is CH or N; with the provisos that (a) when Z is phenyl, W is other than methylene substituted by phenyl, and (b) when Q is CH and n is 1, Z is other than hydroxy, (C₁—C₄) alkoxy and —O[⊖] (alkali metal)[⊕].
2. A compound as claimed in claim 1 wherein Q is CH, n is 1, and W is methylene.
3. A compound as claimed in claim 2 wherein Z is hydrogen.
15 4. A compound as claimed in claim 1 wherein Q is N, n is 1, W is methylene and Z is methyl or phenyl.
5. A compound as claimed in claim 1 wherein Q is N, n is 1, W is phenyl-substituted methylene, and Z is (C₁—C₄) alkoxy.
6. A process for preparing a compound as claimed in claim 1 substantially as described herein.
20 7. A process as claimed in claim 6 substantially as herein before described in any one of the Examples.
8. A compound as claimed in claim 1 which has been prepared by a process as claimed in either of claims 6 and 7.
9. The acetal of the formula:—

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SPECIFICATION NO 2092133B

The following amendments were allowed under Section 27 on 16 March 1984:

Page 1, line 6, *delete* anti-inflammatory and

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8 June 1984

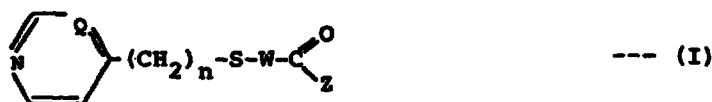
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pyrimidyl mercaptan via 4-pyrimidylmethylisothiuronium bromide. Half as much base is employed in the first stage of the synthesis as compared to Preparation 1, since the free base of the starting material is employed for this preparation.

Claims

- 5 1. A compound of the formula:

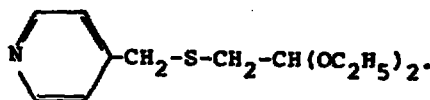
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wherein:—

- n is 1 or 2;
 W is methylene or methylene substituted with either a methyl or a phenyl group;
 10 Z is hydroxy, (C₁—C₄) alkoxy, hydrogen, methyl, phenyl, or —O[⊖] (alkali metal)[⊕] Q is CH or N; with the provisos that (a) when Z is phenyl, W is other than methylene substituted by phenyl, and (b) when Q is CH and n is 1, Z is other than hydroxy, (C₁—C₄) alkoxy and —O[⊖] (alkali metal)[⊕].
 2. A compound as claimed in claim 1 wherein Q is CH, n is 1, and W is methylene.
 3. A compound as claimed in claim 2 wherein Z is hydrogen.
 15 4. A compound as claimed in claim 1 wherein Q is N, n is 1, W is methylene and Z is methyl or phenyl.
 5. A compound as claimed in claim 1 wherein Q is N, n is 1, W is phenyl-substituted methylene, and Z is (C₁—C₄) alkoxy.
 6. A process for preparing a compound as claimed in claim 1 substantially as described herein.
 20 7. A process as claimed in claim 6 substantially as herein before described in any one of the Examples.
 8. A compound as claimed in claim 1 which has been prepared by a process as claimed in either of claims 6 and 7.
 9. The acetal of the formula:—

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