

(Table III) from the authentic hydrazide obtained from ethyl *N*-(2-pyridyl)oxamate.

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Supplementary Material Available. Eleven pages of elemental analytical results for the compounds will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 X 148 mm, 24X reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for \$4.00 for photocopy or \$2.00 for microfiche, referring to code number JCED-74-288.

Benzenesulfonamides of Primary Aminopyridines and Primary Aminoquinolines

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Sulfonamides of 12 aminopyridines and aminoquinolines are prepared. For the preparation of these sulfonamides, pyridine is a more suitable solvent than acetic acid.

The preparation of sulfonamides of primary and secondary amines is a well-known avenue to the classification and identification of such compounds. However, the benzenesulfonamides of a number of common aminopyridines and aminoquinolines have not been reported. Twelve such sulfonamides are described here. Since the completion of this work, three of the derivatives have been reported with melting points in substantial agreement with our data. They are indicated in Table I.

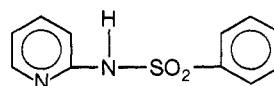
Various modifications of the original Hinsberg method have been suggested. The ones cited here (1, 6, 7, 10, 11, 13) all use nonaqueous solvents. The variants used by Mills and Breckenridge (7) and Shepherd (11) were the basis of the present study. The former used pyridine as the solvent, whereas Shepherd used glacial acetic acid, with sodium acetate as catalyst. While interpreting the reaction in relation to amine basicity, Shepherd suggested that the pyridine method might be improved by adding triethylamine in certain cases.

Published procedures involve washing the product with acid to remove the substrate. In the present cases the products themselves are also basic, and the acid wash is

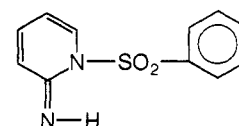
inadvisable. However, simple recrystallization from diluted ethanol sufficed to produce the pure derivative in one to three recrystallizations.

In addition to the new cases shown in Table I, we found that 2-aminopyridine, 2-amino-3-methylpyridine, and 2-amino-5-methylpyridine failed to produce the sulfonamide in glacial acetic acid, and 8-aminoquinoline gave 92% of crude product in the acid solvent. Table I shows that, with 3-aminopyridine and 3-aminoquinoline, the acetic acid method gave lower yields, and it failed entirely with four others. On the other hand, with 4-aminoquinoline, the pyridine methods (B and C) gave only intractable oils, and the acid method (A) gave 59% of derivative. Thus, in general, the observations of Winterbottom (14) are supported; namely, that acetic acid is inferior to pyridine or entirely unsuitable as a solvent for 2- and 4-aminopyridines.

The precise structure of similar derivatives of certain 2- and 4-amino-substituted pyridines has been studied (2, 3, 5, 12). Whether structure I or II applies in these cases is not debated here. In the cases of the monosulfonamides reported here, the products are those obtained by the methods indicated, and are suitable for identification



I



II

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Table I. Benzenesulfonamides^a

Amine used	Method	Crude yield, %	Mp, °C	Empirical formula
3-Aminopyridine	B	85	188.1–189.1	C ₁₁ H ₁₀ N ₂ O ₂ S
3-Aminopyridine	A	16	...	...
4-Aminopyridine	C	81 ^b	291–292	C ₁₁ H ₁₀ N ₂ O ₂ S
2-Amino-4-methylpyridine	B	88 ^b	222.5–223.5	C ₁₂ H ₁₂ N ₂ O ₂ S
2-Amino-6-methylpyridine	B	89 ^b	135.0–136.0	C ₁₂ H ₁₂ N ₂ O ₂ S
2-Aminoquinoline	B	73 ^b	171.5–172.5	C ₁₅ H ₁₂ N ₂ O ₂ S
3-Aminoquinoline	C	93	157.7–159.2	C ₁₅ H ₁₂ N ₂ O ₂ S
3-Aminoquinoline	A	36	...	...
5-Aminoquinoline	B	97	206–207 ^c	C ₁₅ H ₁₂ N ₂ O ₂ S
6-Aminoquinoline-HCl	B	57	222.5–224	C ₁₅ H ₁₂ N ₂ O ₂ S
4-Aminoquinoline	A	59 ^{d,e}	240.5–243.5	C ₁₆ H ₁₄ N ₂ O ₂ S ^e
8-Aminoquinoline	C	90	157.7–158.7 ^f	C ₁₆ H ₁₄ N ₂ O ₂ S
6-Methoxy-8-aminoquinoline	B	98	164.3–165.3	C ₁₆ H ₁₄ N ₂ O ₃ S
6-Methoxy-8-aminoquinoline	A	44	...	...
5-Bromo-8-aminoquinoline	A	78	170.5–171.5 ^g	C ₁₅ H ₁₁ BrN ₂ O ₂ S

^a Elemental analyses (C,H,N) in agreement with theoretical values were obtained and submitted for review. ^b Method A gave no yield. ^c Lit. (8) mp 202–203°C. ^d Methods B and C gave only oils. ^e Analysis indicates monohydrate. ^f Lit. (9) mp 161–161.5°C. ^g Lit. (4) mp 172.5–173°C.

purposes. However, all derivatives mentioned here are soluble in dilute NaOH except that of 5-bromo-8-aminoquinoline which cannot have the structure of type II. Pending further confirmation, type I structures are preferred.

Experimental

All melting points were taken with a Fisher-Johns hot-stage apparatus and are corrected. Except where indicated, all analyses were by Weiler and Strauss, 164 Banbury Road, Oxford, England.

2-Amino-4-methylpyridine, 2-amino-5-methylpyridine, and 2-amino-6-methylpyridine were supplied by the Reilly Tar and Chemical Co. (courtesy of Frank E. Cislak). The 5-bromo-8-aminoquinoline was prepared in this laboratory and had a melting point of 104°C. (Lit. 109–

111°C). All other substrates were from the usual sources of supply and had observed melting points in close agreement with the literature, except that the observed value for 6-aminoquinoline hydrochloride was indefinite. Table I gives the results.

Method A. The method of Shepherd was followed by refluxing amine with a 25% excess of benzenesulfonyl chloride dissolved in glacial acetic acid (1:10 v/v), while an equimolar quantity of sodium acetate was added in portions. At the end of the reflux period, water was added to dissolve the sodium chloride. The cooled solution was neutralized with dilute ammonium hydroxide (1:1) and the crude benzenesulfonamide collected. The dried product was decolorized with charcoal and then recrystallized to a constant melting point from ethanol:water, either 10:1 (v/v) or 2:1 (v/v).

Method B. The method of Mills and Breckenridge was adapted by refluxing the amine with 25% excess benzenesulfonyl chloride dissolved in pyridine. After an hour of heating, the reaction mixture was poured into ice water. The precipitate was collected and purified as in Method A.

Method C. This was the same as Method B except that an equimolar amount of triethylamine was added after the first 5 min of refluxing.

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