

### Experimental Section<sup>3</sup>

**General Method for the Preparation of (2*R*:2'*R*)-, (2*S*:2'*S*)-, and *meso*-2,2'-Bithiirane.**—A cooled solution of KSCN (16 g) in H<sub>2</sub>O (50 ml) was added to the 1,2:3,4-diepoxybutane (4.3 g) and the reaction mixture was kept at 3–7° for 1 hr while stirring. After additional stirring for 4.5 hr at 15–20° the precipitated material was filtered off and washed (H<sub>2</sub>O) and the filter cake was extracted (CHCl<sub>3</sub>, 200 ml). The CHCl<sub>3</sub> solution was dried (Na<sub>2</sub>SO<sub>4</sub>) and the solvent was removed *in vacuo* to give the crude product (about 3 g). After one recrystallization from EtOH (15 ml, 99.9%) (under filtration) while avoiding a long heating period, the bithiirane (about 2.3 g) was obtained. The analytical samples were purified by sublimation *in vacuo* (12 mm, 40–50°). The physical properties are listed in Table I.

TABLE I  
(2*R*:2'*R*)-, (2*S*:2'*S*)-, AND *meso*-2,2'-BITHIIRANE<sup>a</sup>

Configuration	Mp, °C	[α] <sub>D</sub> <sup>20</sup> , deg (CHCl <sub>3</sub> ) at mμ				
		365	436	446	578	589
2 <i>R</i> :2' <i>R</i> <sup>b</sup>	80–81	+66.2	–92.6	–89.2	–82.5	–80.3
2 <i>S</i> :2' <i>S</i>	80–80.5	–67.2	+92.1	+89.1	+82.4	+80.0
<i>meso</i> <sup>c</sup>	99–100					

<sup>a</sup> Analytical results obtained for C, H, S were within 0.25% of the theoretical values for the formula C<sub>4</sub>H<sub>6</sub>S<sub>2</sub>. <sup>b</sup> Prepared from (2*S*:3*S*)-1,2:3,4-diepoxybutane. <sup>c</sup> Prepared from *meso*-1,2:3,4-diepoxybutane.

(3) H. Gürtler gave technical assistance. Analyses were performed by G. Cornali and W. Egger. Melting points are corrected and were taken in open glass capillaries using a Hershberg apparatus.

### Derivatives of 4-Aminobenzenesulfonanilide

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In a search for more potent sulfonamide compounds, we have been preparing a series of derivatives of 4-aminobenzenesulfonanilide; we now wish to report the synthesis of 4-(*p*-nitrobenzenesulfonamido)succinanic acid and 4-(*p*-aminobenzenesulfonamido)succinanic acid.

### Experimental Section<sup>1</sup>

**4-Nitrosuccinanic Acid.**—A mixture of 14 g (0.1 mole) of 4-nitroaniline, 10 g (0.1 mole) of succinic anhydride, 50 ml of anhydrous dioxane, and a few drops of H<sub>2</sub>SO<sub>4</sub> was refluxed overnight, cooled, and poured into a 10% solution of Na<sub>2</sub>CO<sub>3</sub>. The clear solution was stirred for 1 hr and then acidified with AcOH. The yield was 24 g (100%), mp 193–194°.

**4-Aminosuccinanic acid** was prepared by the procedure of Landsteiner and Van der Scheer.<sup>2</sup>

**4-(*p*-Nitrobenzenesulfonamido)succinanic Acid.**—To a thoroughly stirred mixture of 5.5 g (0.026 mole) of 4-aminosuccinanic acid and 3 g (0.052 mole) of Na<sub>2</sub>CO<sub>3</sub> in 30 ml of H<sub>2</sub>O, was slowly added a solution of 5 g (0.026 mole) of *p*-nitrobenzenesulfonyl chloride in 30 ml of dioxane. After addition, the mixture was stirred at room temperature for 30 min and then filtered. The compound was crystallized (Me<sub>2</sub>CO–H<sub>2</sub>O); yield 70%, mp 216–218°. Anal. (C<sub>16</sub>H<sub>15</sub>N<sub>3</sub>O<sub>7</sub>S) C, H, N, S.

**4-(*p*-Aminobenzenesulfonamido)succinanic acid** was prepared following the same procedure used for 4-aminosuccinanic acid.

(1) Melting points were taken on a Fisher-Johns block and are uncorrected. Analyses were performed by Microanalytical Laboratory, Oxford, England. The infrared spectra were determined with a Perkin-Elmer 137 and were as expected.

(2) K. Landsteiner and J. Van der Scheer, *J. Exptl. Med.*, **56**, 399 (1932).

There was obtained 2 g (71%) of white flakes, mp 189–190° (Me<sub>2</sub>CO–H<sub>2</sub>O). Anal. (C<sub>16</sub>H<sub>17</sub>N<sub>3</sub>O<sub>7</sub>S) C, H, N, S.

The nitro sulfanilamide analog was as effective as sulfanilamide *in vitro* against *Staphylococcus aureus* at 1000 μg/ml; the effective concentration of the amino derivative was 2000 μg/ml. Both compounds had an oral LD<sub>50</sub> of 1.5 g/kg in rats.<sup>3</sup>

(3) Personal communication from Dr. N. Ercoli, Instituto de Zoología Tropical, Universidad Central de Venezuela, Caracas, Venezuela.

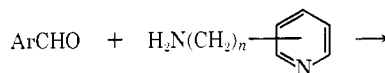
### Preparation of Some ω-N-(Substituted Benzyl)aminoalkylpyridines

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In our earlier paper<sup>1</sup> we reported the preparation of some ω-pyridylalkyl benzamide and benzoate derivatives which showed sedative activity. Continuing our work in this series we now report the preparation of some substituted ω-N-benzylaminoalkylpyridines.



The ω-aminoalkylpyridine was treated in a nonpolar solvent (*e.g.*, benzene, toluene, xylene) with an equivalent amount of an aromatic aldehyde. The resulting Schiff bases were reduced in good yield with NaBH<sub>4</sub> in anhydrous EtOH. The products are listed in Table I.

**Biological Effects.**—According to Dews' method the compounds showed sedative activity against the exciting effect of desoxyephedrine (DOE);<sup>2</sup> some have a strong antihypertensive effect. It appeared that the sedative and antihypertensive activity of our series was affected by the aryl substituent and the position of alkyl chain in the pyridine. The most active compound was 2-[β-(3,4-dimethoxybenzylamino)ethyl]pyridine (**11**). Its most important data are the following therapeutic ratios for action [LD<sub>50</sub>/ED<sub>50</sub> (mg/kg)]: decrease of spontaneous motility in the mouse, 15.7 (ip); antagonism against DOE in the mouse, 11.8 (ip); hypotensive activity in the dog, >>20 (iv).

### Experimental Section<sup>3</sup>

**2-[β-(3,4-Dimethoxybenzylamino)ethyl]pyridine (**11**).**—3,4-Dimethoxybenzaldehyde (49.8 g, 0.3 mole) in 200 ml of xylene was refluxed with 36.6 g (0.3 mole) of 2-(β-aminoethyl)pyridine for 2 hr in an apparatus equipped with a Marcusson H<sub>2</sub>O separatory adapter. During this period 5.4 ml (0.3 mole) of H<sub>2</sub>O was collected. The xylene was removed by distillation, the residue was dissolved in 300 ml of anhydrous EtOH, 18 g (0.4 mole) of NaBH<sub>4</sub> was added, and the mixture refluxed for 2 hr. The complex was decomposed by the addition of H<sub>2</sub>O, the EtOH was removed by distillation, and the residue was extracted three times with 100 ml of C<sub>6</sub>H<sub>6</sub>. The organic extracts were combined, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered, and evaporated. The residue was distilled: bp 183–185° (0.05 mm), yield 71.5 g (87%). The oily

(1) O. H. Hankovszky and K. Hideg, *J. Med. Chem.*, **9**, 151 (1966).

(2) P. B. Dews, *Brit. J. Pharmacol.*, **8**, 46 (1953).

(3) Melting points were obtained on a Boetius apparatus and are uncorrected. Where analyses are indicated only by symbols of the elements, analytical results obtained for those elements were within 0.4% of the theoretical values.