

Isolation of *N*-Methylmorpholine from the Seeds of *Cassia occidentalis* L. (Coffee Senna)

N-Methylmorpholine was isolated from the seeds of *Cassia occidentalis* L. (coffee senna) and the identity was established by comparison of infrared

and mass spectra, melting point and mixture melting point with a sample of synthetic *N*-methylmorpholine hydrochloride.

C*assia occidentalis* L. (coffee senna) is an annual legume, naturalized from the tropics, which grows in waste areas of the southeastern and southwestern United States. The roasted seeds of coffee senna, known as Mogdad coffee, or Stephanie coffee, have been used as a coffee substitute (Bruere, 1942; Burkart, 1947; Ferraz de Menzes, 1952), although they are toxic before roasting (Bruere, 1942).

Livestock poisoning due to the ingestion of the seeds of coffee senna was noticed in 1913 and 1914 (Brocq-Rousseu and Bruere, 1925; Moussu, 1925), when horses were poisoned after being fed oats mixed with the seeds in variable proportions. Recently, widespread muscle degenerations in cattle have been observed by feeding trials (Henson *et al.*, 1965; Mercer *et al.*, 1967; O'Hara *et al.*, 1969).

Toxic albumin (Moussu, 1925), chrysarobin, and toxalbumin (Brocq-Rousseu and Bruere, 1925; Bruere, 1942) were reported to be toxic principles of the seed. Several anthraquinone derivatives (Watt and Breyer-Brandwijk, 1962), notably physcione (3-methyl-6-methoxy-1,8-dihydroxyanthraquinone) (King, 1957) have been isolated from the seed.

A toxic volatile base with molecular weight 198, m.p. 82.5–83.5° C, was also isolated in these laboratories (Puleo, 1966), but it was not further characterized due to the very low yield of the base (6 mg per 13.6 kg). Based on the results of low resolution mass spectra, possible molecular formulas of the base were suggested to be $C_{11}H_{22}N_2O$, $C_{10}H_{18}N_2O_2$, or $C_9H_{14}N_2O_3$.

EXPERIMENTAL

Infrared spectra were recorded with a Perkin-Elmer Model 337 grating infrared spectrophotometer.

Mass spectra were obtained with a CEC Model 21-110B high resolution mass spectrometer.

Melting points were determined with a Thomas Hoover capillary melting point apparatus, and they were uncorrected.

The dried, ground seeds (3 kg) were extracted three times with ethanol containing 3% tartaric acid at 50° to 60° C. The filtered extracts were combined (about 20 l.) and concentrated *in vacuo* to about one tenth of their original volume. The concentrated solution was diluted with two volumes of water and made acidic (pH ~2.0) with dilute sulfuric acid.

The solution was filtered and extracted with benzene to remove some nonpolar substances.

The aqueous solution was made basic (pH ~11.0) with concentrated sodium hydroxide (with cooling) and the base content was extracted with chloroform. The base was converted to acid salt by the addition of concentrated hydrochloric acid to the chloroform extracts and the solvent was removed *in vacuo*. The residue was taken up in dilute hydrochloric acid, and the reddish brown pigment was removed by extracting with chloroform. The aqueous solution containing the base was made basic with concentrated sodium hydroxide, and extracted three times with chloroform. The combined chloroform extracts were dried over anhydrous magnesium sulfate and filtered. Dry hydrogen chloride in ether was added to the chloroform solution, and the solvents, ether and chloroform, were removed *in vacuo*. The hydrochloride of the base was crystallized as needles (150 mg) from 2-propanol. Recrystallization from 2-propanol gave small cubes of this salt, m.p. 208–208.5° C; ir (KBr) cm^{-1} 2480, 2620, and 2695 ($R_3NH^+Cl^-$), and 1110 ($-C-O-C-$); mass spectrum 70 eV m/e 101 (M^+ , found: 101.0844; calcd: 101.0841 as $C_5H_{11}NO$), 71 ($M^+ - CH_2O$, found: 71.0734; calcd: 71.0735 as C_4H_9N), and 43 ($M^+ - C_3H_6O$, found: 43.0421; calcd: 43.0422 as C_2H_5N).

N-Methylmorpholine, Technical grade, was purchased from Eastman Organic Chemicals, distilled, and converted into hydrochloride, and crystallized in the same manner as above, m.p. 208–208.5° C [lit. (Knorr, 1889) 205° C]; ir (KBr) cm^{-1} 2480, 2620, and 2695 ($R_3NH^+Cl^-$), and 1110 ($-C-O-C-$); mass spectrum 70 eV m/e 101 (M^+ , found: 101.0842; calcd: 101.0841 as $C_5H_{11}NO$).

DISCUSSION

The infrared and mass spectra of the natural *N*-methylmorpholine hydrochloride were essentially identical when they were compared with those of an authentic sample. An admixture of the hydrochloride of the natural and authentic *N*-methylmorpholine did not depress the melting point of the reference compound. *N*-Methylmorpholine was synthesized

by Knorr (1889). This is probably the first case of the isolation of *N*-methylnorpholine from the plant kingdom.

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