NOTES.

1-*Aza*bicyclo[1 : 2 : 2]*heptane*. By G. R. CLEMO and V. PRELOG.

1-Aza*bicyclo*[1 : 2 : 2]HEPTANE has been synthesised in two ways: by the action of ammonia on 1 : 5-dibromo-3-bromomethylpentane (Prelog and Cerkovnikov, *Annalen*, 1936, **525**, 294) and by intramolecular quaternary salt formation from 4-piperidylcarbinol through the 4-bromomethylpiperidine, which was not isolated (Clemo and Metcalfe, J., 1937, 1523). The former authors described the compound as crystalline, whereas Clemo and Metcalfe obtained an oil. Prelog and Cerkovnikov meanwhile carried out the intramolecular salt-formation of 4-iodomethylpiperidine and obtained the same crystalline product. After exchange of specimens and seeding, it was clear that the difference was due to supercooling, for the product of Clemo and Metcalfe then crystallised and melted at 78—79°. We emphasise these observations, the high m. p. being a characteristic property of such bridged cyclic structures. The ease of formation (75·4% of the theoretical yield) of the strained molecule is noteworthy. A third synthesis of this interesting compound will be described elsewhere.

4-Iodomethylpiperidine Hydriodide.—4-Piperidylcarbinol (2 g.), prepared by reduction of synthetic ethyl piperidine-4-carboxylate (Hanousek and Prelog, *Coll. Czech. Chem. Comm.*, 1932, **4**, 259), was heated for 4 hours at 100° in a sealed tube with red phosphorus (0·8 g.) and hydriodic acid (6 c.c., 70%) (see Clemo and Metcalfe, *loc. cit.*). Water (25 c.c.) was added, the phosphorus separated from the hot solution, and the filtrate evaporated. On cooling, the white *hydriodide* crystallised (4·74 g.; 77·2%). By further evaporation, more of the white product was obtained (total yield, nearly theoretical). For analysis it was recrystallised from acetone–ethyl acetate; m. p. 132—133° (corr.) (Found: N, 3·9. $C_6H_{12}NI,HI$ requires N, 4·0%).

1-*Aza*bicyclo[1 : 2 : 2]*heptane.*—4-Iodomethylpiperidine hydriodide (4·5 g.) in water (300 c.c.) was stirred while N/2-sodium hydroxide (256 c.c.) was dropped in during 2½ hours at 45°. After cooling, benzenesulphonyl chloride (8 g.) was added during a further ½ hour's stirring. The steam-volatile base neutralised 9·83 c.c. of N-hydrochloric acid (75·4% of the theoretical). The base, isolated in the usual way, crystallised to a camphor-like mass. The m. p. of the vacuum-distilled base is higher than recorded in the first publication, *viz.*, 78—79°. The picrate (from acetone–alcohol) melts at 285° (decomp.) (corr.). The product of Clemo and Metcalfe melted, after seeding, at the same temperature.—UNIVERSITY OF DURHAM, KING'S COLLEGE, NEWCASTLE-UPON-TYNE, and UNIVERSITY OF ZAGREB, YUGOSLAVIA. [*Received, February* 18*th*, 1938.]

Crystalline Salts derived from p-*Aminophenylstibonic Acid.* By WILLIAM H. GRAY and IVAN D. LAMB.

OF the large number of organic antimony compounds prepared in the course of chemotherapeutic investigations, but few, and those of types unsuited to the purpose, have been obtained crystalline. The drugs which have found application in the treatment of kala-azar, such as the diethylamine salt and glucoside of *p*-aminophenylstibonic acid, and the product of interaction of this acid with carbamide (Gray, Trevan, Bainbridge, and Attwood, *Proc. Roy. Soc.* 1931, *B*, **108**, 54), as well as their precursors " stibacetin " (sodium *p*-acetamidophenylstibonate) and *p*-aminophenylstibonic acid, have been obtained hitherto only in an amorphous condition. It is therefore of interest to record the preparation of " stibacetin " and sodium *p*-aminophenylstibonate in crystalline form.

If a concentrated aqueous solution of " stibacetin " is allowed to evaporate slowly at room temperature, the salt separates in micro-crystals, consisting of masses or rosettes of thin needles. These have also been obtained by dissolving the crude " stibacetin " in 2 parts of hot water and allowing the solution to cool. Some batches yield the crystals more readily than others. They form a thick paste and are difficult to filter or wash. They are best isolated by centrifuging and washing with a little water and then with alcohol, and can be recrystallised from slightly less than 2 parts of hot water; the yield is poor. So obtained, the product is nearly colourless, but gives a slightly yellow solution in 2 parts of cold water. It does not melt, but decomposes at about 300°. A trace of the sodium chloride used for salting-out the crude " stibacetin " still remains. This crystalline form is almost identical in composition with ordinary " stibacetin," consisting of complex molecules containing 2—3 acetamidophenylstibonic acid residues to 1 atom of sodium [Found for the air-dried substance: H_2O, 13·7. Found for the substance dried at 80° in a vacuum: NaCl, 0·3; C, 29·7; H, 3·2; N, 4·5; Sb, 39·3; Na, 3·2; atomic ratios Sb : N = 1·00; Sb : Na = 2·36. Calc. for $(CH_3{\cdot}CO{\cdot}NH{\cdot}C_6H_4)_3Sb_3O_7HNa$: C, 31·9; H, 2·8; N, 4·7; Sb, 40·4; Na, 2·5. Calc. for $(CH_3{\cdot}CO{\cdot}NH{\cdot}C_6H_4)_2Sb_2O_5HNa$: C, 31·2; H, 2·8; N, 4·6; Sb, 39·5; Na, 3·7%].

Crystalline sodium *p*-aminophenylstibonate is obtained by prolonged treatment of " stibacetin " with alkali. The ambiguity in the published accounts with regard to the time required for the completion of this hydrolysis has been mentioned elsewhere (Gray, Trevan, Bainbridge, and Attwood, *loc. cit.*, p. 59). When " stibacetin " (27 g.) in 7% sodium hydroxide solution (224 c.c.) is heated for 7 hours at 90°, the acetyl group is completely removed. This is shown by the precipitation by acetic acid of *p*-aminophenylstibonic acid having without purification the composition $NH_2{\cdot}C_6H_4{\cdot}SbO_3H_2,4/3H_2O$, in agreement with that of the purified substance described by Schmidt (*Annalen*, 1922, **429**, 145). Under these conditions the alkaline solution, if kept for several days, deposits, together with a small amount of finely divided material poorer in carbon, which is removed by levigation, large crystals of sodium *p*-aminophenylstibonate, which when dried over sulphuric acid at room temperature consist of the dihydrate $NH_2{\cdot}C_6H_4{\cdot}SbO_3HNa,2H_2O$ (12·8 g.). This may be dissolved in cold water and recrystallised by the addition of an equal volume of acetone (yield, 6·3 g.). It forms large, almost colourless, rectangular plates, soluble in 14 parts of water at 20° (Found: C, 22·4; H, 3·7; N, 4·4; Sb, 37·7; Na, 7·2. Calc. for $C_6H_7O_3NSbNa,2H_2O$: C, 22·4; H, 3·4; N, 4·4; Sb, 37·8; Na, 7·1%). The water of crystallisation is not lost completely below 160°, and at this temperature the substance begins to darken.—THE WELLCOME CHEMICAL RESEARCH LABORATORIES, LONDON, and WELLCOME CHEMICAL WORKS, DARTFORD. [*Received, February 18th*, 1938.]