2-(Benzohydrylmercaptomethyl)-imidazoline and Some Related Compounds

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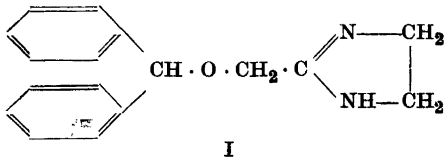
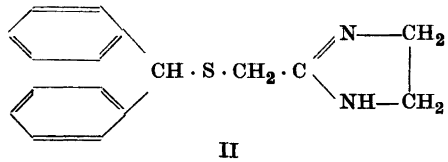
Following the synthesis of 2-(benzohydryloxymethyl)-imidazoline (I) some years ago [1] it was considered of interest to investigate the pharmacological properties of its sulphur analogue (II).



I



II

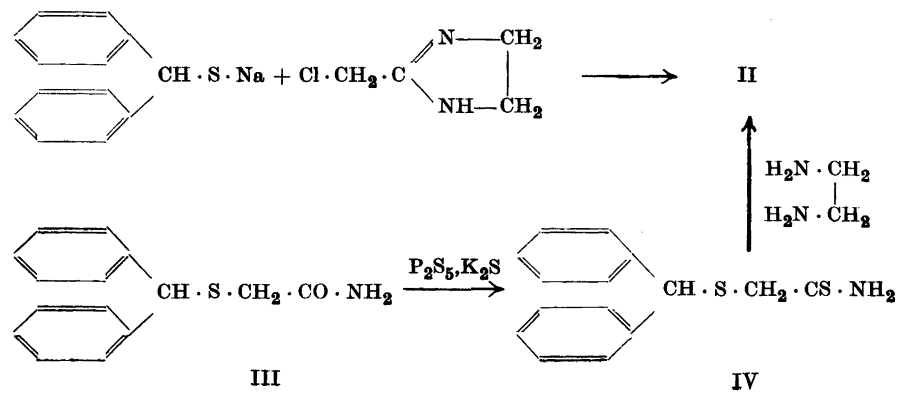
This compound was prepared by the reaction of benzohydryl mercaptan with 2-(chloromethyl)-imidazoline in the presence of sodium ethoxide. Alternatively it could be obtained by the treatment of (benzohydrylmercapto)-acetamide with phosphorus pentasulphide and potassium sulphide and reaction of the resulting thioamide with ethylenediamine.

The new imidazoline was tested for antihistaminic and antispasmodic properties on isolated guinea pig intestine. Its effect on spasms induced by histamine and acetyl choline was only 1/20 and 1/2 respectively of that of the oxygen analogue (I).

In connection with the synthesis of the compound II (benzylmercapto)-thioacetamide, 2-(benzylmercaptomethyl)-imidazoline and the ethyl ester and amide of (triphenylmethylmercapto)-acetic acid were prepared and are recorded in this note.

EXPERIMENTAL. *2-(Benzohydrylmercaptomethyl)-imidazoline (II).*

Method A. Benzohydrylmercaptane [2] (12.5 g, 80 %) and 2-(chloromethyl)-imidazoline hydrochloride [3] (7.75 g) were added to a solution of sodium (2.3 g) in absolute ethanol (100 ml). The mixture was refluxed with stirring for one hour and filtered and an ethereal solution of oxalic acid was added until precipitation ceased. The crude *oxalate* (14.2 g) was recrystallised twice from ethyl acetate; m.p. 171–171.5°. (Found: C 61.0; H 5.43. $C_{19}H_{20}N_2O_4S$ (372.4) requires C 61.3; H 5.41 %).



III IV

The *free base*, obtained by treatment of an aqueous suspension of the oxalate with dilute sodium hydroxide, melted at 115—116° after recrystallisation from light petroleum. (Found: C 72.6; H 6.29; S 11.2. $C_{17}H_{18}N_2S$ (282.4) requires C 72.3; H 6.42; S 11.4 %). Its *hydrochloride* melted at 189.5—191° (from acetone-ethanol 3 : 1). (Found: C 64.2; H 5.86; Cl 11.3. $C_{17}H_{19}ClN_2S$ (318.9) requires C 64.0; H 6.00; Cl 11.1 %).

Method B. A mixture of (benzohydrylmercapto)-acetamide [4] (5.2 g), phosphorus pentasulphide (1.8 g), potassium sulphide (1.7 g) and toluene (20 ml) was heated on the water bath for one hour with occasionally shaking. The supernatant liquid was decanted and the residue was extracted with hot toluene (20 ml). The combined toluene solutions yielded on cooling yellow crystals (4.5 g), m.p. 72—73°. Recrystallisation from toluene removed the colour, but the m.p. was not raised. Analysis indicated, that the reaction product was an addition compound containing approximately one mole of the initial amide (III) and one mole of the expected *thioamide* (IV). (Found: C 66.7; H 5.71; S 18.4. $C_{30}H_{30}N_2OS_3$ (530.7) requires C 67.9; H 5.70; S 18.1 %).

It should be noted, that (benzohydryloxy)-acetamide and the corresponding thioamide form a similar addition compound [5].

The amide-thioamide product obtained above (3.1 g) was dissolved in toluene (25 ml) and refluxed with anhydrous ethylenediamine (0.75 g) for three hours. After cooling, the toluene solution was extracted with aqueous sodium carbonate and with water, and the 2-(benzohydrylmercaptomethyl)-imidazoline was isolated as the oxalate by the addition of ethereal oxalic acid. The crude oxalate (1.5 g) was recrystallised twice from ethyl acetate; m.p. 171—172° undepressed on admixture with the oxalate prepared by method A above. (Found: C 60.9; H 5.50. $C_{19}H_{20}N_2O_4S$ (372.4) requires C 61.3; H 5.41 %).

(Benzylmercapto)-thioacetamide. (Benzylmercapto)-acetamide [6] (10 g) was treated with phosphorus pentasulphide (5.0 g) and potassium sulphide (4.7 g) in toluene (55 ml) as described above. The crude thioamide (3.3 g) was recrystallised from ethanol; m.p. 78—78.5°. (Found: N 6.92; S 32.2. $C_9H_{11}NS_2$ (197.3) requires N 7.10; S 32.5 %).

2-(Benzylmercaptomethyl)-imidazoline oxalate. This compound was prepared from (benzylmercapto)-thioacetamide (3.0 g) and ethylenediamine (1.0 g) in the same manner as the corresponding benzohydryl compound (method B). The crude oxalate (1.5 g) was recrystallised from acetone; m.p. 138—139°. (Found: C 53.0; H 5.58; N 9.50. $C_{13}H_{16}N_2O_4S$ (296.3) requires C 52.7; H 5.44; N 9.45 %).

Ethyl (triphenylmethylmercapto)-acetate. (Triphenylmethylmercapto)-acetic acid [7] (20 g) was dissolved in hot ethanol (50 ml) and conc. sulphuric acid (5 ml) was added. A vigorous reaction occurred, and after a few minutes the ester separated as an oil. The reaction mixture was poured into water (500 ml) and the ester was extracted with ether. The ether extract was dried and the solvent evaporated giving a crystalline residue (19.0 g) which was recrystallised from ethanol; m.p. 93—94°. (Found: C 76.1; H 6.12; S 8.73. $C_{23}H_{22}O_2S$ (362.5) requires C 76.2; H 6.12; S 8.84 %).

(Triphenylmethylmercapto)-acetamide. The ethyl ester obtained above (6.4 g) was dissolved in ethanol (40 ml), and the solution was saturated with ammonia at − 20° and heated in a sealed vessel at 100° overnight. On cooling, the amide (4.7 g) separated; m.p. 145—146° after recrystallisation from ethanol. (Found: N 4.26; S 9.55. $C_{21}H_{19}NOS$ (333.4) requires N 4.20; S 9.62 %).

1. Dahlbom, R., and Sjögren, B. *Acta Chem. Scand.* **1** (1947) 777.
2. Klenk, M. M., Suter, C. M., and Archer, S. *J. Am. Chem. Soc.* **70** (1948) 3846.
3. Klarer, W., and Urech, E. *Helv. Chim. Acta* **27** (1944) 1762.
4. Dahlbom, R., and Österberg, L.-E. *Acta Chem. Scand.* **2** (1948) 856.
5. Djerassi, C., and Scholz, C. R. *J. Org. Chem.* **13** (1948) 830.
6. Gabriel, S. *Ber.* **12** (1879) 1641.
7. Holmberg, B. *J. prakt. Chem.* **141** (1934) 93.

Received February 1, 1952.

Some 9-Aminoacylcarbazoles

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The interesting spasmolytic properties of a series of 10-dialkylaminoacylphenothiazines (I) prepared in this laboratory [1,2] prompted us to study the effect of the replacement of the phenothiazine moiety of the molecule by carbazole. For this reason some 9-dialkylaminoacylcarbazoles (II) were synthesised by essentially the same method as was used for the