2-(β-DIALKYLAMINOETHYLMERCAPTO)-2-IMIDAZOLINES

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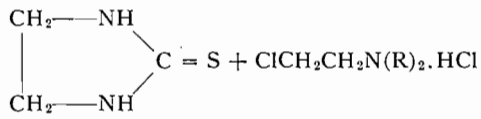
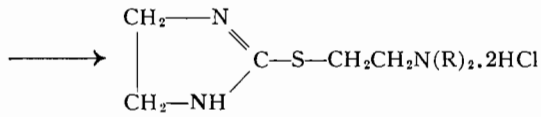
The reaction (1) of imidazoline-2-thione (I) with alkyl or aralkyl halides readily gives the corresponding 2-alkylmercapto or 2-aralkylmercapto-2-imidazoline salts. This reaction has been used by us for the preparation of a series of 2-(β-dialkylaminoethylmercapto)-2-imidazolines (II). 2-Benzhydrylmercapto-2-imidazoline was also prepared by this method.



I



II

These compounds were screened by our Pharmacology Department. Some of them were found to have mild analgesic activity.

EXPERIMENTAL[1]

2-(β-Dimethylaminoethylmercapto)-2-imidazolinium Chloride Hydrochloride

Imidazoline-2-thione[2] (10 g., 0.093 mole) and β-dimethylaminoethylchloride hydrochloride (13.4 g., 0.093 mole) were dissolved in 175 ml. of isopropanol and refluxed for 48 hours. The solution was then evaporated to about 75 ml. On cooling, 12 g. of product separated out, m.p. 179–183° C. Two recrystallizations from isopropanol raised the melting point to 183.5–184.5° C. Calc. for $C_7H_{17}N_3SCl_2$: C, 34.15; H, 6.96; S, 13.02; Cl, 28.80. Found: C, 34.22; H, 7.02; S, 13.02; Cl, 28.89.

2-(β-Diethylaminoethylmercapto)-2-imidazolinium Chloride Hydrochloride

In the same manner as the above procedure, imidazoline-2-thione (7.8 g., 0.075 mole) and β-diisopropylaminoethylchloride hydrochloride (15.1 g., 0.075 mole) gave 20 g. of product, m.p. 217–219° C. One recrystallization from ether–ethanol raised the melting point to 218–219° C. Calc. for $C_{11}H_{25}N_3SCl_2$: N, 13.91; S, 10.60; Cl, 23.47. Found: N, 15.05; S, 11.96; Cl, 25.82.

2-(β-Diisopropylaminoethylmercapto)-2-imidazolinium Chloride Hydrochloride

This compound, m.p. 188–190° C., was prepared in a 92% yield by the same procedure as were the previous two homologues. One recrystallization from ethanol gave an analytically pure material, m.p. 193–194° C. Calc. for $C_9H_{21}N_3SCl_2$: N, 15.32; S, 11.69; Cl 25.86. Found: N, 15.05; S, 11.96; Cl, 25.82.

[1]*All melting points are uncorrected.*
[2]*Sharples Chemical Inc., Philadelphia 9, Pa.*

2-(β-Diisopropylaminoethylmercapto)-2-imidazoline (Free Base)

2-(β-Diisopropylaminoethylmercapto)-2-imidazolinium chloride hydrochloride (12.5 g., 0.0415 mole) was dissolved in a 100 ml. of methanol and a solution of sodium methoxide (4.55 g., 0.083 mole) in 100 ml. of methanol was slowly added with stirring. The solution was then filtered to remove the precipitated sodium chloride and the filtrate evaporated down *in vacuo* at room temperature, leaving 7 g. of product as a viscous oil. Attempts to induce this oil to crystallize have not been successful to-date. The free base decomposed readily on heating with the production of a mercaptan-like odor. It was characterized by conversion to its acid salts.

Free base (1.0 g.) was dissolved in 10 ml. of ether and excess hydrobromic acid in a little isopropanol was added. The 2-(β-diisopropylaminoethylmercapto)-2-imidazolinium bromide hydrobromide precipitated as an oil which crystallized on trituration with an ether–isopropanol mix to yield 1.3 g. with m.p. 202–205° C. One recrystallization from ether–ethanol raised the melting point to 206–207° C. Calc. for $C_{11}H_{25}N_3SBr_2$: N, 10.74; S, 8.19; Br, 40.85. Found: N, 10.72; S, 8.37; Br, 40.92.

The free base was also converted to its dihydrogen sulphate addition salt by an identical procedure. The salt melted at 145–146° C. after two recrystallizations from ether–isopropanol. Calc. for $C_{11}H_{27}N_3S_3O_8$: SO_4 ion, 15.04; N, 9.87. Found: SO_4 ion, 15.03; N, 9.73.

2-Benzhydrylmercapto-2-imidazolinium Bromide Hydrobromide

Imidazoline-2-thione (2.55 g., 0.025 mole) and benzhydrylbromide (6.2 g., 0.025 mole) were dissolved in 20 ml. of ethanol and refluxed for 2 hours. The ethanol was then removed *in vacuo* and the oil residue crystallized from an isopropanol–benzene mix to yield 6.2 g. of product, m.p. 135–150° C. Two recrystallizations from ether–isopropanol raised the melting point to 174–176° C. Calc. for $C_{16}H_{17}N_2SBr_2$: C, 55.02; H, 4.91; N, 8.02; Br, 22.89. Found: C, 55.10; H, 5.04; N, 8.00; Br, 22.78.

ACKNOWLEDGMENT

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1. HOFMAN, K. Heterocyclic compounds. Imidazole and its derivatives. Part I. Interscience Publishers, Inc., New York. 1953.

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