the two sources contain most of the common amino acids with the exception of methionine and hydroproline. From previous experience [3, 4] we know that the spots of these two amino acids would appear on the two-dimentional chromatograms with the amounts of hydrolyzed material used in the present investigation if they were present in amounts, normally occuring in proteins and plasma filtrates [3, 5]. Our results thus would seem to corroborate those of Dent and Rose [1]. However, it may be pointed out that Bence-Jones protein according to Devine [6] contains 0.6 per cent of methionine. This means that even on the chromatograms where 0.66 mg of hydrolyzed protein was analyzed (Fig. 1) the smallest amount of methionine (8 μg), which would give a spot on the paper, was not present. When larger amounts of material were analyzed clearly separated spots were not obtained. Devine [6] also reported that Bence-Jones protein did not contain hydroxyproline.

No attempt has been made to compare the amino acid content of the two samples of protein from a quantitative point of view but it is obvious from an inspection of the two series of chromatograms with different amounts of total nitrogen applied to the paper that the sizes and colour intensities of the spots are very similar. Microbiological determinations of the amino acids are at present carried out and will definitively decide on this point.

1. Dent, C. E., and Rose, G. *Biochem. J.* **43** (1948 liv.
2. Consden, R., Gordon, A. H., and Martin, A. J. P. *Biochem. J.* **38** (1944) 224.
3. Ågren, G. In press.
4. de Verdier, C. H., and Ågren, G. *Acta Chem. Scand.* **2** (1948) 783.
5. Block, R. J., and Bolling, D. *The amino acid composition of proteins and foods.* (1945).
6. Devine, J. *Biochem. J.* **35** (1941) 433.
7. Brand, E., and Edsall, J. T. *Ann. Rev. Biochem.* **16** (1947) 223.

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Some New Phenothiazine Derivatives of Pharmacological Interest

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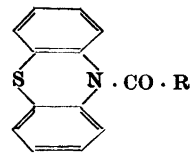
If phenothiazine (1 mole), dissolved in boiling benzene, is allowed to react with a halogeneacylhalogenide (1.5 mole), hydrogene halogenide is evolved and the resulting 10-halogeneacylphenothiazine separates from the cooled reaction mixture.

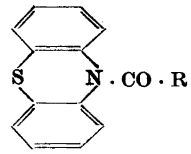
Table 1. Halogeneacylphenothiazines.



R	M. p. °C
$-CH_2 \cdot Cl$	115—116.5
$-\overset{CH_3}{\underset{H}{C}}-Br$	147.5—148.5
$-CH_2 \cdot CH_2 \cdot Cl$	142—143
$-\overset{C_2H_5}{\underset{H}{C}}-Br$	120—121

The halogene compounds react easily with primary, secundary and cyclic amines (cyclohexyl-, dimethyl-, diethylamine and piperidine) when heated with the amine (2.6 mole) to 70° in benzene solution (sealed tube). The reaction mixture is filtered and the filtrate evaporated. The residue is recrystallised or, when oily, transferred to hydrochloride.

Table 2. Alkylaminoacylphenothiazines.



Compound no.	R	M. p. °C
I	$-CH_2 \cdot N(CH_3)_2$	114.5—116
II	$-CH_2 \cdot N(C_2H_5)_2$	58 —59
III	$-CH_2 \cdot$ N-ring	164—165
IV	$-CH_2 \cdot NH-$ ring	124—126
V	$-CH(CH_3) \cdot N(C_2H_5)_2$	99.5—100.5
VI	$-CH(CH_3) \cdot$ N-ring	110—111
VII	$-CH(C_2H_5) \cdot N(CH_3)_2$	98—99
VIII	$-CH(C_2H_5) \cdot N(C_2H_5)_2 \cdot HCl$	203 (dec.)
IX	$-CH(C_2H_5) \cdot$ N-ring $\cdot HCl$	216 (dec.)

An Improved Synthesis of Ethyl *Iso*propylidenecyanoacetate and the Construction of a New Water Separator

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Ethyl *iso*propylidenecyanoacetate was first prepared by Komppa [1] by condensation of acetone and ethyl cyanoacetate by means of diethylamine. The reaction mixture was kept for one month at room temperature, and the yield of ethyl isopropylidenecyanoacetate was about 8 %.

A better yield was obtained by Scheiber and Meisel [2], when a mixture of one mole of ethyl cyanoacetate, 3 moles of acetone, and 0.2 mole of zinc chloride and aniline was boiled for 8 hours, thus yielding 40 % of ethyl *iso*propylidenecyanoacetate.

These compounds have been subject to preliminary pharmacological tests (S. Wiedling). They all show a rather high local anesthetic power, for instance a 0.7 % solution of compound V has the same duration as a 2 % solution of Xylocaine-HCl (pH 5.6) but a longer time of onset when tested on rabbit cornea. The antihistaminic effect was rather weak, when tested on isolated guinea-pig intestine, for instance compound I excerted about 1/5 of the effect of Benadryl. The compounds had a good antispasmodic activity, compound V was twelve times more active than Benadryl when tested against acetylcholine on isolated guinea-pig intestine. Preliminary toxicity tests show that compound V has a Dl_{50} about 2 g/kg when injected subcutaneously on mice.

Complete chemical and pharmacological results will be reported later.

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