## ALKYLATION OF MALONIC ESTERS

## IN DIMETHYLFORMAMIDE

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The course of the alkylation of malonic esters depends on the strength of the base used, the structure of the alkylating agent, and the nature of the solvent [1, 2]. According to existing technology for the production of sodium pentobarbital by alkylating malonic ester, sodium ethoxide and ethyl alcohol are used as base and solvent. Metal alcoholates are usually bases strong enough for effective alkylation, whereas the effect of the solvent becomes important in the second alkylation, when the acidity of the ethyl alcohol competes with the acidity of the monoalkyl-malonic ester, and the necessary condition of the second alkylation is that the ethyl alcohol should be carefully distilled off and replaced by other solvents. In connection with this, the use of dimethylformamide (DMF) as solvent is of great interest [3]. According to the literature, alkylation is accelerated in aprotic solvents, such as DMF, the order of introduction of the alkyl groups being of no importance [4, 5].

According to the technological system in force, the malonic ester is first alkylated with ethyl bromide, and then with 2-bromopentane. The yield of ethylmalonic ester (1) is 73.9%, the content of the principal substance being 83.4%. The yield of ethyl-(1-methylbutyl)-malonic ester (II) is 47.2% (on the basis of I), and its purity is 76.7%.

The use of DMF makes it possible to change the order of alkylation, which allows the purity of the products to be increased, their yield to be increased, and the duration of the process to be reduced. The yield of 1-methylbutylmalonic ester (III) reaches 75.5% (purity 97.4%), and the yield of II is increased to 73.5%, the content of the principal substance being 94.7%. The overall yield of II, on the basis of the malonic ester, was increased by 20% in DMF. In the two stages, the alkylation time was cut to 4 hours in comparison with 24 hours. It is to be supposed that the higher purity of II will allow sodium pentobarbital preparations of higher purity to be obtained.

## EXPERIMENTAL

Gas-liquid chromatography was carried out on a LKhM-7A chromatograph, with a detector registering the thermal conductivity at 140°, the liquid phase being 5% SE-30 siloxane elastomer on silanized chromosorb P (80-100 mesh) and the carrier gas being helium.

<u>1-Methylbutylmalonic Ester (III).</u> 106.4 g of malonic ester are added at 50° to a solution of sodium ethoxide (from 15.3 g of sodium and 210 ml of absolute ethyl alcohol), the alcohol is distilled off at atmospheric pressure until the temperature in the mass is  $110-115^\circ$ , the reaction mixture is cooled to 40°, and 120 ml of dry DMF added. The residual alcohol is distilled off under vacuum (400-420 mm). The solution is then cooled to 20°, and 85 ml of 2-bromoethane added. The reaction mass is slowly heated to 110° and stirred for 2 hours (on termination of the reaction, the medium is neutral). The mixture is cooled to 20°, 120 ml of water added, and the organic layer distilled under high vacuum. 118.5 g of III are obtained; the purity is 97.4%. Yield 75.5%, bp 88-100° (4 mm),  $n_{20}^{20} = 1.4275$ .

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Ethyl-(1-methylbutyl)malonic Ester (II). 96.7 g of III are added at 60° to sodium alcoholate (from 10.3 g of sodium and 102 ml of absolute ethyl alcohol), the alcohol is distilled off at atmospheric pressure until the temperature in the mass is 115°, the mass is then cooled to 40°, 100 ml of dry DMF are added, and the residual alcohol is carefully distilled off under vacuum. The reaction mixture is cooled to 20°, 35 ml of ethyl bromide is added, and the mass is slowly heated to 110° and stirred for 2 hours (on termination of the reaction, the medium is neutral). The mixture is cooled to 15-20°, 110 ml of water added, and the organic layer distilled. 84.3 g of II are obtained; the purity is 94.7%. Yield 73.5%, bp 116-121° (7 mm),  $n_D^{20} = 1.4355$ .

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