SYNTHESES OF HETEROCYCLIC COMPOUNDS

Volumes 3 and 4

Edited by

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TRANSLATED FROM RUSSIAN

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СИНТЕЗЫ ГЕТЕРОЦИКЛИЧЕСКИХ СОЕДИНЕНИЙ

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SINTEZY GETEROTSIKLICHESKIKH SOEDINENII

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SYNTHESES OF HETEROCYCLIC COMPOUNDS

Volume 3

PUBLISHER'S FOREWORD

The publishers were highly pleased with the enthusiastic reception afforded Volumes 1 and 2 of this series, and fully expect that the present volumes will be of equal value to the Western scientific community.

In order to make this book even more useful, certain minor changes have been made in organization, namely, the pagination for the two volumes was made consecutive, and a combined index was prepared instead of separate indexes at the end of each volume. In every other respect the treatment of Volumes 3 and 4 is consistent with that of Volumes 1 and 2.

PREFACE

Volume 3 of "Syntheses of Heterocyclic Compounds," like Volumes 1 and 2, contains material on the synthesis of furan derivatives; it describes laboratory methods for the preparation of thirty compounds of this series.

In selecting material for this volume, the Editorial Board has tried to include furan derivatives which, by virtue of their structures and functional groups, may be of interest as intermediates in the synthesis of compounds of more complex structure. The Editorial Board considers that, from this point of view, the methods given for the preparation of aldehydes (5-benzyl-2-furaldehyde, 5-p-methylbenzyl-2-furaldehyde, 4,5-dimethyl-2-furaldehyde) and dicarboxylic acids (5,5'-methylenedi-2-furoic, 5-[(carboxymethylthio)methyl]-2-furoic, 5-carboxy-2-furanacetic acids) are of particular interest and open up new possibilities of synthesis in this series.

In the compilation of "Other Methods of Preparation," literature published up to the end of 1956 has been reviewed.

A. L. Mndzhoian

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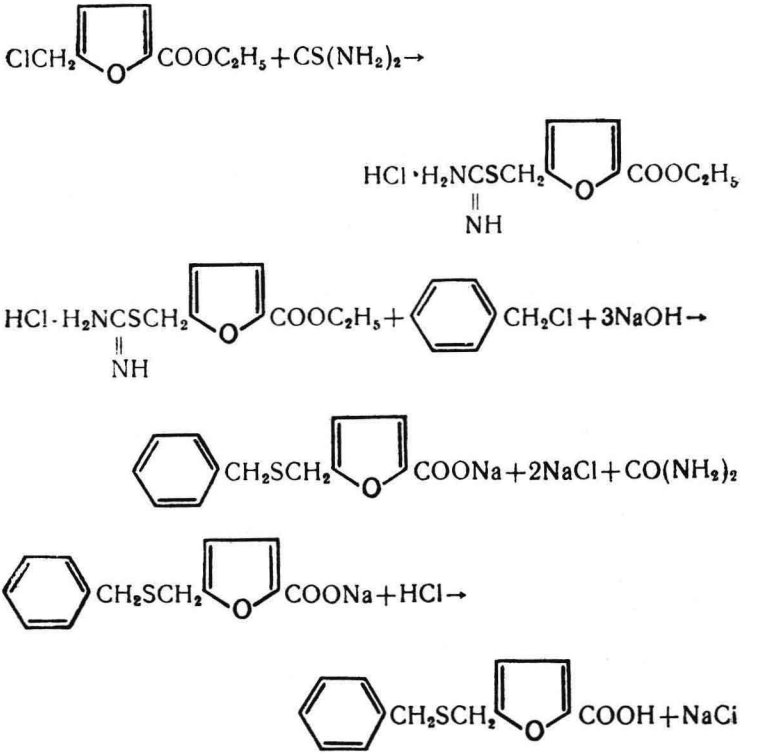
5-(BENZYLTHIOMETHYL)-2-FUROIC ACID



Proposed by A. L. Mndzhoian and A. A. Aroian
Checked by V. G. Afrikian and A. A. Dokhikian

PREPARATION

Ethyl 5-(Amidinothiomethyl)-2-furoate Hydrochloride. A mixture of 37.7 g (0.2 mole) of freshly distilled ethyl 5-(chloromethyl)-2-furoate (see CB translation of Vol. 1 of this work, p. 30), 15.2 g (0.2 mole) of thiourea, and 40 ml of absolute methanol was prepared in a 250-ml round-bottomed flask fitted with reflux condenser protected by a calcium chloride tube. The mixture was boiled in a water bath for 4 – 5 hours, and then, while still hot, it was poured into a 500-ml beaker; the flask was rinsed with 5 ml of absolute methanol (Note 1), which was then added to the bulk of the mixture. The solution was cooled with running water from the mains and stirred with a glass rod while 175 – 200 ml of dry ether was added.

The product separated as an oily layer, which later turned into a finely crystalline substance. The crystals were filtered off at the pump, washed with 50 ml of dry ether, and dried in the air; m.p. 158 – 159° (Note 2).

Yield 50.4 – 52.1 g (95.1 – 98.3%) (Note 3).

5-(Benzylthiomethyl)-2-furoic Acid. A mixture of 26.5 g (0.1 mole) of ethyl 5-(amidinothiomethyl)-2-furoate hydrochloride, 18.9 g (0.15 mole) of benzyl chloride, and 50 ml of ethanol was prepared in a 500-ml three-necked round-bottomed flask fitted with a stirrer, which entered through a seal, a dropping funnel, and a reflux condenser. The mixture was stirred in a boiling water bath for 15 – 20 minutes; the bath was then removed, and over a period of one hour a solution of 20 g (0.5 mole) of sodium hydroxide in 200 ml of 75% ethanol was added. Heating and stirring were continued further for 4 – 5 hours; the reflux condenser was then replaced with one set for distillation, and the alcohol was distilled off completely.

Water (100 ml) was added to the residue, and the alkaline solution was washed with 50 ml of ether. The washed solution was heated in a boiling water bath to remove residual ether, cooled, and poured into a beaker containing 100 – 150 g of ice and 60 ml of concentrated hydrochloric acid (the mixture was then acid to Congo red). The 5-(benzylthiomethyl)-2-furoic acid that separated was filtered off, washed with 50 ml of cold water, and dried in the air. The crude product amounted to 26.3 – 27.8 g and melted at 117 – 118°.

For purification the acid was dissolved in 100 – 110 ml of 50% acetic acid, and the resulting solution was boiled for 5 – 10 minutes with 1.5 – 2 g of animal charcoal and filtered through a hot filter. The product was washed with 25 – 30 ml of cold water, pressed out well on the filter, and dried in the air; m.p. 123 – 124°.

Yield 22.1 – 23.2 g (89.0 – 93.4%) (Note 4).

5-(Benzylthiomethyl)-2-furoic acid ($C_{13}H_{12}O_3S$; mol. wt. 248.30) crystallizes in the form of fine needles, readily soluble in alcohol and acetic acid, poorly soluble in ether, benzene, and water.

NOTES

1. If a large amount of methanol is used, addition of a very