solution was evaporated, and the residue was dissolved in benzene and passed through a column filled with silica gel (100/160 $\mu$) with elution by chloroform. The solvent was removed from the eluate by evaporation to give 0.1 g (20%) of 1-methyl-3-phenylindole with mp 63-65 deg C. Mass spectrum: $[M^+]$ 207. The product had $R_f$ 0.52. According to the data in [10], this compound has mp 65 deg C.

1-Methyl-3-phenyl-2-iminoindoline (IIIa). A 1.7-g (0.075 mole) sample of phosphorus pentasulfide was added to a solution of 2.4 g (0.1 mole) of phenylacetic acid N'-methyl-N'-phenylhydrazide in 24 ml of absolute ether, and the mixture was refluxed in a stream of argon for 8 h. Complete disappearance of the starting hydrazide was observed by TLC after 1 h. The mixture was then cooled, and the resulting precipitate was removed by filtration, washed twice with dioxane and ether, and dried to give 1.7 g (66%) of crude salt III with mp 172-210 deg C. The precipitate was made alkaline with 1 N sodium hydroxide solution, and the mixture was refluxed for 5 min. The insoluble material [0.98 g (45%)] was removed by filtration, washed twice with water, and dissolved completely in acetone. The product was precipitated by the addition of water, and the precipitate was refluxed for 10 min in 50% ethanol containing activated charcoal. The hot ethanol solution was filtered, and the filtrate was cooled. The resulting crystals were separated and recrystallized from absolute ethanol to give 280 mg of 1-methyl-3-phenyl-2-iminoindoline with mp 110-112 deg C. Mass spectrum: $[M^+]$ 222. Found: N 12.2%. Calculated N 12.6%. UV spectrum (in methanol), $\lambda_{max}(\log \varepsilon)$: 272 (3.89) and 300 nm (3.84).

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# SYNTHESIS OF ARYL β-HETERYLETHYL KETONES

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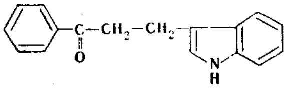
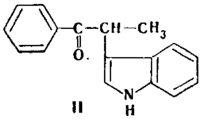
UDC 547.751.547.589

The decarboxylation of $\beta$-aroyl-$\alpha$-heterylpropionic acids in vacuo leads to the formation of the corresponding ketones.

To solve the problem of the direction of nucleophilic attack by enamines of the indole and pyrrole type at the ethylene bond of $\beta$-aroylacrylic acids we have previously accomplished the decarboxylation of $\beta$-benzoyl-$\alpha$-(3-indolyl)propionic acid [1]. The structure of the resulting ketone could be represented by the following formulas, depending on the structure of the starting acid:



I



II

The PMR signals of the $-CH_2-CH_2-$ or $CH-CH_3$ fragments constitute a criterion for the identification of the two alternative structures. On the basis of the spectra obtained (from the absence of signals of a $CH_3$

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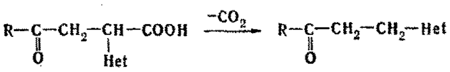
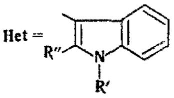
group) it was shown that the investigated compound has structure I. On the basis of these data we developed a preparative method for the synthesis of aryl β-heteryl- and thienyl β-heterylethyl ketones by decarboxylation in vacuo of α-substituted β-aroyl- and β-thienoylacrylic acids.



$$\underset{\text{III}}{R-\underset{\underset{O}{\|}}{C}-CH_2-\underset{\underset{Het}{|}}{CH}-COOH} \xrightarrow{-CO_2} \underset{\text{IV}}{R-\underset{\underset{O}{\|}}{C}-CH_2-CH_2-Het}$$

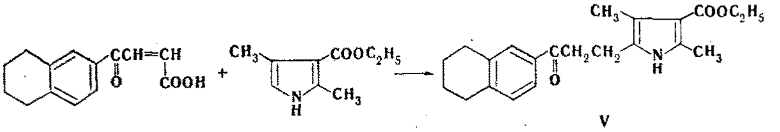


We have previously carried out the decarboxylation in glycerol at 200 deg C [1]. However, under these conditions the starting acids were not decarboxylated or the reaction led to the formation of a mixture of the acid and ketone. It was established that the optimal variant is decarboxylation by vacuum distillation. The structures of the synthesized ketones were confirmed by data from the IR and PMR spectra.

The absorption band characteristic for the carboxyl carbonyl group at 1700-1710 $cm^{-1}$ vanishes in the IR spectra of the ketones. On the basis of the PMR spectra of the ketones one can confidently assert that they are aryl β-heterylethyl ketones. Thus the spectrum of IVa contains the signal (a multiplet of the $A_2B_2$ type) of a $-CH_2-CH_2-$ fragment at 2.90-3.45 ppm. The NH signal is located at weakest field (a broad singlet at 10.67 ppm). Overlapped multiplets of aromatic protons and a singlet signal of the α proton of an indole ring are found at 6.80-8.00 ppm.

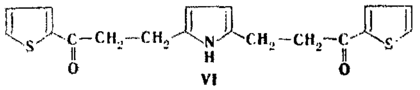
The formation of ketones IVa-h provides evidence for the addition of the indole at the α-carbon atom of β-aroylacrylic acids in accordance with the theoretical concepts of the orientation of attack at an α,β-disubstituted ethylene bond. The ketones were identified, and their oximes and 2,4-dinitrophenylhydrazones were obtained (Table 1). It was demonstrated by thin-layer chromatography (TLC) that the oximes are individual products rather than mixtures of the syn and anti isomers.

Aryl β-(3-heteryl)ethyl ketones can be obtained in some cases directly from β-aroylacrylic acids and pyrrole derivatives. Thus the reaction of β-(tetrahydro-2-naphthoyl)acrylic acid with substituted pyrrole leads to ketone V.

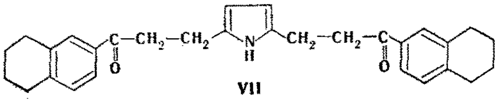


V

β-Aroylacrylic acids react peculiarly with pyrrole. It has been previously shown that the reaction of benzoyl- and toluylacrylic acids leads to the formation of certain amounts of the diketones [2]. We studied the reaction of β-thienoylacrylic and tetrahydronaphthoylacrylic acids with pyrrole. The results of the experiments showed that pyrrole is alkylated in the 2 and 5 positions to give diketones VI and VII, the products of decarboxylation of the dicarboxylic acids, rather than the expected dicarboxylic acids. The structure of the diketones was confirmed by data from the IR and PMR spectra.



VI



VII

It must be noted that the reaction of β-aroyl- and β-indoylacrylic acids with indole and its derivatives leads only to the formation of β-aroyl-α-substituted propionic acids [1] and β-indoyl-α-substituted propionic acids [3].

β-(Tetrahydro-2-naphthoyl)-α-indolylpropionic acid and its derivatives, the synthesis of which is described in the present paper, behave like the previously investigated β-aroylacrylic acids.

According to the literature data, β-aroyl-α-aminopropionic acids are reduced with lithium aluminum hydride to give either the alcohol or the lactone [4]. In order to synthesize alcohols of the indole and pyrrole series we studied the conditions for the reduction of the ketones and the starting acids. In contrast to β-aroyl-α-aminopropionic acids, we were unable to reduce β-aroyl-α-(3-heteryl)propionic acids in the presence of potassium hydroxide to the corresponding lactones. Attempts to reduce the same acids and aryl β-(α-heteryl)ethyl ketones to the corresponding alcohols in methanol by the methods in [5] were also unsuccessful.

## EXPERIMENTAL

The IR spectra of the compounds were recorded with a UR-10 spectrometer. The PMR spectra were recorded with an HA-100 spectrometer. The synthesized oximes were chromatographed on Silufol in an ether–benzene system (1 : 1).

**β-(Tetrahydro-2-naphthoyl)-α-(3-indolyl)propionic Acid.** A mixture of 2.3 g (0.01 mole) of tetrahydronaphthoylacrylic acid and 1.17 g (0.01 mole) of indole in 10 ml of dry benzene was heated on a water bath for 12 h, and the resulting precipitate was removed by filtration to give 2.34 g (67.3%) of a product with mp 188-190 deg C (from methanol). IR spectrum: 1665, 1705 (C=O); 3410 cm$^{-1}$ (NH). Found: C 76.2; H 6.0; N 3.6%. $C_{22}H_{21}NO_3$. Calculated: C 76.0; H 6.1; N 3.7%. The methyl ester had mp 146°C (from methanol). Found: N 4.1%. $C_{23}H_{24}NO_3$. Calculated: N 3.8%. The method described above was also used to obtain β-(tetrahydro-2-naphthoyl)-α-[1-(β-cyanoethyl)-3-indolyl]propionic acid, with mp 180-181 C (from methanol), in 84.6% yield. IR spectrum: 1665 and 1705 cm$^{-1}$ (C=O). Found: C 72.8; H 6.6; N 6.9%. $C_{25}H_{29}N_2O_3$. Calculated: C 72.5; H 6.4; N 6.6%. The methyl ester had mp 176-177 C (from methanol). Found: C 75.2; H 6.4; N 6.9%. $C_{26}H_{26}N_2O_3$. Calculated: C 75.3; H 6.3; N 6.7%.

**6-Tetrahydro-4-naphthyl-4-indolyl-2,3,4,5-tetrahydro-3-pyridazinone.** A mixture of 1 g (0.004 mole) of β-(tetrahydro-2-naphthoyl)-α-(3-indolyl)-propionic acid and 3 ml of 80% hydrazine hydrate was heated on a water bath for 2 h, and the resulting precipitate was washed with hot alcohol to give 0.75 g (76.5%) of a product with mp 160-162 deg C. Found: N 12.9%. $C_{22}H_{21}N_3O$. Calculated: N 12.5%. The same method was used to obtain 0.7 g (70.7%) of 6-tetrahydro-4-naphthyl[1-(β-cyanoethyl)-3-indolyl]-2,3,4,5-tetrahydro-3-pyridazinone with mp 178-180 deg C. Found: N 14.1%. $C_{25}H_{24}N_4O$. Calculated: N 14.1%.

**p-Toluyl β-(2,4-Dimethyl-3-carbethoxypyrrolyl)ethyl Ketone.** A 1.9-g (0.01 mole) sample of p-toluyl-β-(2,4-dimethyl-3-carbethoxy-5-pyrrolyl)propionic acid was added to 20 ml of glycerol heated to 140 deg C. Decarboxylation was completed by heating the reaction mixture at 200 deg C for 10-15 min until a clear solution formed. It was then cooled, and 70 ml of water was added. The next day, the resulting ketone was removed by filtration to give 1.7 g (70%) of a product with mp 120 deg C (from alcohol). IR spectrum: 1656 (conjugated ketone C=O) and 1694 cm$^{-1}$ (conjugated ester C=O). Found: C 72.6; H 7.3; N 4.6%. $C_{19}H_{23}NO_3$. Calculated: C 72.8; H 7.4; N 4.5%. The oxime had mp 159-160 deg C (from alcohol). The dinitrophenylhydrazone had mp 203 deg C (from alcohol).

**Tetrahydro-2-naphthyl β-(2,4-Dimethyl-3-carbethoxy-5-pyrrolyl)ethyl Ketone (V).** A mixture of 2.3 g (0.01 mole) of β-tetrahydronaphthoylacrylic acid and 1.5 g (0.01 mole) of 2,4-dimethyl-3-carbethoxypyrrole was refluxed in 10 ml of benzene for 6 h, and the resulting precipitate was removed by filtration, washed with alkali, and recrystallized from methanol to give 2.5 g (73.5%) of a product with mp 146-148 deg C. IR spectrum: 1665 (conjugated ketone C=O), 1700 (conjugated ester C=O), and 3340 cm$^{-1}$ (NH). Found: C 73.9; H 7.3; N 4.8%. $C_{21}H_{25}NO_3$. Calculated: C 74.3; H 7.4; N 4.5%. The oxime had mp 112 deg C (from alcohol). The dinitrophenylhydrazone had mp 201 deg C (from alcohol).

**2,5-Bis(3-keto-3-thienylpropyl)pyrrole (VI).** A mixture of 3.6 g (0.02 mole) of thienoylacrylic acid and 0.67 g (0.01 mole) of pyrrole in 15 ml of benzene was refluxed for 12 h, and the resulting precipitate was removed by filtration and purified by boiling in methanol to give 3.2 g (72.6%) with mp 158-160 deg C. IR spectrum: 1650 (C=O) and 3330 cm$^{-1}$ (NH). Found: C 62.8; H 5.1; N 4.2%. $C_{20}H_{17}NO_6S_2$. Calculated: C 62.9; H 4.9%; N 4.3%. 2,5-Bis[3-keto-3-(tetrahydro-2-naphthyl)]pyrrole (VII), with mp 173-175 deg C (from methanol), was similarly obtained in 62% yield. IR spectrum: 1650 (C=O) and 3330 cm$^{-1}$ (NH). Found: C 81.2; H 7.2; N 3.3%. $C_{30}H_{33}NO_2$. Calculated: C 81.6; H 7.5; N 3.2%.

**Aryl β-(3-Indolyl)ethyl Ketones (IV).** A 4.7-g (0.016 mole) sample of β-aroyl-α-(3-indolyl)propionic acid was vacuum distilled at 270-300 deg C (3 mm) to give an oil, which crystallized when it was cooled. The crystalline mass was washed with alkali and water, dried, and recrystallized from alcohol. IR spectrum: 1670-1678 cm$^{-1}$ (C=O) (Table 1). The oximes and 2,4-dinitrophenylhydrazones of the ketones were obtained in alcohol or pyridine.

TABLE 1. Aryl β-(3-Heteryl)ethyl Ketones IV

| Compound | R | R′ | R″ | mp, °C | Found, % |  |  | Empirical formula | Calculated, % |  |  | Yield, % | mp, °C |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  | C | H | N |  | C | H | N |  | Oxime | Dinitrophenylhydrazone |
| IV a | $C_6H_5$ | H | H | 127—128 | 82,2 | 6,3 | 5,5 | $C_{17}H_{15}NO$ | 81,9 | 6,3 | 5,6 | 63 | 172 | 188—189 |
| IV b | $C_6H_5$ | H | $CH_3$ | 138—139 | 81,8 | 6,3 | 5,0 | $C_{18}H_{17}NO$ | 82,1 | 6,5 | 5,3 | 59 | 260—265 | — |
| IV c | n-$CH_3C_6H_4$ | H | H | 142 | 82,3 | 6,4 | 5,6 | $C_{18}H_{17}NO$ | 82,1 | 6,5 | 5,3 | 60 | 159—160 | 205 |
| IV d | n-$CH_3C_6H_4$ | $CH_2CH_2CN$ | H | 132—133 | 79,6 | 6,6 | 8,8 | $C_{21}H_{20}N_2O$ | 79,7 | 6,4 | 8,8 | 79 | 76—78 | 160—162 |
| IV e | n-$CH_3C_6H_4$ | H | $CH_3$ | 258—260 | 82,6 | 6,9 | 6,4 | $C_{19}H_{19}NO$ | 83,2 | 6,9 | 6,1 | 62 | 270—271 | — |
| IV f | n-$CH_3OC_6H_4$ | H | H | 125—126 | 77,6 | 5,8 | 5,3 | $C_{18}H_{17}O_2$ | 77,4 | 6,1 | 5,0 | 84 | 138 | 197—198 |
| IV g | $C_{10}H_{11}$ | H | H | 112—113 | 82,8 | 6,8 | 4,8 | $C_{21}H_{21}NO$ | 83,1 | 7,0 | 4,6 | 54 | 154 | — |
| IV h | $C_{10}H_{11}$* | $CH_2CH_2CN$ | H | Hygroscopic | 80,6 | 6,7 | 8,0 | $C_{24}H_{24}N_2O$ | 80,9 | 6,8 | 7,9 | 52 | 123—125 | 88—90 |

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* 1,2,3,4-Tetrahydro-6-naphthyl.

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# REACTION OF 3-MERCAPTOINDOLE AND ITS ETHYL DERIVATIVES WITH ACETYLENE

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UDC 547.752

1-Vinyl-3-vinylthioindole, 1-vinyl-3-ethylthioindole, and 1-ethyl-3-vinylthioindole, respectively, were obtained by the reaction of 3-mercaptoindole, 3-ethylthioindole, and 1-ethyl-3-mercaptoindole with acetylene. 3-Mercaptoindole reacts with acetylene in aqueous media to give 3-vinylthioindole. The structures of the vinyl derivatives of 3-mercaptoindole obtained were proved by means of IR and PMR spectroscopy and the results of elementary analysis.

Indole reacts with acetylene under pressure in the presence of an alkaline catalyst under rather severe temperature conditions to give 1-vinylindole [1]. There is no information in the literature regarding the synthesis of vinyl derivatives of 3-mercaptoindole. The introduction of an SH group in the 3 position of the indole molecule leads to the development of a new reaction center that is capable, together with the imino group, of reaction with acetylene.

We have found that the reaction of acetylene with indoles I-III under the conditions of the vinylation of indole (at 220 deg C for 30 min) proceeds with pronounced resinification. Vinyl derivatives were isolated in no greater than 3-5% amounts. Lowering the reaction temperature 40 deg C made it possible to obtain 1-vinyl-3-vinylthioindole (IV) and 1-vinyl-3-ethylthioindole (V) in good yields (up to 70%). A further decrease in the reaction temperature to 150-160 deg C reduces the yields of vinylthioindoles IV and V, respectively, to 35 and 23%; the formation of the product of the addition of one molecule of acetylene – 3-vinylthioindole (VII) – is observed in the case of 3-mercaptoindole. We were unable to obtain monovinyl derivative VII in high yield in dioxane. Vinyl sulfide VII was obtained in 60% yield in the reaction of 3-mercaptoindole with acetylene in water in the presence of an equimolar amount of KOH.

I-III IV-VII

I $R=R'=H$; II $R=C_2H_5$, $R'=H$; III $R=H$, $R'=C_2H_5$; IV $R=R'=CH=CH_2$;
V $R=CH=CH_2$, $R'=C_2H_5$; VI $R=C_2H_5$, $R'=CH=CH_2$; VII $R=H$, $R'=CH=CH_2$

We assume that, as in the case of cyclic thioamides, acetylene adds initially to the more nucleophilic sulfur atom in the vinylation of mercaptoindole I. Considerably milder conditions than in the reaction of indole with acetylene are necessary for this. Evidence for this is also provided by the relative ease of formation of 1-ethyl-3-vinylthioindole (VI), the yield of which at 120 deg C reaches 60%. Due to its electron-acceptor effect, the vinylthio grouping formed in the case of mercaptoindole I in the 3 position of the indole ring promotes greater polarizability of the N–H bond, as a consequence of which the addition of a second molecule of acetylene to the nitrogen atom occurs under milder conditions than addition to indole itself.

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