# SUBSTITUTED ARYLAMIDES OF DITHIOCARBOXYLIC ACIDS

## XIII* SYNTHESIS OF 2,3-DISUBSTITUTED THIAZOLIDIN-4-ONES

A. D. Grabenko, L. N. Kulaeva, and P. S. Pel'kis

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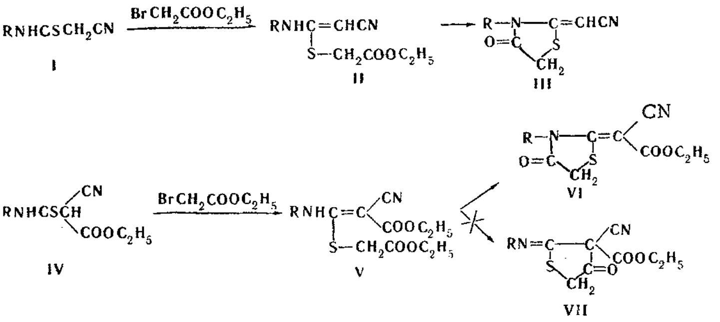
The S-substituted derivatives formed by the reaction of arylamides of cyanothioacetic acid and the esters of arylamides of cyanomonothiomalonic acid with ethyl bromoacetate are cyclized to 2-cyanomethylidene-3-arylthiazolidin-4-ones (III) and 2-carbethoxycyanomethylidene-3-arylthiazolidin-4-ones (VI) rather than to tetrahydrothiophenone derivatives as previously proposed in [1,2].

Among the substituted thiazolidin-4-ones one finds substances which have high physiological activity [3,4]. They also serve as the intermediates in the synthesis of cyanin dyes [5] and other organic substances.

Thiazolidinones are primarily obtained by the reaction of thiocarboxamides with α-halocarboxyl compounds [6]. It was of interest to synthesize new thiazolidin-4-one derivatives starting from the arylamides of cyanothioacetic acid (I), previously described by us [7], and from the esters of arylamides of cyanomonothiomalonic acid (IV) by reaction with ethyl bromoacetate:



The reaction initially gives intermediates II and V, which are then cyclized to III and VI.

A product to which Ruhemann [1] assigned, without proof, the tetrahydrothiophenone structure (VII), was isolated from the reaction of IV with ethyl chloroacetate. Barnikow and co-workers [2], on carrying out the same reaction, isolated intermediate V, which according to their data, also cyclizes to derivative VII; they assumed the VII structure on the basis of the absence of a characteristic absorption band for the NH group and on the basis of the presence of an absorption band at 1743-1753 cm$^{-1}$.

The IR spectra of the compounds obtained by us have absorption frequencies characteristic for the thiazolidine ring at 1530-1509 cm$^{-1}$ (very strong), 1380 cm$^{-1}$ (strong), and 1290 cm$^{-1}$ (strong) [8] and do not contain the strong valence vibration bands of substituted thiophenes [9] at 1402-1444 and 1339-1365 cm$^{-1}$. The absorption bands at 1709-1754 cm$^{-1}$ can be ascribed to the carbonyl group vibrations for substituted thiazolidin-4-ones [9].

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*See Zh. Organ. Khim., 4, 234 (1968) for Communication XII.

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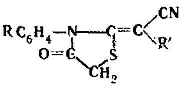
TABLE 1. 2,3-Substituted Thiazolidin-4-ones



| Compound | R | R′ | Mp, °C | Reaction conditions | Empirical formula | N, % |  | Yield, % |
|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  | Found | Calc. |  |
| IIIa | H | H | 185—186 | Refluxing alcohol for 1.5 h | $C_{11}H_8N_2OS$ | 12,77 | 12,96 | 74 |
| IIIb | p-$C_2H_5O$ | H | 155—156 | Same | $C_{13}H_{12}N_2O_2S$ | 10,56 | 10,77 | 55 |
| IIIc | p-Br | H | 150—151 | Same | $C_{11}H_7BrN_2OS$ | 9,45 | 9,49 | 48 |
| VIa | H | $C_2H_5OOC$ | 210—211 | Room temperature for 2 h | $C_{14}H_{12}N_2O_3S$ | 9,68 | 9,72 | 85 |
| VIb | p-$C_2H_5O$ | $C_2H_5OOC$ | 175—176 | Same | $C_{16}H_{16}N_2O_4S$ | 8,21 | 8,43 | 73 |
| VIc | p-$NO_2$ | $C_2H_5OOC$ | 225—227 | Same | $C_{14}H_{11}N_3O_5S$ | 12,39 | 12,61 | 32 |

If the final product did have the VII structure, refluxing it with mineral acids should have brought about cleavage of the N=C bond to form the amine and the tetrahydrothiophene-2,4-dione derivative. The starting material was isolated after refluxing the compounds obtained by us in alcoholic hydrochloric acid (1:1) for 15 h, and no traces of amine were found in the hydrochloric acid solution.

Thus, one can assume that S-substituted derivatives II and V are initially formed by the reaction between ethyl bromoacetate and arylamides of cyanothioacetic acid or esters of the arylamides of cyanomonothiomalonic acid and are then cyclized to 2-cyanomethylidene-3-arylthiazolidin-4-ones (III) and 2-carbethoxycyanomethylidene-3-arylthiazolidin-4-ones (VI) rather than to thiophenone derivatives.

## EXPERIMENTAL

S-Carbethoxymethyl-p-phenetidide of Cyanothioacetic Acid (II, R = p-$C_2H_5O$, $C_6H_4$). Ethyl bromoacetate [0.8 g (0.005 mole)] was added to a solution of 1.1 g (0.005 mole) of cyanothioacetic acid p-phenetidide in alcoholic ethoxide (0.1 g of sodium in 15 ml of absolute alcohol) at room temperature. The crystalline precipitate that formed in several hours was filtered, air-dried, and crystallized from alcohol to give 0.81 g (70%) of II with mp 137 deg. Found %: N 9.50. $C_{15}H_{18}N_2O_3S$. Calc. %: N 9.15.

S-Carbethoxymethylcyanothioacetic acid p-bromoanilide (II, R = p-Br, $C_6H_4$) was obtained in 30% yield under similar conditions and did not melt up to 350 deg. Found %: N 8.03. $C_{13}H_{13}BrN_2OS$. Calc. %: N 8.21.

The light yellow crystalline products obtained are soluble in most organic solvents.

The substituted thiazolidin-4-ones were obtained under similar conditions. The data on the constants and yields of the compounds synthesized are presented in Table 1.

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