HYDROACRIDINES AND RELATED COMPOUNDS.

21.* SYNTHESIS OF 2-(2-THIENYL)HYDROQUINOLINES
AND 2,7-DITHIAHYDROACRIDINES

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UDC 547.836'818'731'831.3.07:541.63:542.942

A number of sulfur-containing 1,5-diketones were synthesized and subjected to reaction with primary amines to give derivatives of 2-(2-thienyl)hydroquinolines and 2,7-dithiahydroacridines that contain 1,4-dihydropyridine and benzoxazolino-tetrahydropyridine structures. The oxidation of some of the dihydropyridine derivatives was studied.

Continuing our research on the reaction of 1,5-diketones with primary amines [1] we studied the reaction of sulfur-containing 1,5-diketones Ia-d and IIa, b with primary amines in order to obtain compounds that have antioxidant activity. Diketone Ic was obtained in [2], whereas we synthesized the remaining ketones for the first time: Ia, b were synthesized by heating the Mannich base of α-acetothienone with the corresponding cyclanone at 140-150°C, Ia was synthesized by the addition of cyclohexanone to p-hydroxybenzalacetothienone, and IIa, b were synthesized by diketone condensation of 2,2-dimethyltetrahydro-4-thiopyrone with the corresponding aldehydes.

The reaction of the indicated diketones with primary amines yielded 1,4-dihydropyridine derivatives IIIa-d and IVa-c, while the reaction of diketones Ib and IIb with o-aminophenol


leads to, respectively, V and VI with a benzoxazolinotetrahydropyridine structure, as in the case of other 1,5-diketones [3]. Complex mixtures of products with high percentages of the starting diketones are formed in a number of cases (diketones Ia and Id) during attempts to carry out the reaction with primary amines; we were unable to isolate reaction products.

The IR spectra of IIIa-d contain two \( \text{C}=\text{C} \) absorption bands, one at 1630-1640 cm\(^{-1}\), and the other at 1680 cm\(^{-1}\). The \( \text{C}=\text{C} \) absorption in the spectra of Va-c also has the form of a doublet with one band at 1660-1670 cm\(^{-1}\) and the other at 1690-1700 cm\(^{-1}\). The spectra of IIc and IVb also contain absorption at 1720 cm\(^{-1}\) (COOCH\(_3\)). The spectra of V and VI do not contain OH absorption, and the region of \( \text{C}=\text{C} \) absorption contains a single band at 1640 cm\(^{-1}\) in the case of V and at 1670 cm\(^{-1}\) in the case of VI. The position of the \( \text{C}=\text{C} \) absorption band in the spectrum of V indicates the formation of an azoline ring on the side of the alicyclic fragment of diketone Ib.

The 1,4-dihydropyridine derivatives obtained proved to be more resistant to oxidation than the previously investigated decahydroacridines. Thus diketone IIa reacts with aniline and CCl\(_4\) [4] to give pyridinium salt VII in relatively low yield, while p-aminobenzoic acid virtually does not undergo reaction under these conditions. Compound IVb decolorizes methylene blue almost an order of magnitude more slowly than 10-(p-carbomethoxyphenyl)decahydroacridine. Water-soluble carboxylate VIII reduces acridine to acridan under mild conditions; however, it does not reduce benzalacetophenone and benzalaniline, which are readily reduced by the analogous carboxylate of the decahydroacridine series [1].

We have demonstrated the possibility of the one-step synthesis of thia analogs of sym-octahydroacridinium salts in the case of the reaction of 2,2-dimethyltetrahydrothiopyrone, benzaldehyde, and aniline in the presence of CCl\(_4\) and p-toluenesulfonic acid, as in the synthesis of sym-octahydroacridinium salts [5]. The corresponding salt (IX) was obtained in 40% yield.

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The IR spectra of mineral oil suspensions and solutions of the compounds in chloroform were recorded with a UR-20 spectrometer. The course of the reactions and the purity of the compounds obtained were monitored by thin-layer chromatography (TLC) on Silufol and activity II Al\(_2\)O\(_3\). The characteristics of the synthesized compounds are presented in Table 1.

1-(a-Thienyl)-3-(2-oxocycloalkyl)propan-1-ones (Ia, b). 2-(3-Dimethylamino-1-propanonyl)thiophene was refluxed with a twofold molar excess of the corresponding cyclanone until dimethylamine liberation ceased (50 h in the case of Ia, as compared with 2 h in the case of Ib), after which the excess cyclanone was removed by distillation at reduced pressure. In the case of Ia the residue was distilled in vacuo with collection of the fraction with bp 172-176°C (6 mm) in the form of a viscous oil, which gradually began to crystallize. In the case of Ib the residue was passed through activity II Al\(_2\)O\(_3\), and diketone Ib was eluted with diethyl ether; the residue after removal of the ether from the eluate by distillation was crystallized.

1-(a-Thienyl)-3-(p-hydroxyphenyl)-3-(2-oxocyclohexyl)propan-1-one (Id). An equimolar (with respect to the chalcone) amount of NaOH in the form of a 40% aqueous solution was added with stirring to a solution of p-hydroxybenzylidene-\( \alpha \)-acetothienone and a threefold molar excess of p-hydroxybenzylidene-\( \alpha \)-acetothienone and a threecold molar excess of cyclohexanone in ethanol (20 ml per gram of chalcone). After 24 h, the mixture was acidified with HCl (1:1) and diluted with a twofold volume of water. The liberated oil crystallized immediately, and Id was removed by filtration, washed with aqueous ethanol and water, and dried.

5,5'-Methylenebis(2,2-dimethyltetrahydro-4-thiopyrone) (IIa) and 5,5'-Benzylidenebis-(2,2-dimethyltetrahydro-4-thiopyrone) (IIb). An equimolar amount of a 2 N alcohol solution of NaOH was added with stirring to a heated (to 80°C) sample of 2,2-dimethyltetrahydro-4-thiopyrone, after which a 35% aqueous solution of formaldehyde or an alcohol solution of