REACTION OF 1,3-DIPHENYLBARBITURIC AND 1,3-DIPHENYL-2-THIOBARBITURIC ACIDS WITH DIAZOTIZED SULFANILAMIDES

Ch'ang Feok Hung and A. M. Khaletskii

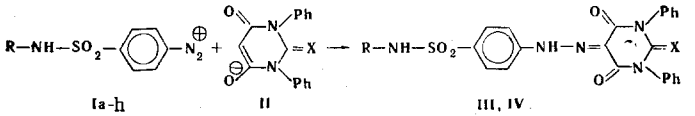
UDC 547.854.5

The reaction of 1,3-diphenylbarbituric and 1,3-diphenyl-2-thiobarbituric acids with diazotized sulfaniiimides gives 1,3-diphenylalloxan and 1,3-diphenyl-2-thioalloxan phenylhydrazones.

The products of the reaction of diazonium salts with 5-unsubstituted and 5-monosubstituted barbituric and thiobarbituric acids have been known for a long time [1]. Azo coupling with 1,3-diphenylbarbituric and 1,3-diphenyl-2-thiobarbituric acids has received little study. Only products of the coupling with diazotized aniline and p-nitroaniline have been described [2,3], but no proof for the structures of the compounds was presented, and the yields were not indicated.

The aim of this work was a study of the possibility of the coupling of variously substituted diazotized sulfanilamides with 1,3-diphenylbarbituric and 1,3-diphenyl-2-thiobarbituric acids and the elucidation of the structures of the reaction products.

The azo coupling was carried out in alkaline media with equimolecular amounts of the reacting substances, and, in all cases, led to almost quantitative yields of the reaction products (Table 1), regardless of the character of the substituent in the diazo component:



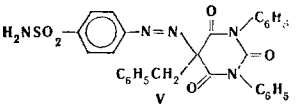
Ia-h II III, IV

a) R = H; b) R = C(=NH)NH$_2$; c) R = COCH$_3$; d) R = 2-thiazolyl e) R = 4-methyl-2- thiazolyl f) R = 5-ethyl-1,3,4-thiazol-2-yl; g) R = 2-pyridyl; h) R = 4,6-dimethyl-2-pyrimidyl

III X = O; IV X = S

Compounds III and IV are yellow or orange, chromatographically homogeneous, crystalline substances that were slightly soluble in ethanol, acetic acid, and water, and quite soluble in aqueous alkali solutions with the formation of colored solutions. Two absorption bands of similar intensity are observed in the UV spectra of these solutions (Table 1): one up to 250 nm, and the other at 362-390 nm. The long-wave band of most of thio compounds IV is bathochromically shifted by 12-13 nm as compared with the spectra of their oxygen analogs.

A model compound with a fixed p-sulfamidophenylazo group (V) in ethanol absorbs in the same region as the p-aminobenzenesulfamide and 5-benzylbarbituric acid (Fig. 1) used for its synthesis, which is characteristic for compounds with two isolated chromophores [4]. The spectrum of an ethanol solution of the product of coupling of diazotized sulfanilamide with 1,3-diphenylbarbituric acid has two absorption bands – one with a maximum at 250 nm, and the other at 385 nm – which indicates conjugation of the chromophores, which is possible in the hydrazone form (IIIa) and impossible in the azodiketo form (A).



V

Leningrad Institute of Pharmaceutical Chemistry. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1276-1279, September, 1971. Original article submitted March 12, 1970.

TABLE 1. Arylhydrazones of 1,3-Diphenylalloxan (III) and 1,3-Diphenyl-2-thioalloxan (IV)

Comp.	mp, °C	Spectral characteristics			$R_f \times 100$[b]			Empirical formula	Found, %		Calc., %		Yield, %
		λ_{max}, nm	lg ε	$\nu_{C=O}$; $\nu_{C=N}$, cm^{-1}	A	B	C		N	S	N	S	
IIIa	158—160[c]	238; 362	4,30; 4,23	1732, 1684, 1677, 1650	88	82	77	$C_{22}H_{17}N_5O_5S$	14,8	7,0	15,1	6,9	94
IIIb	163—164[d]	<224; 365	>4,37; 4,36	1737, 1679, 1666, 1642	45	62	67	$C_{23}H_{19}N_7O_5S$	19,3	6,7	19,4	6,3	90
IIIc	175—176[e]	<224; 364	>4,27; 4,44	1737, 1695, 1668	25	9	64	$C_{23}H_{19}N_5O_6S$	13,7	6,6	13,9	6,3	96
IIId	170—172[e]	236; 366	4,25; 4,30	1734, 1670, 1663	84	48	63	$C_{25}H_{18}N_6O_5S_2$	14,9	12,3	15,4	11,7	87
IIIe	283—285[c]	<224; 367	>4,36; 4,44	1747, 1679	59	18	57	$C_{26}H_{21}N_7O_5S_2$	17,2	11,3	17,0	11,1	93
III f	296—297[f]	237; 363	4,44; 4,35	1729, 1682, 1645, 1632	53	26	60	$C_{27}H_{21}N_6O_5S$	15,4	6,4	15,5	5,9	92
IIIg	185—186[e]	239; 364	4,38; 4,36	1737, 1687, 1679, 1642	92	27	64	$C_{28}H_{23}N_7O_5S$	17,3	5,5	17,2	5,6	87
IVh	205—207[f]	249; 366	4,26; 3,82	1776, 1737, 1710, 1694, 1658	87	80	69	$C_{22}H_{17}N_5O_4S_2$	14,6	13,4	14,6	13,4	89
IVa	254—255[d]	<224; 378	>4,33; 4,32	1684, 1632	40	43	63	$C_{23}H_{19}N_7O_4S_2$	18,6	11,7	18,8	12,3	92
IVb	303—304[d]	<224; 376	>4,42; 4,39	1721, 1700, 1671	10	6	62	$C_{23}H_{19}N_5O_5S_2$	13,3	12,6	13,5	12,3	96
IVc	250—252[d]	249; 390	4,33; 4,25	1782, 1713, 1668	88	31	63	$C_{25}H_{18}N_6O_4S_3$	15,0	17,1	14,9	17,1	91
IVd	220—221[d]	<224; 382	>4,42; 4,01	1745, 1718, 1668	6	7	50	$C_{26}H_{20}N_6O_4S_3$	14,4	16,5	14,6	16,7	89
IVe	264—265[d]	243; 379	4,39; 4,28	1774, 1734, 1696, 1658	71	12	60	$C_{26}H_{21}N_7O_4S_3$	16,5	15,7	16,6	16,3	94
IV f	190—192[d]	235; 375	4,48; 4,09	1780, 1705, 1666, 1640	89	44	61	$C_{27}H_{21}N_6O_4S_2$	14,8	11,7	15,1	11,5	89
IVg	210—212[d]	238; 377	4,27; 4,33	1781, 1725, 1663	90	18	65	$C_{28}H_{23}N_7O_4S_2$	16,4	10,7	16,7	10,9	90
Vh	155—156[d]	251; 316	4,33; 4,10	1756, 1700	82	85	87	$C_{29}H_{23}N_5O_5S$	12,4	5,6	12,6	5,8	93

[a] In 0.1 N NaOH.

[b] A) Activity II Al_2O_3 + 2% CH_3COOH; chloroform–hexane–absolute ethanol (1 : 1 : 1). B) Activity II Al_2O_3 + 2% 0.1 N NaOH; ethyl acetate–butanol–acetone–10% NH_4OH (3 : 3 : 4 : 1). C) Activity III Al_2O_3; C_2H_5OH–CH_3COOH (9 : 1).

[c] From aqueous ethanol.

[d] From water.

[e] From acetic acid–ethanol.

[f] From ethanol.

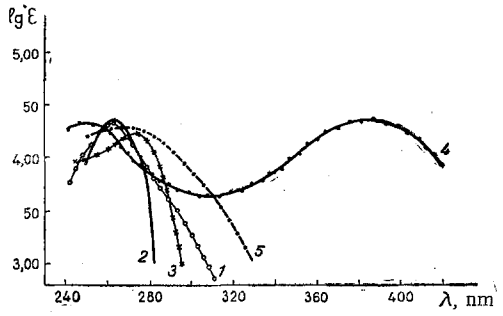
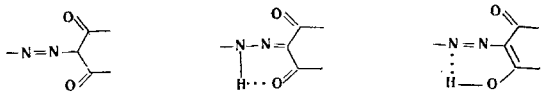


Fig. 1. Electronic spectra of alcohol solutions of: 1) sulfanilamide (I); 2) 1,3-diphenylbarbituric acid (II); 3) 5-benzyl-1,3-diphenylbarbituric acid (III); 4) p-sulfamidophenylhydrazone of 1,3-diphenylalloxan (IV); 5) 5-benzyl-5-(p-sulfamidophenylazo)-1,3-diphenylbarbituric acid (V).

The IR spectra of 1,3-diphenylbarbituric and 1,3-diphenyl-5-benzylbarbituric acids and of model compound V contain a weak band at 1742-1756 cm^{-1}, which can be ascribed to the absorption of the C=O bond of the urea fragment, and an intense band with a maximum and a shoulder (or two maxima) at 1689-1720 cm^{-1}, which is apparently associated with the absorption of the β-dicarbonyl fragment of the molecules [5,6]. The spectrum of IIIa is characterized by a band at 1732 cm^{-1}, which can also be ascribed to $\nu C_2=O$ absorption, and an intense broad band with maxima at 1684, 1675 (shoulder), and 1650 cm^{-1}, which are apparently caused by the C=O stretching vibration of the 4,6-dicarbonyl grouping and the C=N bond. Similar absorption bands are also characteristic for the spectra of the products of the azo coupling of 1,3-diphenylbarbituric acid with other diazotized sulfanilamides and also for the thio analogs of the hydrazones (IV) (Table 1).

Thus the spectral data exclude the azodiketo form (A) of the products of azo coupling and are evidence in favor of the hydrazone forms II and IV, possibly with intramolecular hydrogen bonding (B). The azo-enol form (C) is also unlikely, since the form of the UV spectrum of IIIa does not change in acidified ethanol.



Our conclusions are in agreement with those of other authors regarding the structures of similar products of the coupling of diazotized aromatic amines with 1,2-diphenyl-3,5-dioxopyrazolidine [7].

In contrast to V, which is incapable of keto-enol tautomerism, hydrazones IIIa-h and IVa-h are less mobile during chromatography on alkaline aluminum oxide and more mobile on acidic aluminum oxide or when an acidic system of solvents is used. Moreover, the thiobarbituric acid derivatives are less mobile than their oxygen analogs (Table 1) on alkaline aluminum oxide.

EXPERIMENTAL

General Method for the Preparation of 1,3-Diphenylalloxan and 1,3-Diphenyl-2-thioalloxan Hydrazones (IIIa-h, IVa-h). A 0.001 mole sample of the appropriate sulfanilamide was dissolved in 2 ml of water and 0.5 ml of 10% sodium hydroxide, the solution was cooled to 0-5°, 0.0011 mole of sodium nitrite in 0.5 ml of water was added, and 1 ml of 18% hydrochloric acid was then added with stirring. A solution of 0.001 mole of 1,3-diphenylbarbituric [8] or 1,3-diphenyl-2-thiobarbituric acid [8] in 4 ml of 10% sodium hydroxide was added to the precipitate. After stirring at 0-5° for 20 min, the mixture was acidified with acetic acid, allowed to stand for 2 h, and the precipitate was removed by filtration and dried in a vacuum desiccator. The precipitate was recrystallized from a suitable solvent and dried in vacuo. The properties of the synthesized compounds are presented in Table 1.

5-Benzyl-5-(p-sulfamidophenylazo)-1,3-diphenylbarbituric Acid (V). A 0.001 mole sample of p-aminobenzenesulfamide in 1 ml of concentrated hydrochloric acid was cooled to 0-5°, and 0.0011 mole of sodium nitrite in 1 ml of water was added with stirring. A solution of 0.001 mole of 5-benzyl-1,3-diphenylbarbituric acid [9] in 6 ml of 10% sodium hydroxide was then added, the mixture was stirred at 0.5° for 10 min, acidified with acetic acid, and allowed to stand for 3 h. The precipitate was removed by filtration and dried in a vacuum desiccator. It was then recrystallized from alcohol–water and vacuum dried. The properties of compounds V are presented in Table 1.

The UV spectra of solutions in ethanol and in 0.1 N aqueous NaOH were recorded with an SF-4A spectrophotometer in thin (10 mm) layers and concentrations of $2 \cdot 10^{-5}$ M. The IR spectra of mineral oil suspensions were obtained with an IKS-14 spectrophotometer. The chromatography was carried out in a thin,

loose layer of "for chromatography" Al_2O_3, produced by the Donetsk Chemical Reagent Plant, on 12 by 12 plates with a range of 10 cm and a layer thickness of 0.5 mm. The substances to be chromatographed were applied in about 0.001 ml (1% ethanol solutions) amounts. All of the substances were detected in UV light.

LITERATURE CITED

1. O. Kühling, Ber., 31, 1972 (1898).
2. M. A. Whiteley, J. Chem. Soc., 91, 1330 (1907).
3. A. Mossini, Ann. Chim. Farm., 47 (1939); Chem. Abstr., 34, 2175 (1940).
4. C. N. R. Rao, Electronic Spectra in Chemistry [Russian translation], Moscow (1964), p. 70.
5. Yu. N. Sheinker and Yu. I. Pomerantsev, Zh. Fiz. Khim., 30, 79 (1956).
6. S. Goenechea, Z. Anal. Chem., 218, 416 (1966).
7. V. G. Yakutovich, B. L. Moldaver, Yu. P. Kitaev, and Z. S. Titova, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 877 (1968).
8. N. V. Koshkin, Zh. Obshch. Khim., 5, 1460 (1935).
9. E. Grimaux, Bull. Soc. Chim. France, 31, No. 4, 146 (1879).