QUINONES

XLIX * CONDENSATION OF ARYL-p-BENZOQUINONES WITH β-AMINOCROTONATE ESTERS

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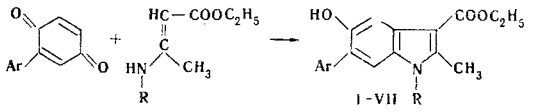
A number of 2-methyl-3-carbethoxy-5-hydroxy-6-arylindole derivatives were obtained by the condensation of aryl-p-benzoquinones with β-aminocrotonate esters and N-substituted β-aminocrotonate esters. The position of the aryl substituent was established by means of the NMR spectra.

The condensation of p-quinones with β-aminocrotonate ester, N-substituted β-aminocrotonate esters, and acetylacetone imines is one of the most convenient methods for the synthesis of 5-hydroxyindole derivatives [1-3]. The problem of the proof of the structures of the 5-hydroxyindole derivatives obtained by the condensation of β-aminocrotonate ester, and its analogs with unsymmetrical p-quinones was recently simplified by means of NMR spectroscopy [4]. This not only extends the range of application of the method but also makes it possible to investigate the problems of orientation during the reaction of β-aminocrotonate esters with monosubstituted p-benzoquinones.

In this paper we have studied the reaction of aryl-p-benzoquinones [5,6] with β-aminocrotonate, N-methyl-β-aminocrotonate, and N-benzyl-β-aminocrotonate esters.

The reaction was carried out under the conditions described in a paper by one of our co-workers [3]. The reaction yielded 2-methyl-3-carbethoxy-5-hydroxy-6-arylindoles (I-VII) in yields of 11-16% and considerable amounts of dark resinous products.



Methylation of 5-hydroxyindoles I, III, and IV with dimethyl sulfate gave 5-methoxy derivatives VIII-X. The aryl substitient in the 5-hydroxyindoles I-VII is in the 6-position, as established by means of the NMR spectra. The NMR spectra of I-VII contain two distinct singlets, which should be ascribed to the indole ring protons, in addition to proton signals from the aryl substituents. Singlets can occur only when these protons are in the 4 and 7 positions. The chemical shifts of the protons in the 4 and 7 positions of the indole ring are presented in Table 2.

In connection with the fact that the C-4 proton is found at weaker field relative to the C-7 proton of indole itself [7], we assigned the weak-field signals observed during investigation of I-VII to the protons in the 4 position, while the signals observed at stronger field were assigned to the protons in the 7 position. The substantiation of this assignment is apparent when the spectra of I, III, and IV are compared with the

*See [8] for Communication XLVIII.

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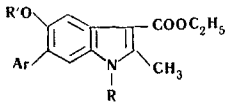
TABLE 1



Compound	R	R_1	Ar	Mp (crystallization solvent)	Empirical formula	Found, %				Calc., %				Yield, %
						C	H	N	Cl	C	H	N	Cl	
I	CH_3	H	C_6H_5	221—222 Acetone	$C_{19}H_{19}NO_3$	73,50	6,21	4,65	—	73,76	6,18	4,52	—	16,2
II	CH_3	H	4-ClC_6H_4	258—259 Acetone	$C_{19}H_{18}ClNO_3$	66,64	5,33	4,07	10,37	66,38	5,28	4,07	10,31	15
III	CH_3	H	2,4-$Cl_2C_6H_3$	243—244 Acetone	$C_{19}H_{17}Cl_2NO_3$	60,78	4,84	3,75	18,77	60,59	4,55	3,70	18,74	15,6
IV	CH_3	H	4-$NO_2C_6H_4$	272—273 Acetone	$C_{19}H_{18}N_2O_5$	64,67	5,20	7,80	—	64,40	5,12	7,90	—	14,1
V	H	H	C_6H_5	237—238 Methanol	$C_{18}H_{17}NO_3$	72,83	5,96	4,71	—	73,20	5,80	4,74	—	11
VI	H	H	4-ClC_6H_4	264—265 Methanol	$C_{18}H_{16}ClNO_3$	65,25	4,82	4,07	10,53	65,55	4,89	4,24	10,74	16,5
VII	$CH_2C_6H_5$	H	C_6H_5	198—199 Alcohol	$C_{25}H_{23}NO_3$	78,15	5,90	3,87	—	77,93	6,01	3,76	—	16,3
VIII	CH_3	CH_3	C_6H_5	143—145 Alcohol	$C_{20}H_{21}NO_3$	74,60	6,60	4,45	—	74,27	6,54	4,33	—	79
IX	CH_3	CH_3	2,4-$Cl_2C_6H_3$	168—170 Alcohol	$C_{20}H_{19}Cl_2NO_3$	61,45	4,83	3,46	17,73	61,23	4,88	3,57	18,07	75
X	CH_3	CH_3	4-$NO_2C_6H_4$	193—195 Alcohol	$C_{20}H_{20}N_2O_5$	64,92	5,65	7,56	—	65,20	5,47	7,60	—	88

TABLE 2. Chemical Shifts of the C-4 and C-7 Protons of 2-Methyl-3-Carbethoxy-5-hydroxy(methoxy)-6-arylindole Derivatives

Protons	Compounds *							
	I	VIII	II	III	IX	IV	X	VI
4-H	7,77	7,89	7,62	7,84	9,92	7,88	7,91	7,89
7-H	7,16	7,20	7,22	7,18	7,18	7,34	7,37	—†

*All spectra were obtained in CF_3COOH with tetramethylsilane as the internal standard.

†The signal from the 7-H proton is covered by the signal of the benzyl group attached to the nitrogen.

spectra of the corresponding 5-methoxyindoles (VIII, IX, and X). Replacement of the hydroxyl group by a methoxy results in a shift of the weak-field signal, which is natural if the weak-field signal belongs to the C-4 proton in the ortho position with respect to the group being replaced.

EXPERIMENTAL

2-Methyl-3-carbethoxy-5-hydroxy-6-arylindoles (I-VII). A solution of 0.05 mole of β-aminocrotonate ester in 100 ml of dichloroethane was added to 0.05 mole of the arylquinone. The solution was heated to the boiling point, and three fourths of the volume of solvent was removed by distillation. The residue was cooled and allowed to stand overnight. The resulting crystals were filtered and washed with ether. The data for I-VII are presented in Table 1.

2-Methyl-3-carbethoxy-5-methoxy-6-arylindoles (VIII-X). Sodium hydroxide [20 ml (2 N)] was added to a solution of 0.01 mole of 5-hydroxy-6-arylindole in 30 ml of dioxane, and the reaction mixture was stirred at room temperature for 40 min with 0.02 mole of dimethyl sulfate. The resulting precipitate was filtered and washed with water. The data for VIII-X are presented in Table 1.

LITERATURE CITED

1. A. N. Grinev, N. K. Kul'bovskaya, and A. P. Terent'ev, Zh. Obsch. Khim., 25, 1355 (1955).
2. A. N. Grinev, V. I. Shvedov, and I. P. Sugrobova, Zh. Obsch. Khim., 31, 2298 (1961).
3. A. N. Grinev, V. I. Shvedov, and E. K. Panisheva, Zh. Organ. Khim., 1, 2051 (1965).
4. R. Allen and M. Weiss, J. Org. Chem., 33, 198 (1968).
5. D. Kvalnes, J. Am. Chem. Soc., 56, 2478 (1934).
6. P. Bassard and P. L'Ecuyer, Can. J. Chem., 36, 700 (1958).
7. P. Black and M. Heffernan, Austr. J. Chem., 18, 353 (1965).
8. V. I. Shvedov, G. N. Kurilo, and A. N. Grinev, Khim.-Farmats. Zh., 4, 7 (1970).