THE REACTION OF QUINOL-6-YLMETHYLENEAMINES WITH DIALKYLPHOSPHITES. SYNTHESIS OF QUINOL-6-METHYLENEAMINES AND OF DIALKYL ESTERS OF ARYLAMINO(QUINOL-6-YL)METHYLPHOSPHONIC ACIDS

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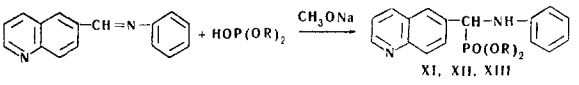
Syntheses of quinol-6-ylmethyleneamines are described. The addition of dialkyl phosphites to the azomethine grouping of the quinol-6-ylmethyleneamines in the presence of sodium methoxide has been studied. Eighteen new dialkyl esters of arylamino(quinol-6-yl)methylphosphonic acids have been synthesized.

In the development of investigations in the field of 6-substituted quinolines [1, 2], we have studied the reaction of quinol-6-ylmethyleneamines with dialkyl phosphites.

For this purpose we have extended [1] the synthesis of quinol-6-ylmethyleneamines and the condensation of quinoline-6-aldehyde with aromatic and heterocyclic amines. Quinol-6-ylmethyleneaniline (I), quinol-6-ylmethylene-m-toluidine (II), quinol-6-ylmethylene-p-toluidine (III), quinol-6-ylmethylene-o-anisidine (IV), quinol-6-ylmethylene-p-anisidine (V), and quinol-6-ylmethylene-p-phenetidine (VI) have been obtained in good yield. The reaction of the aldehyde with monomethyl-substituted α-aminopyridines and α-aminoquinolines by heating the components in ethanolic solution has yielded 3-methyl-, 4-methyl-, and 5-methyl-2-(quinol-6-ylmethyleneamino)-pyridines (VII, VIII, IX) and 2-(quinol-6-ylmethyleneamino)quinoline (X).

The quinol-6-ylmethyleneamines synthesized consist of colorless crystalline substances (except for IV) soluble in organic solvents, sparingly soluble in diethyl ether, and insoluble in water. The azomethines I–VI were characterized in the form of the picrates and VII–X as the dipicrates (see Table 1).

The reaction of the quinol-6-ylmethyleneamines with dialkyl phosphites was carried out by the method described previously [3–5] in the presence of a sodium alkoxide. The condensation of I with dimethyl, diethyl, and diisopropyl phosphites gave the dimethyl, diethyl, and diisopropyl esters of phenylamino-(quinol-6-yl) methylphosphonic acids (XI–XIII), respectively.



XI, XII, XIII

The products of the reaction of II and III and quinol-6-ylmethylene-β-naphthylamine [1] with dialkyl phosphites were the dialkyl esters of m-tolylamino-(quinol-6-yl)methylphosphonic acid (XIV, XV, XVI), of p-tolylamino(quinol-6-yl)-methylphosphonic acid (XVII, XVIII, XIX), and of β-naphthylamino(quinol-6-yl)-methylphosphonic acid (XX, XXI).

The condensation of the azomethines IV–VI gave esters of o-methoxyphenylamino-(quinol-6-yl)methylphosphonic acid (XXI, XXIII), of p-methoxyphenylamino(quinol-6-yl)methylphosphonic acid (XXIV, XXV, XXVI), and of p-ethoxyphenylamino(quinol-6-yl)-methylphosphonic acid (XXVII, XXVIII).

It was impossible to perform the addition of dialkyl phosphites to the azomethine groupings of di(quinol-6-ylmethylene)-p-phenylenediamine [1] or to the azomethines VII–X.

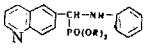
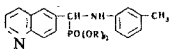
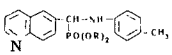
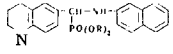
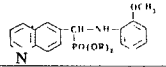
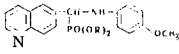
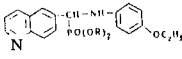
Table 1

Characteristics and Conditions of Synthesis of the Quinol-6-ylmethyleneamines

Compound	Amounts of reactants, g		Amount of ethanol, ml	Mp, °C	Empirical formula	N, %		yield, %	Picrates			
	quinoline-6-aldehyde	amine				found	calculated		mp, °C	empirical formula	N, % found	N, % calculated
I	1.5	0.89	—	98–99	$C_{16}H_{12}N_2$	12.16	12.07	90.6	214–215	$C_{16}H_{12}N_2 \cdot C_6H_3O_7N_3$	14.85	15.18
II	2.0	1.36	—	80–81	$C_{17}H_{14}N_2$	11.02	11.38	93.6	226–227	$C_{17}H_{14}N_2 \cdot C_6H_3O_7N_3$	14.93	14.74
III	1.5	1.02	—	98–99	$C_{17}H_{14}N_2$	11.72	11.38	92.0	233–235	$C_{17}H_{14}N_2 \cdot C_6H_3O_7N_3$	15.14	14.74
IV	2.0	1.56	5	Viscous liquid	$C_{17}H_{14}ON_2$	10.97	10.68	89.0	195–196	$C_{17}H_{14}ON_2 \cdot C_6H_3O_7N_3$	14.56	14.26
V	3.0	2.35	10	112–113	$C_{17}H_{14}ON_2$	11.00	10.68	80.0	224–225	$C_{17}H_{14}ON_2 \cdot C_6H_3O_7N_3$	14.67	14.26
VI	3.8	3.30	10	106–107	$C_{18}H_{16}ON_2$	9.78	10.14	97.4	210–211	$C_{18}H_{16}ON_2 \cdot C_6H_3O_7N_3$	13.70	13.86
VII	2.0	1.37	5	89–90	$C_{16}H_{13}N_3$	17.26	17.00	89.0	236–237	$C_{16}H_{13}N_3 \cdot 2C_6H_3O_7N_3$	17.57	17.87
VIII	2.5	1.72	5	120–121	$C_{16}H_{13}N_3$	17.31	17.00	77.0	234–235	$C_{16}H_{13}N_3 \cdot 2C_6H_3O_7N_3$	17.64	17.87
IX	2.2	1.51	5	97–98	$C_{16}H_{13}N_3$	16.83	17.00	81.2	260–261	$C_{16}H_{13}N_3 \cdot 2C_6H_3O_7N_3$	18.02	17.87
X	2.1	1.92	5	168–169	$C_{19}H_{13}N_3$	14.52	14.84	85.5	267–268	$C_{19}H_{13}N_3 \cdot 2C_6H_3O_7N_3$	17.36	17.00

Table 2

Characteristics and Conditions for the Synthesis of Dialkyl Esters of Arylamino(quinol-6-yl)methylphosphonic Acids

Compound No.	Compound	R	Amounts of reactants, g: azomethine	Amounts of reactants, g: dialkylphosphite	Mp, °C	Empirical formula	Found, %: N	Found, %: R	Calculated, %: N	Calculated, %: P	Yield, %	Picrates: mp, °C	Picrates: empirical formula	Picrates: found, %: N	Picrates: found, %: P	Picrates: calculated, %: N	Picrates: calculated, %: P
XI		CH_3	0.50	0.30	157—158	$C_{18}H_{19}O_3N_2P$	8.33	8.79	8.18	9.06	87.8	170—171	$C_{18}H_{19}O_3N_2P \cdot C_6H_3N_3O_7$	12.03	5.17	12.26	5.43
XII		C_2H_5	0.50	0.37	122—123	$C_{20}H_{23}O_3N_2P$	7.72	8.62	7.56	8.37	62.5	162—163	$C_{20}H_{23}O_3N_2P \cdot C_6H_3N_3O_7$	11.42	5.52	11.67	5.17
XIII		C_3H_7-*i*	0.50	0.45	154—155	$C_{22}H_{27}O_3N_2P$	7.33	8.11	7.03	7.78	46.5	165—166	$C_{22}H_{27}O_3N_2P \cdot C_6H_3N_3O_7$	11.33	4.80	11.16	4.94
XIV		CH_3	0.50	0.28	142—143	$C_{19}H_{21}O_3N_2P$	7.52	8.97	7.86	8.71	69.4	120—121	$C_{19}H_{21}O_3N_2P \cdot C_6H_3N_3O_7$	11.58	5.37	11.96	5.30
XV		C_2H_5	0.60	0.40	117—118	$C_{21}H_{25}O_3N_2P$	7.41	8.42	7.29	8.07	53.7	113—114	$C_{21}H_{25}O_3N_2P \cdot C_6H_3N_3O_7$	11.18	5.28	11.42	5.05
XVI		C_3H_7-*i*	0.60	0.50	125—126	$C_{23}H_{29}O_3N_2P$	6.51	7.36	6.79	7.52	30.0	116—117	$C_{23}H_{29}O_3N_2P \cdot C_6H_3N_3O_7$	10.54	5.20	10.92	4.83
XVII		CH_3	0.50	0.28	167—168	$C_{19}H_{21}O_3N_2P$	7.60	8.02	7.86	8.71	87.5	172—173	$C_{19}H_{21}O_3N_2P \cdot C_6H_3N_3O_7$	11.65	5.60	11.96	5.30
XVIII		C_2H_5	0.60	0.41	153—154	$C_{21}H_{25}O_3N_2P$	7.02	8.42	7.29	8.07	75.2	174—175	$C_{21}H_{25}O_3N_2P \cdot C_6H_3N_3O_7$	14.20	4.81	11.42	5.05
XIX		C_3H_7-*i*	0.60	0.50	154—155	$C_{23}H_{29}O_3N_2P$	7.04	7.33	6.79	7.52	68.0	175—176	$C_{23}H_{29}O_3N_2P \cdot C_6H_3N_3O_7$	10.62	5.28	10.92	4.83
XX		CH_3	1.00	0.50	157—158	$C_{22}H_{21}O_3N_2P$	7.46	8.27	7.14	7.91	36.0	134—135	$C_{22}H_{21}O_3N_2P \cdot C_6H_3N_3O_7$	11.53	5.04	11.26	4.99
XXI		C_3H_7-*i*	1.10	0.80	158—159	$C_{26}H_{29}O_3N_2P$	6.98	6.70	6.24	6.91	11.5	130—132	$C_{26}H_{29}O_3N_2P \cdot C_6H_3N_3O_7$	10.62	4.81	10.34	4.58
XXII		CH_3	1.42	0.75	150—151	$C_{19}H_{21}O_4N_2P$	7.38	8.63	7.52	8.33	50.0	161—162	$C_{19}H_{21}O_4N_2P \cdot C_6H_3N_3O_7$	11.83	5.58	11.64	5.15
XXIII		C_3H_7-*i*	1.45	1.14	149—150	$C_{23}H_{29}O_4N_2P$	6.83	7.51	6.54	7.24	38.1	162—163	$C_{23}H_{29}O_4N_2P \cdot C_6H_3N_3O_7$	10.81	5.23	10.65	4.71
XXIV		CH_3	1.30	0.68	176—177	$C_{19}H_{21}O_4N_2P$	7.85	8.14	7.52	8.33	76.1	114—115	$C_{19}H_{21}O_4N_2P \cdot C_6H_3N_3O_7$	11.35	5.01	11.64	5.15
XXV		C_2H_5	1.00	0.65	156—157	$C_{21}H_{25}O_4N_2P$	6.68	7.98	7.00	7.75	78.9	108—109	$C_{21}H_{25}O_4N_2P \cdot C_6H_3N_3O_7$	11.36	5.25	11.13	4.92
XXVI		C_3H_7-*i*	1.00	0.80	165—166	$C_{23}H_{29}O_4N_2P$	6.71	7.56	6.54	7.24	64.4	114—115	$C_{23}H_{29}O_4N_2P \cdot C_6H_3N_3O_7$	10.38	4.94	10.65	4.71
XXVII		CH_3	1.40	0.70	141—142	$C_{20}H_{23}O_4N_2P$	7.46	7.68	7.25	8.03	92.2	164—165	$C_{20}H_{23}O_4N_2P \cdot C_6H_3N_3O_7$	11.10	5.21	11.38	5.04
XXVIII		C_2H_5	1.30	0.82	145—146	$C_{22}H_{27}O_4N_2P$	5.98	7.66	6.76	7.48	87.1	128—129	$C_{22}H_{27}O_4N_2P \cdot C_6H_3N_3O_7$	10.52	4.48	10.88	4.82

The dialkyl esters of arylamino(quinol-6-yl)methylphosphonic acids that were synthesized consisted of crystalling substances soluble in organic solvents, sparingly soluble in ether, and insoluble in water.

The picrates of the esters were obtained (see table 2).

EXPERIMENTAL

Synthesis of the quinol-6-ylmethyleneamines (I-X). A mixture of quinoline-6-aldehyde (mp 75-76° C) and an amine (in equimolecular amount) in solution in ethanol or in the absence of a solvent was heated in the water bath for 1 hr. After the reaction product had been cooled or the ethanol had been evaporated off, rapid crystallization took place. The majority of the azomethines were recrystallized from benzene (5-8 ml), **II** and **VI** from a mixture of benzene and petroleum ether, and **V** and **X** from ethanol.

Quinol-6-ylmethyleneaniline has been synthesized previously [6] by heating the aldehyde and aniline hydrochloride. Crystals with mp 99° C. The yield was not given and the picrate was not prepared.

The picrates of the azomethines **I-VI** and the dipicrates of **VII-X** were obtained by heating the components in glacial acetic acid (Table 1).

Synthesis of the dialkyl esters of **arylamino(quinol-6-yl)methylphosphonic acids (XI-XXVIII).** To a mixture of a quinol-6-ylmethyleneamine and a dialkyl phosphite (~25% excess) was added 0.2-0.3 ml of a saturated anhydrous methanolic solution of sodium methoxide. When the mixture was stirred vigorously, the reaction took place with the evolution of heat and it was completed by heating at 80-85° C for 1-2 min. The reaction products were obtained in the form of crystalline masses or viscous liquids crystallizing on standing (in the cold). Dry ethyl ether was added, the mixture was stirred, and the crystals were filtered off. The majority of the esters were crystallized from xylene (3-5 ml), while the esters **XXII-XXVI** were crystallized from ethanol (2-3 ml).

The picrates of the esters **XI-XXI** were prepared in and crystallized from glacial acetic acid; the picrates of **XXII** and **XXVIII** were obtained in xylene solution and crystallized from ethanol (Table 2).

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