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SYNTHESIS AND PROPERTIES OF *sym*-TRIAZENE DERIVATIVES

13*. SYNTHESIS OF 6-SUBSTITUTED 2,4-DIALKYL(ARYL)THIO-*sym*-TRIAZENES FROM IMINO ESTERS OF CARBOXYLIC ACIDS

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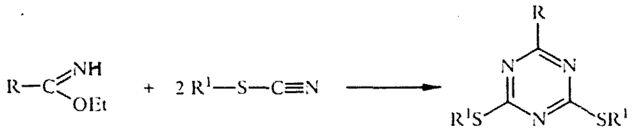
*6-Substituted 2,4-dialkyl(aryl)thio-*sym*-triazenes are synthesized by condensation of imino esters of carboxylic acids with thiocyanates.*

In a continuation of studies on the synthesis of *sym*-triazine derivatives by condensations involving imino esters of carboxylic acids [2-6], we report here on the preparation of 6-substituted 2,4-dialkyl(aryl)thio-*sym*-triazines. The literature has limited information on the preparation and properties of *sym*-triazines of this kind [7-10]. At the same time, these compounds are of interest as potentially biologically active substances and also as stabilizers and additives to polymeric materials, hydrocarbon fuels, and lubricating oils.

Previously, we have shown that the reaction of imino esters of acids in the furanic series with methyl thiocyanate leads to furyl-substituted 2,4-dimethylthio-*sym*-triazines [6]. In the present work, we have investigated the possibility of using this method to obtain 2,4-dialkyl(aryl)thio-*sym*-triazines containing a sterically hindered phenol, 5-nitrofuran, indole, or pyridine group. For this purpose we studied the condensation of the ethylimino esters of carboxylic acids Ia-g with methyl-(IIa), benzyl-(IIb), and 4-hydroxy-3,5-ditert-butylphenylthiocyanate (IIc).



I a-g   II a-c   III a-n

Ia, IIIa-c, R = 4-HO-3,5-(t-Bu)$_2$C$_6$H$_2$SCH$_2$; Ib, IIId, e R = 5-nitrofuryl-2; Ic, IIIf R = β-(5-nitrofuryl-2)vinyl; Id, IIIg-i R = indolyl-3; Ie, IIIj R = indolyl-3-methyl; If, IIIk R = pyridyl-2; Ig, III*l*-n R = pyridyl-3; IIa, IIIa, d, f, g, j-*l* R^1 = Me; IIb, IIIb, h, m R^1 = PhCH$_2$; IIc, IIIc, e, i, n R^1 = 4-HO-3,5-(t-Bu)$_2$C$_6$H$_2$

It was established that when ethylimino esters Ia-g are boiled with thiocyanates IIa-c (1:2 mole ratio) in acetone (8-18 h), 2,4-dialkyl(aryl)thio-6-R-*sym*-triazines (IIIa-n) are formed in good yields. The nitriles and amides of the corresponding acids were found as by-products in the reaction mixture by means of TLC.

When the mole ratio of imino ester Ib to thiocyanate IIa was changed to 1:1-1:1.5, the yield of corresponding *sym*-triazine IIId decreased to 44-47%. Increasing the amount of methylthiocyanate (IIa) in the reaction mixture to 1:3-1:4 had no effect on the yield of compound IIId.

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*For paper 12, see [1].

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TABLE 1. Characteristics of the Compounds Synthesized

Compound	Molecular formula	mp, °C	R_f*2	PMR Spectrum, δ, ppm, KSSV (J), Hz*3	Yield, %
IIIa	$C_{20}H_{29}N_3OS_3$	145...146	0,64 (a)	1,62 (18H, s, *t*-Bu), 2,48 (6H, s, MeS), 3,90 (2H, s, CH$_2$), 5,08 (1H, s, OH), 7,22 (2H, s, H$_{arom}$)	76
IIIb	$C_{32}H_{27}N_3OS_3$	136...137	0,75 (a)	1,76 (18H, s, *t*-Bu), 3,35 (4H, s, CH$_2$), 3,84 (2H, s, CH$_2$), 5.20 (1H, s, OH), 6,80...7,10 (10H, m, Ph), 7,30 (2H, s, H$_{arom}$)	73
IIIв	$C_{46}H_{65}N_3O_3S_3$	157...158,5	0,44 (a)	1,66...1.74 (54H, br.s., *t*-Bu), 3,95 (2H, s, CH$_2$), 5,10 (1H, s, OH), 5,18 (2H, s, OH), 7,14...7,21 (6H, br.s. H$_{arom}$)	62
IIIг	$C_9H_8N_4O_3S_2$	164...165	0,58 (b)	2,40 (6H, s, MeS), 6,48 (1H, d, 3-H furan , J_{34} = 3,6), 6,95 (1H, d, 4-H furan)	78
IIIд	$C_{35}H_{44}N_4O_5S_2$	160...161,5 decomp.	0,63 (b)	1,70 (36H, s, *t*-Bu), 5,12 (2H, s, OH), 6,59 (1H, d, 3-H furan , J_{34} = =3,8), 7,03 (1H, d, 4-H furan), 7,24 (4H, s, H$_{arom}$)	68
IIIe	$C_{11}H_{10}N_4O_3S_2$	178...180	0,70 (b)	2,54 (6H, s, MeS), 6,55 (1H, d, 3-H furan , J_{34} = 3,4), 6,87 (1H, d, 4-H furan), 7,25 (1H, d, α-CH=, $J_{\alpha\beta}$ = 15,0), 7,54 (1H, d, β-CH=)	70
IIIж	$C_{13}H_{12}N_4S_2$	190...192	0,62 (c)	2,40 (6H, s, MeS), 7,14...7,52 (4H, m, H$_{arom}$), 7,78 (1H, d, 2-H indole J_{12} = 2,7), 8,10 (1H, br.s. NH)	65
IIIз	$C_{25}H_{20}N_4S_2$	182...184	0,50 (c)	3,54 (4H, s, CH$_2$), 6,92...7,33 (14H, m, H$_{arom}$), 7,80 (1H, d, 2-H indole J_{12} = 3,0), 8,14 (1H, br.s. NH)	58
IIIи	$C_{30}H_{48}N_4O_2S_2$	218...219	0,45 (c)	1,64 (36H, s, *t*-Bu), 5,18 (2H, s, OH), 7,10 (4H, s, H$_{arom}$), 7,25...7,50 (4H, m, H$_{arom}$), 7,72 (1H, d, 2-H furan , J_{12} = 2,5), 8,12 (1H, br.s. NH)	54
IIIк	$C_{14}H_{14}N_4S_2$	140...141,5	0,77 (c)	2,52 (6H, s, MeS), 3,94 (2H, s, CH$_2$), 7,08...7,40 (4H, m, H$_{arom}$), 7,60 (1H, d, 2-H indole , J_{12} = 2,8), 8,05 (1H, br.s., NH)	78
IIIл	$C_{10}H_{10}N_4S_2$	172...173	0,48 (b)	2,47 (6H, s, MeS), 7,24...7,68 (4H, m, H$_{arom}$),	84
IIIм	$C_{10}H_{10}N_4S_2$	187...188	0,40 (b)	2,50 (6H, s, MeS), 7,08...7,42 (4H, m, H$_{arom}$)	87
IIIн	$C_{22}H_{18}N_4S_2$	169...170	0,65 (b)	3,62 (4H, s, CH$_2$), 6,84...7,35 (14H, m, H$_{arom}$)	
IIIo	$C_{36}H_{46}N_4O_2S_2$	205...206,5	0,58 (a)	1,66 (36H, s, *t*-Bu), 5,15 (2H, s, OH), 7,14 (4H, s, H$_{arom}$), 7,26...7,52 (4H, m, H$_{arom}$).	75

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*Compounds IIIa, d, f, k, *l*, n were recrystallized from ethanol, IIIb, j, m from aqueous ethanol, and IIIe, g-i from aqueous DMF.

*2Solvent system shown in parentheses.

*3Spectra of compounds IIIa-c, j-m were taken in acetone-D$_6$, of compounds IIIa, d-h, n in DMSO-D$_6$.

It must be noted that in none of the cases were cyclocondensation products of the "2:1" type, i.e., 2-alkylthio-4,6-R^2-*sym*-triazines, found in the reaction mixture, nor were products of the homocyclotrimerization of the initial carboxylic acid imino ester (i.e., 2,4,6-tri-R-substituted *sym*-triazines) or of thiocyanates IIa-c (i.e., 2,4,6-trialkyl(aryl)thio-*sym*-triazines).

In reactions with imino esters Ia-g, methylthiocyanate (IIa) is more reactive than thiocyanates IIb, c. For example, when the imino ester of indol-3-carboxylic acid (Id) is boiled with methylthiocyanate (1:2 mole ratio) in acetone for 10 h, the yield of *sym*-triazine IIIg is 63-65%. Under analogous conditions, imino ester Id and thiocyanate IIc give the corresponding *sym*-triazine, IIIi, in 52-54% yield after boiling for 17-18 h. Reactions involving thiocyanate IIc at higher temperatures (80-100°C) in other solvents were found to give tars from which we could not extract individual compounds.

In the IR spectra of the synthesized *sym*-triazines, IIIa-n, absorption bands of varying intensities were found at 1555-1530, 1430-1420, 1125-1090, 1025-1005, 815-805, and 695-680 cm^{-1}. These are characteristic of the stretching, breathing, out-of-plane, and in-plane vibrations of *sym*-triazine [1-6, 11, 12]. Along with these vibrations, the spectra of compounds IIIa-c, e, i, n also have absorption bands arising from the sterically hindered phenol group: a narrow band at 3650-3635 cm^{-1} corresponding to the stretching vibration of an unassociated OH group in shielded phenols [13]; two bands of medium intensity at 1265-1240 cm^{-1}, characteristic of vibrations of the Ar–OH bond in shielded phenols [14]; and also two groups of absorption bands at 885-870 and 830-820 cm^{-1}, resulting from the out-of-bending vibrations of a tetrasubstituted benzene ring.

In the PMR spectra (Table 1) of *sym*-triazines IIIa, d, f, j-*l* the signals of the methyl group protons are found as singlets with an intensity of six proton units in the 2.40-2.54 ppm range [15]. In the spectra of compounds IIIa-c, e, i, n the singlets from the hydroxylic protons are found in the 5.08-5.20 ppm range, which is characteristic of shielded phenols [13, 16]. The signals from the *tert*-butyl protons occur as singlets in the 1.62-1.76 ppm range. Singlets at 7.14-7.30 ppm arise from the magnetically equivalent protons of the hydroxyaryl groups [13, 16].

EXPERIMENTAL

The IR spectra were taken on a Bruker IFS-48 instrument in tablets with KBr. The PMR spectra were obtained on a Bruker WP-100 SY (100 MHz) instrument, TMS internal standard. The course of the reactions and the purity of the compounds obtained were monitored by means of TLC on Al_2O_3 III st. act. by Brockman in solvent systems of 10:1 benzene:methanol (a), 20:1 chloroform:acetone (b), and 5:1 benzene:methanol (c). Development was with iodine vapor.

The elemental analyses for C, H, N, and S of the synthesized compounds agreed with the calculated values.

Ethylimino esters of 4-hydroxy-3,5-ditert-butylphenylthioacetic (Ia) [3], 5-nitrofuran-2-carboxylic (Ib) [6], (E)-β-(5-nitrofuryl-2) acrylic (Ic) [6], indol-3-carboxylic (Id) [17], indolyl-3-acetic (Ie) [17], pyridine-2-carboxylic (If) [18], and pyridine-3-carboxylic (Ig) [19] acids as well as 4-hydroxy-3,5-ditert-butylphenylthiocyanate (IIc) [20], were prepared by the methods in the references in square brackets.

General Procedure for Preparing 6-Substituted 2,4-Dialkyl(aryl)-thio-*sym*-triazines (IIIa-n). Add a solution of 20 mmoles of thiocyanate IIa-c in 25 ml of acetone dropwise to a stirred solution of 10 mmoles of the ethyliminoester of carboxylic acids Ia-g in 25 ml of acetone. Boil the reaction mixture, with stirring (8-10 h to obtain *sym*-triazines IIIa, d, f, i-n; 12-14 h for the synthesis of *sym*-triazines IIIh, o; 16-18 h to obtain *sym*-triazines IIIc, e, i, n), until the initial imino ester has disappeared (by TLC). Remove the solvent at reduced pressure, chromatograph the residue on silica gel, 40/100 μm (95 × 4.5 cm). Elute products IIIa-f, k-n with a 10:1 hexane:acetone mixture, and products IIIg-i with a 10:1 chloroform:acetone mixture. The resultant compounds are further purified by recrystallization from suitable solvents (see Table 1).

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