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sym-TRIAZINES. 8*. SYNTHESIS AND SOME REACTIONS OF 4,6-DISUBSTITUTED 2-(1H-PYRROLYL)-1,3,5-TRIAZINES

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We have studied the reaction of 2,5-dimethoxytetrahydrofuran with 4,6-disubstituted 2-amino-1,3,5-triazines with the aim of obtaining novel coupled polyheterocyclic systems with potential bioactivity. Reaction conditions were optimized. A series of novel 4,6-disubstituted 2-(1H-1-pyrrolyl)-sym-triazines was obtained. It was found that the product yields depended on the nature of the substituent in the 4 and 6 positions of the triazine ring and on the reaction conditions.

Keywords: 4,6-disubstituted 2-amino-1,3,5-triazines, 2,5-dimethoxytetrahydrofuran, 4-substituted 2-amino-(1,3,5-triazinyl)-6-iminotriphenylphosphoranes, 4-substituted 2-(1H-1-pyrrolyl)-6-(1,2,3-triazol-1-yl)-1,3,5-triazines.

In continuing our study of the synthesis of conjugated heterocyclic systems it seemed reasonable to prepare novel compounds containing 1,3,5-triazine, pyrrole, and 1,2,3-triazole rings together. We have previously reported the synthesis of *sym*-triazine derivatives containing 1,2,3-triazole fragments [2, 3]. The aim of this work is the targeted synthesis of novel and potentially bioactive 4,6-disubstituted 2-(1H-1-pyrrolyl)-1,3,5-triazine derivatives and to study their properties and reactions.

It is known [4] that 4,6-dichloro-2-(N-pyrrolyl)-1,3,5-traizines are formed in about 37% yield as a result of the reaction of 2,4,6-trichloro-1,3,5-triazine with pyrrole or pyrrolyl potassium (lithium) in the presence of $AlCl_3$. However, this method is only suitable for the substitution of the first chlorine in cyanuric chloride.

In [5] it was reported that the primary amino group of alkyl and arylamines can be used as the nitrogen component in the construction of a pyrrole ring *via* reaction with 2,5-dimethoxytetrahydrofuran. The latter can be used as a latent 1,4-dicarbonyl compound giving high yields of the corresponding N-alkyl- or N-aryl-pyrroles.

* For Communication 7 see [1].

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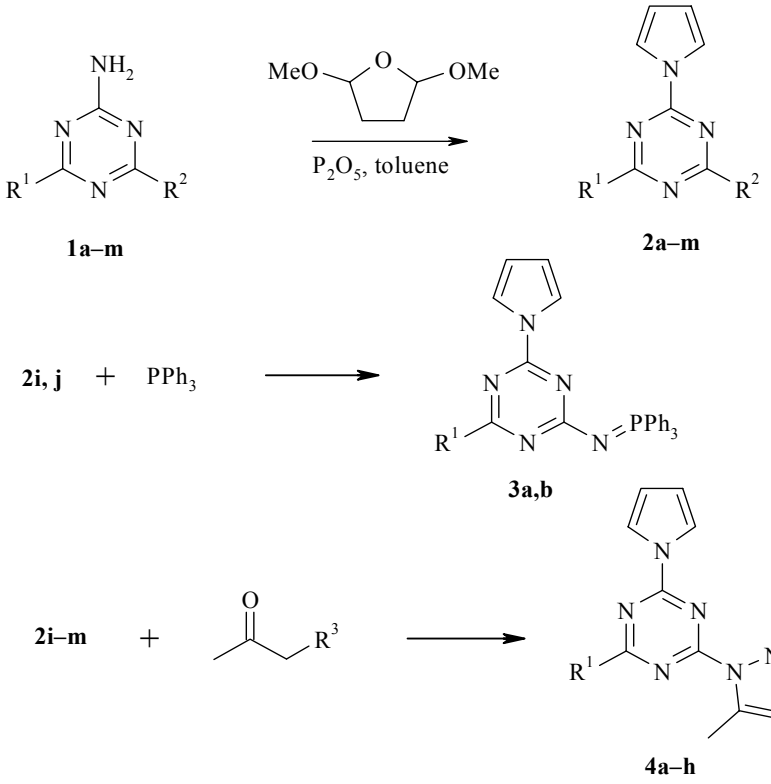
In the case of two compounds the authors in [6] have shown that pyrazolinotriazines containing a primary amino group in their composition can form pyrroles with 2,5-dimethoxytetrahydrofuran in 72 and 83% yields by refluxing for 10 h in a mixture of dioxane and acetic acid.

The starting mono- and diamino *sym*-triazines **1a-m** were prepared by a known method [7]. The physico-chemical and spectroscopic characteristics of some of them are given in Tables 1 and 2.

Studies have shown that the reaction conditions prove to have a marked effect on the reaction time and on the yield of the target compounds. It was found that shortening of the reaction time and improved yields of the 4,6-disubstituted 2-(1H-1-pyrrolyl)-1,3,5-triazines **2a-m** can be achieved by refluxing the reagents in toluene solution in the presence of P_2O_5 using a molar ratio of amino-*sym*-triazine **1** to 2,5-dimethoxytetrahydrofuran to P_2O_5 of 1:1.2:1. The reaction was carried out according to the scheme:



1,2 a $R^1 = NPh_2$, $R^2 = NMe_2$; **b** $R^1 = NPh_2$, $R^2 = NEt_2$; **c** $R^1 = NPh_2$, $R^2 = CN$; **d** $R^1 = NPh_2$, R^2 =1-morpholino; **e** $R^1 = NPh_2$, R^2 =1-piperidino; **f** $R^1 = Ph$, $R^2 = NH_2$; **g** $R^1 = Ph$, R^2 =1-pyrrolyl; **h** $R^1 = OMe$, R^2 = 1-morpholino; **i** $R^1 = NPh_2$, $R^2 = N_3$; **j** $R^1 = NEt_2$, $R^2 = N_3$; **k** $R^1 = NPr_2$, $R^2 = N_3$; **l** $R^1 = N(Me)CH_2Ph$, $R^2 = N_3$; **m** $R^1 = NMePh$, $R^2 = N_3$; **3 a** $R^1 = NPh_2$, **b** $R^1 = NEt_2$; **4 a** $R^1 = NPh_2$, R^3 =Ac; **b** $R^1 = NEt_2$, R^3 =Ac; **c** $R^1 = NPr_2$, R^3 =Ac;**d** $R^1 = N(Me)CH_2Ph$, R^3 =Ac; **e** $R^1 = NPh_2$,R^3 = COOEt; **f** $R^1 = NPr_2$, R^3 = COOEt; **g** $R^1 = N(Me)CH_2Ph$, R^3 = COOEt; **h** $R^1 = NMePh$, R^3 = COOEt

With an equimolar ratio of reagents the reaction time was increased from 1-2 to 2.5-4 h and the yield of target products was lowered by 7-10%. The use of absolute toluene as solvent ensures good solubility of the starting materials and a quite high reaction mixture temperature and leads to high (73-93%) yields of the target products **2a-m**. With the use of a lower boiling solvent (benzene) the reaction time is increased by 3-3.5 h. It should be noted that carrying out the synthesis in glacial acetic acid in agreement with [6, 8] needs more prolonged heating (up to 10 h). The yields of compounds **2a-h** did not exceed 45-55% but those containing an azide group **2i-m** (Tables 1 and 2) were in fact less (up to 30%) and this is evidently associated with side reactions which lead to rapid tarring.

TABLE 1. Physico-chemical Characteristics for Compounds Synthesized **1a-e,g,i-m, 2a-m, 3a,b,** and **4a-h**

Com-pound	IR spectrum, ν, cm^{-1}	^1H NMR spectrum, δ, ppm, SSCC (*J*, Hz)	Molecular ion, *m/z* (I_{rel} %)
1	2	3	4
1a	3330, 3395 (NH_2); 1550, 1580 (C=S, C=N)	2.73 (3H, br. s, NCH_3); 3.00 (3H, br. s, NCH_3); 5.85 (2H, br. s, NH_2); 7.10 (2H, t, *J* = 8.0, *p*-C_6H_5); 7.21 (4H, d, *J* = 8.0, *o*-C_6H_5); 7.27 (4H, t, *J* = 8.0, *m*-C_6H_5)	
1b	3330, 3395 (NH_2); 1540, 1560 (C=S, C=N)	0.92 (3H, br. s, CH_3 in NEt_2); 1.10 (3H, br. s, CH_3 in NEt_2); 3.20 (2H, br. s, CH_2 in NEt_2); 3.50 (2H, br. s, CH_2 in NEt_2); 5.73 (2H, br. s, NH_2); 7.09 (2H, t, *J* = 8.0, *p*-C_6H_5); 7.22 (4H, d, *J* = 8.0, *o*-C_6H_5); 7.27 (4H, t, *J* = 8.0, *m*-C_6H_5)	
1c	3290, 3400 (NH_2); 1500, 1540 (C=S, C=N); 2220 (C≡N)	7.23 (2H, t, *J* = 8.0, *p*-C_6H_5); 7.26 (4H, d, *J* = 8.0, *o*-C_6H_5); 7.37 (4H, t, *J* = 8.0, *m*-C_6H_5); 7.41 and 7.32 (2H, br. s, NH_2)	
1d	3320, 3390 (NH_2); 1530, 1600 (C=S, C=N); 1060, 1095 (C–O–C)	3.55 (8H, br. s, $2NCH_2$, $2OCH_2$); 5.90 (2H, br. s, NH_2); 7.11 (2H, t, *J* = 8.0, *p*-C_6H_5); 7.21 (4H, d, *J* = 8.0, *o*-C_6H_5); 7.28 (4H, t, *J* = 8.0, *m*-C_6H_5)	
1e	3370 (br., NH_2); 1555, 1610 (C=S, C=N)	1.40-1.65 (6H, m, $3CH_2$); 3.52 (4H, br. s, $2NCH_2$); 5.77 (2H, br. s, NH_2); 7.10 (2H, t, *J* = 8.0, *p*-C_6H_5); 7.21 (4H, d, *J* = 8.0, *o*-C_6H_5); 7.27 (4H, t, *J* = 8.0, *m*-C_6H_5)	
1g	3390 (br., NH_2); 1500, 1520, 1590 (C=S, C=N)	6.25 (2H, t, *J* = 2.3, 2CH); 7.88 (2H, t, *J* = 2.3, 2NCH); 7.39 (2H, s, NH_2); 7.48 (2H, t, *J* = 8.0, *m*-C_6H_5); 7.53 (1H, t, *J* = 8.0, *p*-C_6H_5); 8.43 (2H, d, *J* = 8.0, *o*-C_6H_5)	
1i	3290, 3400 (NH_2); 2100 (N_3); 1500, 1540 (C=S, C= N)	6.20 (2H, br. s, NH_2); 7.10-7.35 (10H, m, $2C_6H_5$)	
1j	3400 (br., NH_2) 2100 (N_3); 1560, 1610 (C=S, C=N)	1.03 (6H, t, *J* = 7.7, $2CH_3$ in NEt_2); 3.47 (4H, q, *J* = 7.7, $2CH_2$ in NEt_2); 5.75 (2H, br. s, NH_2)	
1k	3350 (br., NH_2) 2110 (N_3); 1550, 1610 (C=S, C=N)	0.55-0.90 (6H, m, $2CH_3$ in NPr_2); 1.7-1.95 (4H, m, $2CH_2$ in NPr_2); 3.30-3.60 (4H, m, $2CH_2N$ in NPr_2); 5.85 (2H, br. s, NH_2)	
1l	3300, 3390 (NH_2); 2110 (N_3);	3.10 (3H, s, NCH_3); 4.75-4.90 (2H, m, $NCH_2C_6H_5$); 5.90 (2H, br. s, NH_2); 7.20-7.35 (5H, m, C_6H_5)	

TABLE 1. (continued)

1	2	3	**4**
1m	3330, 3395 (NH_2); 2110 (N_3); 1520, 1560, (C=S, C=N)	3.60 (3H, s, NCH_3); 7.23-7.35 (5H, m, C_6H_5); 5.95 (2H, br. s, NH_2)	
2a	1530, 1580, 1600 (C=S, C=N)	2.86 (3H, s, NCH_3); 3.38 (3H, s, NCH_3); 6.07 (2H, t, *J* = 2.3, 2CH); 7.19 (2H, t, *J* = 7.8, *p*-C_6H_5); 7.29 (4H, d, *J* = 7.8, *o*-C_6H_5); 7.31 (4H, t, *J* = 7.8, *m*-C_6H_5); 7.37 (2H, br. t, *J* = 2.3, 2CHN)	356 (45)
2b	1590, 1550, 1620 (C=S, C=N)	1.0 (3H, t, *J* = 7.4, CH_3 in NEt_2); 1.2 (3H, t, *J* = 7.4, CH_3 in NEt_2); 3.30 (2H, q, *J* = 7.4, CH_2 in NEt_2); 3.60 (2H, q, *J* = 7.4, CH_2 in NEt_2); 6.07 (2H, t, *J* = 2.3, 2CH); 7.17 (2H, t, *J* = 7.8, *p*-C_6H_5); 7.29 (4H, d, *J* = 7.8, *o*-C_6H_5); 7.31 (4H, t, *J* = 7.8, *m*-C_6H_5); 7.37 (2H, t, *J* = 2.3, 2CHN)	384 (25)
2c	2220 (CN), 1540, 1565, 1595 (C=S, C=N)	6.35 (2H, t, *J* = 2.3, 2CH); 7.34 (2H, br. s, 2CHN); 7.37 (2H, t, *J* = 7.8, *p*-C_6H_5); 7.44 (4H, d, *J* = 7.8, *o*-C_6H_5); 7.49 (4H, t, *J* = 7.8, *m*-C_6H_5)	338 (60)
2d	1020, 1140 (C–O–C); 1510, 1590, 1610 (C=S, C=N)	3.4–3.9 (8H, m, Σ $2NCH_2$, $2OCH_2$); 6.1 (2H, t, *J* = 2.3, 2CH); 7.21 (2H, t, *J* = 7.8, *p*-C_6H_5); 7.3 (4H, d, *J* = 7.8, *o*-C_6H_5); 7.38 (4H, t, *J* = 7.8, *m*-C_6H_5); 7.38 (2H, t, *J* = 2.3, 2CHN)	398 (75)
2e	1510, 1555, 1625 (C=S, C=N)	1.47 (2H, m, CH_2); 1.6 (2H, m, CH_2); 1.67 (2H, m, CH_2); 3.49 (2H, m, NCH_2); 3.82 (2H, m, NCH_2); 6.08 (2H, t, *J* = 2.3, 2CH); 7.19 (2H, t, *J* = 7.8, *p*-C_6H_5); 7.26 (4H, d, *J* = 7.8, *o*-C_6H_5); 7.31 (4H, t, *J* = 7.8, *m*-C_6H_5); 7.35 (2H, t, *J* = 2.3, 2CHN)	396 (60)
2f	3310, 3390 (NH_2), 1530, 1570, 1620 (C=S, C=N)	6.25 (2H, t, *J* = 2.3, 2CH); 7.3 (2H, br. s, NH_2); 7.48 (2H, t, *J* = 7.8, *m*-C_6H_5); 7.57 (1H, t, *J* = 7.8, *p*-C_6H_5); 8.42 (2H, d, *J* = 7.8, *o*-C_6H_5); 7.78 (2H, t, *J* = 2.3, 2CHN)	237 (70)
2g	1520, 1555, 1605 (C=S, C=N)	6.38 (4H, t, *J* = 2.3, 4CH); 7.57 (2H, t, *J* = 7.8, *m*-C_6H_5); 7.65 (1H, t, *J* = 7.8, *p*-C_6H_5); 7.92 (4H, t, *J* = 2.3, 4CHN); 8.07 (2H, d, *J* = 7.8, *o*-C_6H_5)	287 (100)
2h	1570, 1515, 1600 (C=S, C=N); 1045, 1150 (C–O–C)	3.67 (4H, m, $2NCH_2$); 3.8–3.9 (4H, m, $2OCH_2$); 3.96 (3H, s, OCH_3); 6.18 (2H, t, *J* = 2.3, 2CH); 7.60 (2H, t, *J* = 2.3, 2CHN)	261 (50)
2i	2105 (N_3), 1530, 1565, 1605 (C=S, C=N)	6.30 (2H, t, *J* = 2.3, 2CH); 7.27 (2H, br. s, *J* = 2.3, 2CHN); 7.47 (2H, t, *J* = 7.8, *p*-Ph); 7.54 (4H, d, *J* = 7.8, *o*-Ph); 7.57 (4H, t, *J* = 7.8, *m*-Ph);	354 (45)
2j	2100 (N_3), 1540, 1580, 1600 (C=S, C=N)	1.1 (3H, t, *J* = 7.4, CH_3 in NEt_2); 1.25 (3H, t, *J* = 7.4, CH_3 in NEt_2); 3.35 (2H, q, *J* = 7.4, CH_2 in NEt_2); 3.70 (2H, q, *J* = 7.4, CH_2 in NEt_2); 6.20 (2H, t, *J* = 2.3, 2CH); 7.30 (2H, br. s, 2CHN)	258 (80)
2k	2110 (N_3), 1560, 1585, 1615 (C=S, C=N)	6.20 (2H, t, *J* = 2.3, 2CH); 7.30 (2H, br. s, 2CHN); 0.40-0.75 (6H, m, $2CH_3CH_2CH_2N$); 1.1-1.50 (4H, m, $2CH_2CH_2N$); 3.40-3.70 (4H, m, $2CH_2N$)	286 (70)
2l	2110 (N_3), 1550, 1590, 1610 (C=S, C=N)	6.17 (2H, t, *J* = 2.3, 2CH); 7.35 (2H, br. s, 2CHN); 4.50-4.85 (2H, m, $NCH_2C_6H_5$); 7.25-7.40 (5H, m, C_6H_5)	306 (75)
2m	2120 (N_3), 1520, 1560, 1620 (C=S, C=N)	3.40 (3H, s, NCH_3); 6.27 (2H, t, *J* = 2.3, 2CH); 7.12 (2H, br. s, 2CHN); 7.23-7.35 (5H, m, C_6H_5)	292 (60)

TABLE 1 (continued)

1	2	3	4
3a	1530, 1570, 1615 (C=S, C=N)	6.25 (2H, t, J = 2.3, 2CH); 7.30 (2H, t, J = 2.3, 2CHN); 6.95-7.20 (10H, m, $2C_6H_5$); 7.40-7.65 (15H, m, $3C_6H_5$)	588 (60)
3b	1550, 1590, 1610 (C=S, C=N)	0.60-0.95 (6H, m, $2CH_3$ in NEt_2); 2.90-3.05 (4H, m, $2CH_2$ in NEt_2); 6.20 (2H, t, J = 2.3, 2CH); 7.45 (2H, t, J = 2.3, 2CHN); 7.50-7.75 (15H, m, $3C_6H_5$)	492 (80)
4a	1505, 1575, 1600 (C=S, C=N, N=N), 1690 (C=O)	2.50 (3H, s, $COCH_3$); 2.62 (3H, s, 5'-CH_3); 6.37 (2H, t, J = 2.3, 2CH); 7.00 (4H, m, *o*- and *m*-C_6H_5); 7.38 (1H, m, *p*-C_6H_5); 7.65 (2H, t, J = 2.3, 2CHN)	436 (70)
4b	1540, 1570, 1595 (C=S, C=N, N=N), 1680 (C=O)	1.17–1.27 (6H, m, $2CH_3$ in NEt_2); 2.65 (3H, s, $COCH_3$); 2.90 (3H, s, 5'-CH_3); 3.67 (2H, q, J = 7.3, CH_2 in NEt_2); 3.75 (2H, q, J = 7.3, CH_2 in NEt_2); 6.40 (2H, t, J = 2.3, 2CH); 7.74 (2H, t, J = 2.3, 2CHN)	340 (40)
4c	1540, 1570, 1595 (C=S, C=N, N=N), 1680 (C=O)	0.90 (3H, t, J = 7.5, CH_3 in NPr_2); 0.95 (3H, t, J = 7.5, CH_3 in NPr_2); 1.60-1.75 (4H, m, $2CH_2$ in NPr_2); 2.66 (3H, s, $COCH_3$); 2.9 (3H, s, 5'-CH_3); 3.60 (2H, t, J = 7.5, CH_2N in NPr_2); 3.67 (2H, t, J = 7.5, CH_2N in NPr_2); 6.40 (2H, t, J = 2.3, 2CH); 7.72 (2H, t, J = 2.3, 2CHN)	368 (55)
4d	1525, 1550, 1600 (C=S, C=N, N=N), 1700 (C=O)	2.65 (3H, s, $COCH_3$); 2.85 (3H, s, 5'-CH_3); 3.25 (3H, s, NCH_3); 4.95–5.05 (2H, m, $NCH_2C_6H_5$); 6.40 (2H, m, 2CH); 7.30-7.45 (5H, m, C_6H_5); 7.77 (2H, m, 2CHN)	388 (90)
4e	1500, 1545, 1615 (C=S, C=N, N=N), 1715 (C=O)	1.32 (3H, t, J = 7.4, CH_3 in OEt); 2.60 (3H, s, 5'-CH_3); 4.33 (2H, q, J = 7.4, CH_2 in OEt); 6.36 (2H, t, J = 2.3, 2CH); 7.45 (2H, t, J = 2.3, 2CHN); 7.47 (2H, m, *p*-C_6H_5); 7.50 (8H, m, *o*- and *m*-C_6H_5)	466 (50)
4f	1510, 1550, 1580 (C=S, C=N, N=N), 1710 (C=O)	0.92 (3H, t, J = 7.5, CH_3 in NPr_2); 0.95 (3H, t, J = 7.5, CH_3 in NPr_2); 1.35 (3H, t, J = 7.5, CH_3 in OEt); 1.6-1.75 (4H, m, $2CH_2$ in NPr_2); 2.93 (3H, s, 5'-CH_3); 3.60 (2H, t, J = 7.5, CH_2N in NPr_2); 3.67 (2H, t, J = 7.5, CH_2N in NPr_2); 4.40 (2H, q, J = 7.5, CH_2 in OEt); 6.40 (2H, t, J = 2.3, 2CH); 7.75 (2H, t, J = 2.3, 2CHN)	398 (65)
4g	1515, 1555, 1590 (C=S, C=N, N=N), 1700 (C=O)	1.35 (3H, t, J = 8.0, CH_3 in OEt); 2.95 (3H, s, 5'-CH_3); 3.25 (3H, s, NCH_3); 4.37 (2H, q, J = 8.0, CH_2 in OEt); 5.00 (2H, s, $N\underline{CH_2}C_6H_5$); 6.40 (2H, t, J = 2.3, CH); 7.32 (1H, m, *p*-C_6H_5); 7.38 (4H, m, *o*- and *m*-C_6H_5); 7.75 (2H, t, J = 2.3, 2CHN)	418 (100)
4h	1530, 1580, 1620 (C=S, C=N, N=N), 1700 (C=O)	1.35 (3H, br. m, CH_3 in OEt); 2.75 (3H, br. s, 5'-CH_3); 3.65 (3H, s, NCH_3); 4.35 (2H, br. m, CH_2 in OEt); 6.38 (2H, br. s, 2CH); 7.50 (2H, br. s, 2CHN); 7.35–7.55 (5H, m, C_6H_5)	404 (95)

A steric effect is also an important factor influencing the rate of this reaction. Hence the most reactive are the amino-*sym*-triazines **1a,c,f,h** which contain a low bulk substituent (OCH_3, $N(CH_3)_2$ etc) at positions 4 or 6 of the triazine ring. The greatest reaction times were found in the case of the use of the starting compounds **1d,e** which contain diphenylamine, piperidine, or morpholine substituents together. At the same time, and against expectations, the presence of small volume acceptor groups which lower the nucleophilicity of the amino group (nitrile or azide) markedly increase the rate of formation of the final products. Hence the 2-amino-6-cyano(azido)-*sym*-triazines give the corresponding pyrrolyl-*sym*-triazines **2c,i-m** in good yields (73-93%) even after short (0.5-1 h) refluxing in toluene in the presence of P_2O_5. This is likely connected on one hand with the absence of sterically hindering substituents in the composition of the starting materials and on the other with the use of an aprotoic solvent. It will be recalled that the yields of compounds **2i-m** do not exceed 30% when the reaction is carried out in acetic acid medium (method B, Experimental section).

The composition and structure of the pyrrole *sym*-triazine derivatives **2a-m** were confirmed by IR and ^{1}H NMR spectroscopic and mass-spectrometric data.

The IR spectra of the mono(di)-N-pyrrolyl-*sym*-triazines **2a-m** contain varying intensity maximum absorptions at 1510-1625 cm^{-1} which are characteristic stretching vibrations of a *sym*-triazine ring [9] and substituent in the 4,6 *sym*-triazine ring positions. The spectra of all of the synthesized compounds also show the disappearance of broad absorption stretching bands in the region 3470-3270 cm^{-1} which are assigned to the stretching of the primary amino groups in the *sym*-triazines **1a-m** [10] (Table 1).

The ^{1}H NMR spectra of the synthesized 1,3,5-triazines **2a-m** show all of the proton signals for the substituent groups in positions 4 and 6 of the triazine ring and this is a reliable confirmation of the structure of the compounds obtained (Table 1). It was an interesting experimental fact that the signals for the H-2-5 protons in the majority of the N-substituted pyrroles **1g, 2a-m, 3a,b, 4a-h** appear as triplets with a spin-spin coupling of 2.3 Hz in the range 7.12-7.92 ppm and of intensity two proton units. The signals for the H-3 and H-4 protons in the spectra of the compounds also appear as a triplet in the range 6.07-6.38 ppm, shifted to higher field and typical of N-substituted pyrroles of this type [10].

The mass spectroscopic molcular ions observed in the spectra of compounds **2a-m** also confirm their structure.

With the aim of broadening the series of *sym*-triazine derivatives [2, 11] it was of interest to synthesize iminotriphenylphosphoranes which also contain a pyrrole fragment in their structure. The 4-azido-2-(1H-1-pyrrolyl)-1,3,5-triazines **2i,j** were used as starting materials. The reactions were carried out in benzene solution at 10-15ºC and their completion was monitored by the finish of nitrogen evolution.

The synthesized iminophosphorano-*sym*-triazines **3a,b** (Tables 1 and 2) are colorless, fine crystalline materials.

The IR spectra of compounds **3a,b** show absorption bands in the region 1530-1615 cm^{-1} which are characteristic of C=C stretching vibrations and, in comparison with the spectra of the starting azides **2i-m**, the disappearance of the characteristic azide group band at 2100-2105 cm^{-1}.

The ^{1}H NMR spectra of the compounds **3a,b** also show characteristic signals for the protons of all of the substituents in the *sym*-triazine ring and also multiplet signals for the protons of all three phenyl residues in quite a narrow region (7.40-7.75 ppm) corresponding to fifteen proton units. The mass-spectroscopic data for compounds **3a,b** also confirm their structure.

Bearing in mind the high growth stimulating and antidotal activity [12, 13] of the triazine-triazole biheterocyclic systems previously obtained by us [1, 2] it seemed reasonable to study the possibility of preparing novel *sym*-triazine derivatives which contain triazole and pyrrole rings together.

With this in view we carried out the reaction of the pyrrolyl-*sym*-triazines **2i-m** with acetylacetone and acetoacetic ester in DMF solution in the presence of triethylamine. The target compounds **4a-h** were obtained in high (68-80%) yields (see Scheme and Tables 1 and 2).

TABLE 2. Physico-chemical Characteristics of Synthesized Compounds **1a-e,g,i-m, 2a-m, 3a,b,** and **4a-h**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
1	2	3	4	5	6	7
1a	$C_{17}H_{18}N_6$	66.94 / 66.65	5.89 / 5.92	27.17 / 27.43	202-203	65
1b	$C_{19}H_{22}N_6$	68.48 / 68.24	6.77 / 6.63	24.75 / 25.13	165	70
1c	$C_{16}H_{12}N_6$	66.84 / 66.65	4.44 / 4.20	28.72 / 29.15	186-187	86
1d	$C_{19}H_{20}N_6O$	65.68 / 65.50	5.87 / 5.79	24.01 / 24.12	202-203	73
1e	$C_{20}H_{22}N_6$	69.61 / 69.34	6.37 / 6.40	24.02 / 24.26	211-212	68
1g	$C_{13}H_{11}N_5$	65.99 / 65.81	4.72 / 4.67	29.27 / 29.52	153-154	76
1i	$C_{15}H_{12}N_8$	59.34 / 59.20	4.15 / 3.98	36.60 / 36.82	147-148	80
1j	$C_7H_{12}N_8$	40.49 / 40.38	5.89 / 5.81	53.70 / 53.81	121-122	83
1k	$C_9H_{16}N_8$	45.55 / 45.75	7.00 / 6.83	47.25 / 47.42	110-111	71
1l	$C_{11}H_{12}N_8$	51.70 / 51.56	4.87 / 4.72	43.55 / 43.72	98-99	76
1m	$C_{14}H_{12}N_8$	49.68 / 49.58	4.28 / 4.16	46.04 / 46.26	177-178	70
2a	$C_{21}H_{20}N_6$	70.64 / 70.76	5.74 / 5.66	23.49 / 23.58	168-170	73 (method A)
2b	$C_{23}H_{24}N_6$	71.71 / 71.85	6.37 / 6.29	22.00 / 21.86	116-117	82
2c	$C_{20}H_{14}N_6$	71.13 / 70.99	4.03 / 4.17	24.71 / 24.84	214-215	91
2d	$C_{23}H_{22}N_6O$	69.50 / 69.32	5.62 / 5.57	20.97 / 21.09	173-174	85
2e	$C_{24}H_{24}N_6$	72.54 / 72.70	6.15 / 6.10	21.33 / 21.20	142-143	77
2f	$C_{13}H_{11}N_5$	65.68 / 65.81	4.77 / 4.67	29.54 / 29.52	153-155	76
2g	$C_{17}H_{13}N_5$	70.93 / 71.06	4.47 / 4.56	24.49 / 24.38	185-187	79
2h	$C_{12}H_{15}N_5O_2$	55.01 / 55.16	5.89 / 5.79	26.70 / 26.81	89-90	85
2i	$C_{19}H_{14}N_8$	64.45 / 64.40	4.07 / 3.98	31.58 / 31.62	126-128	93
2j	$C_{11}H_{14}N_8$	50.90 / 51.15	5.70 / 5.46	43.72 / 43.38	—*	77
2k	$C_{13}H_{18}N_8$	54.27 / 54.53	6.67 / 6.34	39.45 / 39.13	—	72
2l	$C_{15}H_{14}N_8$	54.27 / 54.53	4.82 / 4.61	36.85 / 36.58	—*	73
2m	$C_{14}H_{12}N_8$	57.30 / 57.53	4.30 / 4.14	38.40 / 38.83	104-105	77
3a	$C_{37}H_{29}N_6P$	75.58 / 75.49	4.80 / 4.96	14.35 / 14.28	185-186	87
3b	$C_{29}H_{29}N_6P$	70.66 / 70.71	6.01 / 5.93	17.00 / 17.06	156-157	80
4a	$C_{24}H_{20}N_8O$	65.87 / 66.04	4.75 / 4.62	25.56 / 25.68	240-241	75
4b	$C_{16}H_{20}N_8O$	56.56 / 56.56	6.50 / 6.56	32.80 / 32.92	135-136	80

TABLE 2 (continued)

1	2	3	4	5	6	7
4c	$C_{18}H_{24}N_8O$	58.55 58.68	6.50 6.56	30.53 30.42	95-96	71
4d	$C_{20}H_{20}N_8O$	61.80 61.84	5.27 5.19	28.99 28.85	62-63	71
4e	$C_{25}H_{22}N_8O_2$	64.21 64.36	4.60 4.75	24.18 24.02	174-175	73
4f	$C_{19}H_{26}N_8O_2$	57.16 57.27	6.66 6.58	28.01 28.12	84-85	70
4g	$C_{21}H_{22}N_8O_2$	60.35 60.27	5.44 5.30	26.83 26.78	110-111	68
4h	$C_{20}H_{20}N_8O_2$	59.22 59.39	5.08 4.98	27.86 27.71	215-216	78

* oil

It has been found that the rate of the reaction depends significantly on both the structure of the starting azide and on the activity of the dicarbonyl compound. The presence of steric hindrance in the composition of the starting azide increases the reaction time from 0.5-1 h to 10 h when the more active acetylacetone is used and to 48 h in the case of the acetoacetate ester [2].

The synthesized polyheterocyclic systems **4a-h** are white, fine crystalline powders which show good solubility in polar organic solvents and aromatic hydrocarbons. The purity of the compounds obtained was confirmed using TLC and the composition and structure through the results of elemental analysis and from IR, ^{1}H NMR, and mass-spectroscopic data (Table 1).

Hence we have studied the addition-cyclization reactions of different mono- and diamino *sym*-triazine derivatives **1a-m** with 2,5-dimethoxytetrahydrofuran. The dependence of the reaction time on the structure of the substituent occurring in the composition of the amino-1,3,5-triazines and achievement of optimum conditions (P_2O_5, toluene) for the synthesis of the N-substituted pyrrolyl-*sym*-triazines containing different substituents are discussed.

As a result, a series of *sym*-triazine derivatives containing pyrrole, triazole, or iminophosphorane fragments together and with high bioactivity potential has been prepared for the first time.

EXPERIMENTAL

IR spectra were recorded for sample suspensions in vaseline oil on a Specord IR-75 spectrophotometer. ^{1}H NMR spectra were taken on a Bruker DRX-500 (500 MHz) radiofrequency spectrometer using DMSO-d_6 and with TMS as internal standard. Mass spectra were recorded on a Finnigan MAT INCOS50 instrument with 70 eV ionization energy. Elemental analysis of the synthesized compounds was carried out on a Carlo-Erba 1106 analyzer. Monitoring of the reaction course and the purity of the products obtained was carried out using TLC on Silufol UV-254 plates with acetone–hexane (1:1) as eluent.

All of the reagents used were purified by crystallization from a suitable solvent or fractionally distilled immediately before use. Solvents were purified and dried by known methods [14].

4-Dimethylamino-6-diphenylamino-2-(1H-1-pyrrolyl)-1,3,5-triazine (2a). A. A suspension of 2-amino-4-dimethylamino-6-diphenylamino-1,3,5-triazine **1a** (1.0 g, 3.26 mmol), P_2O_5 (0.46 g, 3.26 mmol), and absolute toluene (10 ml) was heated to reflux and 2,5-dimethoxytetrahydrofuran (0.51 g, 3.91 mmol) was added with stirring. The reaction product was refluxed for 1.5-2 h, cooled and then filtered, and the filtrate was evaporated to dryness. The residue was washed with water, dried to constant weight, dissolved in methylene

chloride (10-15 ml), and passed through a silica gel column (1 cm, LC 5/40 μ grade). Additional purification was carried out by crystallization from ethanol. Yield of compound **2a** 0.85 g (73%).

Compounds 2b-i were prepared similarly. The end of the reaction was determined by TLC in each specific case.

B. A solution of compound **1a** (1.0 g, 3.26 mmol) in glacial acetic acid (8 ml) was heated to reflux and 2,5-dimethoxytetrahydrofuran (0.51 ml, 3.91 mmol) was added with stirring. The reaction product was refluxed for 3-3.5 h, cooled, and diluted with cold water (30 ml). The precipitate formed was separated, washed with water to neutral reaction of sparge water, and dried. Purification by method A gave the product compound **2a** (0.55 g, 47%).

4-Diethylamino-2-(1H-1-pyrrolyl)-6-(1,3,5-triazin-2-yl)-iminotriphenylphosphorane (3b). Triphenylphosphine (1.01 g, 3.87 mmol) was added in small portions to a stirred solution of 6-azido-4-diethylamino-2-(1H-1-pyrrolyl)-1,3,5-triazine **2j** (1.0 g, 3.87 mmol) in absolute benzene (15 ml). The reaction product was stirred to the completion of gas bubble formation and left overnight at room temperature. The precipitate formed was filtered off and the mother liquor was evaporated to give an additional amount of product. The precipitates were combined, washed with cold hexane, and dried in air to constant weight. Purification by crystallization from ethanol gave compound **3b** (1.33 g, 80%) as white crystals.

Compound 3a was prepared under the same conditions.

6-(4-Acetyl-5-methyl-1,2,3-triazol-1-yl)-4-dipropylamino-2-(1H-1-pyrrolyl)-1,3,5-triazine (4c). A solution of acetylacetone (0.72 ml, 6.98 mmol) and triethylamine (0.97 ml, 6.98 mmol) in dry DMF (5 ml) was added dropwise to a solution of 6-azido-4-dipropylamino-2-(1H-1-pyrrolyl)-1,3,5-triazine **2k** (1.0 g, 3.49 mmol) in DMF (10 ml) stirred at room temperature. The reaction product was stirred at the same temperature for 3 h and then introduced as a fine jet with stirring into cold water (100 ml). The precipitate of the target product was filtered off, repeatedly washed with water, and dried to give compound **4c** (0.91 g, 71%). The product did not need further purification.

Compounds 4a,b,d were prepared similarly.

4-Dipropylamino-6-(4-ethoxycarbonyl-5-methyl-1,2,3-triazol-1-yl)-2-(1H-1-pyrrolyl)-1,3,5-triazine (4f). A solution of acetoacetic ester (0.89 ml, 6.98 mmol) and triethylamine (0.97 g, 6.98 mmol) in DMF (5 ml) was added to a solution of 4-dipropylamino-6-azido-2-(1H-1-pyrrolyl)-1,3,5-triazine **2k** (1.0 g, 3.49 mmol) in dry DMF (10 ml) with stirring at room temperature. The reaction product was stirred at 30-40ºC for 48 h and treated similarly to compound **4c** to give the target product **4f** (0.97 g, 70%) which did not need further purification.

Compounds 4e,g,h were synthesized similarly.

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