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The 3,5-disubstituted 1-amino-1,3,5-triazine-2,4,6-triones were synthesized in good yields from aromatic aldehyde or ketone ethoxycarbonylhydrazones by treatment with aryl or methyl isocyanates in boiling triethylamine followed by hydrolysis with hydrochloric acid solution.

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Isocyanuric acid derivatives have many industrial applications as crosslinking agents for polyester [1], as additives for flame retardant resin compounds [2] or as antioxidants [3]. Trihydrazone derivatives are used as pesticides [4]. One *N*-amino derivative and one *N*-diamino derivative have been reported in a patent [5], but the syntheses are not clearly described. With the aim to study the cyclic rearrangement of 5-aryl-3-carbamoyl-1,3,4-oxadiazol-2(3*H*)-ones (Scheme 1), we have reported in a previous paper the first synthesis of 3,5-disubstituted 1-acylamino-1,3,5-triazine-2,4,6-triones and of their free amino derivatives [6].

Herein is reported a new very simple synthesis of these heterocycles involving the reaction of ethoxycarbonylhydrazones with aromatic aldehydes or ketones with an excess of aryl or methyl isocyanates in boiling anhydrous triethylamine (Scheme 2).

Under these conditions, addition of isocyanate to ethoxycarbonylhydrazone 1 gave successively semicarbazone derivatives 2 then 3 neither of which were isolated as intermediates. The ring closure of 3 provided benzylidenaminotriazinetriones 4. Methyl isocyanate and several aryl isocyanates were used successfully (Table 1). The reaction time was 30 minutes. Triazinetriones 5 present in small quantities in addition to compounds 4 were formed by trimerization of isocyanates [7] and were easily eliminated by recrystallization. Hydrolysis of triazinetriones 4 with boiling 10% hydrochloric acid solution provided the corresponding 3,5-disubstituted

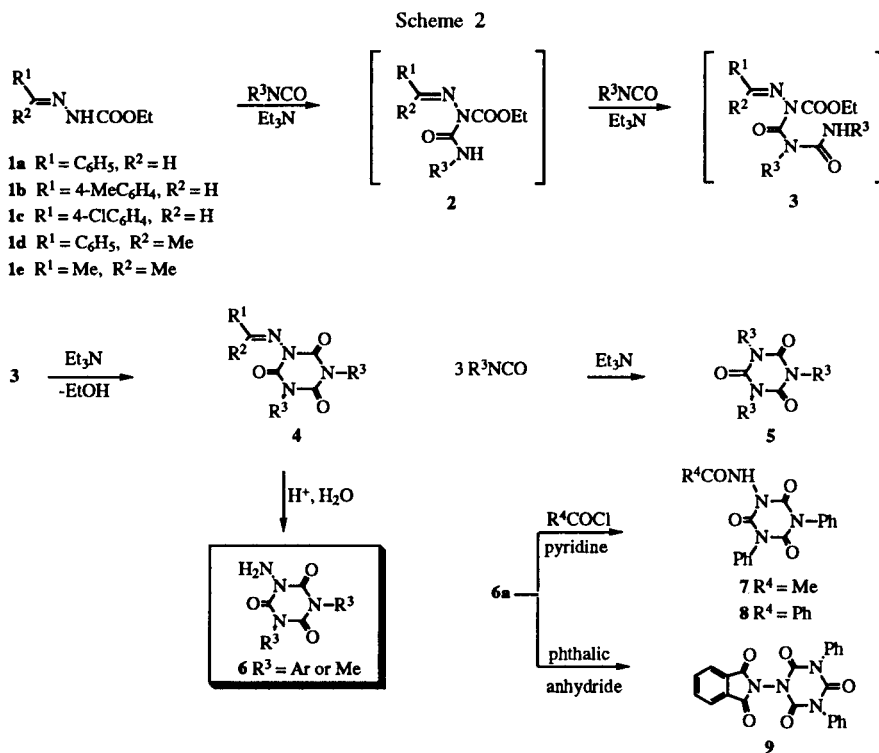
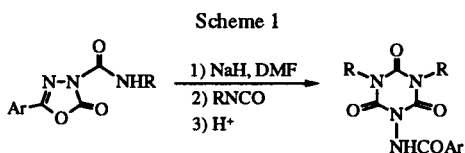


Table 1
1-Amino-1,3,5-triazine-2,4,6-trione Derivatives 4

Compound 4	R ¹	R ²	R ³	Yield% [a]	Mp °C	Formula (molecular weight)	Analysis, %			IR v cm ⁻¹	¹ H NMR [b] δ ppm
							Calcd./Found C	H	N		
a	Ph	H	Ph	79	248 [c]	C ₂₂ H ₁₆ N ₄ O ₃ (384.38)	68.74 68.65	4.20 4.21	14.58 14.65	1770, 1700, 1680, 1610	7.5-8.1 (m, 15H), 8.9 (s, 1H)
b	Ph	H	4-MePh	52	294 [c]	C ₂₄ H ₂₀ N ₄ O ₃ (412.43)	69.89 69.93	4.89 4.87	13.58 13.52	1760, 1700, 1680, 1610	2.2 (s, 6H), 7-8 (m, 13H), 8.8 (s, 1H)
c	Ph	H	4-MeOPh	40	263 [c]	C ₂₄ H ₂₀ N ₄ O ₅ (444.43)	64.86 64.72	4.54 4.60	12.61 12.64	1760, 1700, 1680, 1600	3.8 (s, 6H), 7 (d, 4H), 7.4 (d, 4H), 7.6 (m, 3H), 7.9 (m, 2H), 8.8 (s, 1H)
d	Ph	H	4-ClPh	77	252 [c]	C ₂₂ H ₁₄ Cl ₂ N ₄ O ₃ (453.27)	58.29 58.33	3.11 3.14	12.36 12.31	1770, 1700, 1690, 1600	7.25-8 (m, 13H), 8.8 (s, 1H)
e	Ph	H	3,4-diClPh	30	264 [c]	C ₂₂ H ₁₂ Cl ₄ N ₄ O ₃ (522.16)	50.60 50.54	2.32 2.37	10.73 10.78	1765, 1710, 1695, 1610	7.45-8 (m, 11H), 8.85 (s, 1H)
f	Ph	H	4-BrPh	45	280 [c]	C ₂₂ H ₁₄ Br ₂ N ₄ O ₃ (542.16)	48.73 48.79	2.60 2.54	10.33 10.36	1760, 1700, 1680, 1600	7.3-8 (m, 13H), 8.85 (s, 1H)
g	Ph	H	Me	51	172 [d]	C ₁₂ H ₁₂ N ₄ O ₃ (260.24)	55.38 55.32	4.65 4.59	21.53 21.50	1750, 1700, 1680, 1610	3.2 (s, 6H), 7.5-8 (m, 5H), 8.8 (s, 1H)
h	4-MePh	H	Ph	45	290 [c]	C ₂₃ H ₁₈ N ₄ O ₃ (398.40)	69.33 69.27	4.55 4.61	14.06 13.99	1760, 1700, 1690, 1610	2.3 (s, 3H), 7.2-7.95 (m, 14H), 8.85 (s, 1H)
i	4-ClPh	H	Ph	65	220 [c]	C ₂₂ H ₁₅ ClN ₄ O ₃ (418.82)	63.09 63.00	3.61 3.66	13.38 13.38	1750, 1710, 1690, 1605	7.35-8.05 (m, 14H), 8.85 (s, 1H)
j	Ph	Me	Ph	25	286 [c]	C ₂₃ H ₁₈ N ₄ O ₃ (398.40)	69.33 69.42	4.55 4.51	14.06 14.03	1770, 1700, 1680, 1600	3.3 (s, 3H), 7.25-8.1 (m, 15H)
k	Me	Me	Ph	15	278 [c]	C ₁₈ H ₁₆ N ₄ O ₃ (336.34)	64.28 64.25	4.80 4.83	16.66 16.73	1750, 1700, 1695, 1610	1.95 (s, 3H), 2.1 (s, 3H), 7.35 (m, 10H)

[a] Non-optimized yields. [b] In dimethyl-d₆ sulfoxide. [c] 1-Butanol. [d] Methanol.

Table 2
1-Amino-1,3,5-triazine-2,4,6-triones 6

Compound 6	R ³	Yield % [a]	Mp °C	Formula (molecular weight)	Analysis, %			IR v cm ⁻¹	¹ H NMR [b] δ ppm
					Calcd./Found C	H	N		
a	Ph	93	234 [c]	C ₁₅ H ₁₂ N ₄ O ₃ (296.27)	60.81 60.79	4.05 3.98	18.91 18.87	3300, 3180, 1780, 1705, 1690	5.2 (s, 2H), 7.4 (m, 10H)
b	4-MePh	90	239 [d]	C ₁₇ H ₁₆ N ₄ O ₃ (324.33)	62.95 62.97	4.97 4.91	17.28 17.24	3300, 3200, 1770, 1700, 1680	2.25 (s, 6H), 4.7 (bs, 2H), 7.3 (m, 8H)
c	4-MeOPh	70	214 [e]	C ₁₇ H ₁₆ N ₄ O ₅ (356.33)	57.30 57.31	4.53 4.45	15.72 15.79	3300, 3200, 1770, 1700, 1690	3.8 (s, 6H), 3.9 (bs, 2H), 7-7.5 (m, 8H)
d	4-ClPh	87	272 [e]	C ₁₅ H ₁₀ Cl ₂ N ₄ O ₃ (365.16)	49.33 49.42	2.76 2.71	15.34 15.41	3300, 3180, 1770, 1700, 1680	4.2 (bs, 2H), 7.3-7.7 (m, 8H)
e	3,4-diClPh	75	241 [e]	C ₁₅ H ₈ Cl ₄ N ₄ O ₃ (434.05)	41.50 41.48	1.86 1.89	12.91 12.88	3300, 3180, 1760, 1700, 1695	3.7 (bs, 2H), 7.3-8 (m, 6H)
f	4-BrPh	71	271 [e]	C ₁₅ H ₁₀ Br ₂ N ₄ O ₃ (454.06)	39.67 39.51	2.21 2.19	12.33 12.39	3300, 3200, 1775, 1700, 1680	3.5 (bs, 2H), 7.3-7.7 (m, 8H)
g	Me	72	146 [e]	C ₅ H ₈ N ₄ O ₃ (172.14)	34.88 34.72	4.68 4.70	32.55 32.61	3310, 3220, 1750, 1670(b)	3.15 (s, 6H), 4.45 (bs, 2H)

[a] Non-optimized yields. [b] In dimethyl-d₆ sulfoxide. [c] 1-Butanol. [d] 1-Propanol. [e] Ethanol.

1-amino-1,3,5-triazine-2,4,6-triones **6** in very good yields (Table 2). Structural confirmation of compounds **6** was provided by physicochemical data and chemical reactions. Compound **4a** was regenerated from compound **6a** by treatment with benzaldehyde in acetic acid. Reaction of **6a** with acetyl or benzoyl chloride or phthalic anhydride provided the corresponding acyl derivative **7**, **8** and **9** respectively.

EXPERIMENTAL

Melting points were determined on a Büchi 510 oil heated apparatus and are uncorrected. The ir spectra were recorded on a Perkin Elmer 1310 spectrophotometer as potassium bromide disks. The ¹H and ¹³C nmr spectra were run on a Bruker 200 MHz spectrometer and are reported as δ values (ppm) relative to tetramethylsilane as an internal standard. Reactions were fol-

lowed by tlc on Macherey-Nagel Polygram SIL G/UV₂₅₄ pre-coated plastic sheets. Commercially available organic compounds were used without further purification. Ethoxycarbonylhydrazine [8], and its hydrazones **1a** [9], **1b** [9], **1c** [10], **1d** [11], **1e** [9] were prepared following procedures already published.

General Procedure for the Preparation of 3,5-Disubstituted 1,3,5-Triazine-2,4,6-trione Derivatives **4a-k**.

To a solution of ethoxycarbonylhydrazone **1** (10^{-2} mole) in anhydrous triethylamine (10 ml) was added dropwise at 25°, aryl isocyanate (2.10^{-2} mole) or methyl isocyanate (6.10^{-2} mole) for compound **4g**. The mixture was refluxed for 30 minutes with stirring. **Beware! The trimer 5 which was formed from methyl isocyanate sublimed and could clog the condenser.** In most cases, compounds **4** precipitated. Excess triethylamine was evaporated under reduced pressure. The resulting product was recrystallized from suitable solvents (Table 1).

Acid Hydrolysis of Compounds **4a-k**.

A suspension of triazinetrione **4** (10^{-2} mole) in 10% hydrochloric acid solution (150 ml) was refluxed in a Dean-Stark apparatus. Successive additions of acid solution were required to maintain the initial indicated volume. In most cases, the total hydrolysis was performed when all the solid triazinetrione **4** had disappeared after about 4 hours from the reaction mixture. Upon cooling, the major part of compound **6** crystallized and was removed by filtration. Another part was obtained as a second crop when the resulting filtrate was evaporated under reduced pressure. Compounds **6** were recrystallized from suitable solvents (Table 2).

1-Acetamido-3,5-diphenyl-1,3,5-triazine-2,4,6-trione (**7**).

This compound was obtained by classical method from compound **6a**, using acetyl chloride and pyridine. It was recrystallized from 1-propanol (71%), mp 246°, lit [6] 246°.

1-Benzamido-3,5-diphenyl-1,3,5-triazine-2,4,6-trione (**8**).

This compound was obtained by classical method from compound **6a**, using benzoyl chloride and pyridine. It was recrystal-

ized from acetonitrile (81%). It melted with strong decomposition above 310° [6].

1-Phthalimido-1,3,5-triazine-2,4,6-trione (**9**).

A suspension of 1-amino-3,5-diphenyl-1,3,5-triazine-2,4,6-trione **6a** (0.296 g, 10^{-3} mole) and phthalic anhydride (0.148 g, 10^{-3} mole) in anhydrous xylene (10 ml) was refluxed for 1 hour. Excess xylene was evaporated under reduced pressure. The resulting crude product was recrystallized from ethanol. This compound was obtained in a yield of 85% (0.362 g), mp 220°; ir: 1740-1700 cm^{-1} (v b); ^1H nmr: δ 8.1-7.3 (14 H arom).

Anal. Calcd. for $\text{C}_{23}\text{H}_{14}\text{N}_4\text{O}_5$: C, 64.78; H, 3.30; N, 13.14. Found: C, 64.82; H, 3.28; N, 13.21.

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