Condensed 1,2,4-Triazines. Synthesis and Reactions of Some Condensed Benzo[*e*]*as*-triazines

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2-*o*-Chlorophenyl-2*H*-naphtho[1,2-*d*]*v*-triazole-4,5-quinone condenses with semicarbazide and some of its derivatives at the 4 position and the products cyclize into the corresponding 1,2,4-triazines. Reactions of these triazines with some reagents are described.

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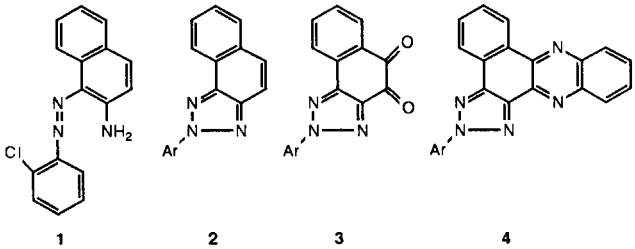
Some 1,2,4-triazines constitute an important class of biologically active compounds [1-8]. In continuation of our previous work in this area [9,10], we now have synthesized a number of new 1,2,4-triazines condensed with the heterocyclic 2-*o*-chlorophenyl-2*H*-naphtho[1,2-*d*]-*v*-triazole moiety. Thus, 2-*o*-chlorophenyl-2*H*-naphtho[1,2-*d*]-*v*-triazole-4,5-quinone (**3**) is prepared by oxidizing 1-(*o*-chlorophenylazo)-2-aminonaphthalene (**1**) with chromium trioxide in acetic acid [12]. The base 2-*o*-chlorophenyl-2*H*-naphtho[1,2-*d*]-*v*-triazole (**2**) is expected to be an intermediate which was not isolated.

The quinone **3** condenses readily with *o*-phenylenediamine to give the phenazine **4**. Condensation of the quinone **3** with semicarbazide, and thiosemicarbazide affords the monosemicarbazone **5a** and the monothiosemicarbazone **5b** respectively. It is believed that condensation takes place with the carbonyl group in position 4 rather than that in position 5. This finds support from the infrared spectral data of compounds **3** and **5b**. Compound **3** shows an absorption band in the region 1685-1690 cm^{-1} attributed to the carbonyl group in position 5, since it is conjugated with the double bonds of the aromatic carbocyclic ring. Delocalization of the π electrons of the carbonyl group reduces the double bond character of the C to O bond, causing absorption at longer wave length as compared with the carbonyl group in position 4 which shows an absorption band at 1725 cm^{-1}. The monothiosemicarbazone **5b** shows an absorption band at 1685 cm^{-1} with the disappearance of the band at 1725 cm^{-1} in the parent quinone.

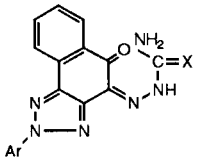
The monosemicarbazone **5a** and the monothiosemicarbazone **5b** were cyclized, by heating in aqueous potasium hydroxide solution into 2-*o*-chlorophenyl-6-hydroxybenzo[*f*]-*v*-triazolo[4,5-*h*]benzo[*e*]-*as*-triazine (**6a**) and its 6-mercapto analog **6b** respectively.

Condensation of the quinone **3** with aminoguanidine bicarbonate in acetic acid afforded 2-*o*-chlorophenyl-6-aminobenzo[*f*]-*v*-triazolo[4,5-*h*]benzo[*e*]-*as*-triazine (**6c**), probably *via* the intermediate guanylhydrazone **5c** which was not isolated. The structure of compound **6c** is inferred from the facts that it gives the correct analytical values and its infrared spectrum shows no absorption bands in the carbonyl region.

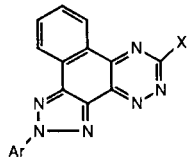
The synthesis of 2-*o*-chlorophenyl-6-chlorobenzo[*f*]-*v*-triazolo[4,5-*h*]benzo[*e*]-*as*-triazine (**6d**) is achieved by heating the hydroxytriazine **6a** with phosphorus oxychloride. Compound **6d** reacts with arylamines, namely, aniline, *o*-chloroaniline and *p*-toluidine and the 6-arylamino compounds **7a-c** are obtained, respectively. Each of



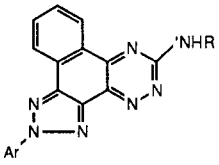
1 **2** **3** **4**



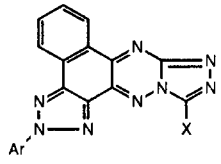
5a, X = O
5b, X = S
5c, X = NH



6a, X = OH
6b, X = SH
6c, X = NH_2
6d, X = Cl



7a, R = C_6H_5
7b, R = C_6H_4Cl-*o*
7c, R = $C_6H_4CH_3$-*p*
7d, R = NH_2
7e, R = N=CH-C_6H_4Cl-*p*
7f, R = N=CH-C_6H_5
7g, R = N=CH-$C_6H_4OCH_3$-*p*
7h, R = N=CH-$C_6H_3(OCH_2O)$



8a, X = H
8b, X = SH

Ar = C_6H_4Cl-*o*

Table

Compound No.	Mp °C	Yield %	Formula (MW)	Analysis % Calcd./Found C	H	N	S	Cl
1	158	57	$C_{16}H_{12}ClN_3$	68.21	4.29	14.91	--	12.58
			(281.74)	67.91	4.02	14.75	--	12.23
3	242	61	$C_{16}H_8ClN_3O_2$	62.05	2.60	13.56	--	11.44
			(309.71)	62.20	2.85	13.44	--	11.23
4	262	75	$C_{22}H_{12}ClN_5$	69.20	3.16	18.34	--	9.28
			(381.83)	69.62	3.01	18.13	--	8.92
5a	259	61	$C_{17}H_{11}ClN_6O_2$	55.67	3.02	22.91	--	9.66
			(366.76)	56.00	3.41	22.64	--	9.52
5b	238	54	$C_{17}H_{11}ClN_6OS$	53.33	2.89	21.95	8.37	9.26
			(382.82)	53.61	2.88	22.33	8.01	9.22
6a	308	34	$C_{17}H_9ClN_6O$	58.54	2.60	24.09	--	10.16
			(348.75)	58.97	2.91	23.94	--	9.98
6b	>300	47	$C_{17}H_9ClN_6S$	55.97	2.48	23.03	8.78	9.71
			(364.81)	56.11	2.37	22.81	8.49	9.52
6c	295	85	$C_{17}H_{10}ClN_7$	58.71	2.89	28.19	--	10.19
			(347.76)	58.53	3.21	28.31	--	9.98
6d	262	91	$C_{17}H_8Cl_2N_6$	55.60	2.19	22.88	--	19.31
			(367.19)	55.94	2.31	22.67	--	20.01
7a	292	58	$C_{23}H_{14}ClN_7$	65.17	3.32	23.13	--	8.36
			(423.86)	65.51	3.24	22.96	--	8.11
7b	244	87	$C_{23}H_{13}Cl_2N_7$	60.27	2.86	21.39	--	15.47
			(458.31)	60.57	3.12	21.11	--	15.31
7c	267	90	$C_{24}H_{16}ClN_7$	65.83	3.68	22.39	--	8.09
			(437.89)	66.12	3.83	22.31	--	7.98
7d	268	80	$C_{17}H_{11}ClN_8$	55.67	3.02	30.55	--	9.66
			(366.78)	55.81	2.97	30.90	--	9.45
7e	307	85	$C_{24}H_{14}Cl_2N_8$	59.39	2.90	23.09	--	14.61
			(485.33)	59.01	3.22	22.75	--	14.23
7f	295	90	$C_{24}H_{15}ClN_8$	63.93	3.35	24.85	--	7.86
			(450.89)	63.70	3.61	24.71	--	7.66
7g	304	87	$C_{25}H_{17}ClN_8O$	62.43	3.56	23.30	--	7.37
			(480.91)	62.81	3.60	23.01	--	7.24
7h	>300	85	$C_{25}H_{15}ClN_5O_2$	60.67	3.05	22.64	--	7.16
			(494.9)	60.52	3.27	22.14	--	7.01
8a	280	86	$C_{18}H_9ClN_8$	57.99	2.43	30.05	--	9.51
			(372.77)	57.95	2.82	29.20	--	9.32
8b	>300	57	$C_{18}H_9ClN_8S$	53.40	2.24	27.68	7.92	8.75
			(404.83)	53.81	2.44	27.70	7.42	8.44

compounds **6b** and **6d** reacts with hydrazine hydrate and gives the 6-hydrazinotriazine **7d**. Compound **7d** undergoes condensation with aromatic aldehydes and the corresponding hydrazones **7e-h** are obtained.

In a similar procedure to that described for the cyclocondensation of 3-hydrazino-1,2,4-triazino[6,5-*f*]benzo[*h*]-quinoline with formic acid and with carbon disulfide [10], we found that the cyclocondensation of the hydrazino compound **7d** with formic acid and with carbon disulfide gives the triazolotriazine **8a** and the mercaptotriazolotriazine **8b** respectively.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra (potassium bromide) were recorded with a Unicam SP 1200 infrared spectrophotometer.

1-(*o*-Chlorophenylazo)-2-aminonaphthalene (**1**).

Compound **1** was prepared by a procedure similar to that described in the literature [12]. To *o*-chloroaniline (6.3 g) was added concentrated hydrochloric acid (12.5 ml) followed by water (12.5 ml). The solution was cooled and diazotized by portionwise addition of aqueous sodium nitrite solution (3.55 g in 6 ml water), keeping the temperature below 5°. The reaction mixture was, then added to a warm solution (40°) of *B*-naphthylamine (7.15 g) and crystalline sodium acetate (2.25 g) in ethanol (50 ml). The red precipitate formed was collected and recrystallized from ethanol into red needles of compound **1** (Table).

2-*o*-Chlorophenyl-2*H*-naphtho[1,2-*d*]-*v*-triazole]-4,5-quinone (**3**).

The quinone **3** was prepared after a procedure similar to that described in the literature [11]. A solution of chromium trioxide (7.0 g) in glacial acetic acid (100 ml) was added, portionwise, to a solution of compound **1** (5.6 g) in a mixture of glacial acetic acid (50 ml) and acetic anhydride (30 ml) keeping the temperature at 40-50°. The temperature was raised to 90° and chromium trioxide (18 g) was added portionwise keeping the

temperature at 90-100°. The reaction mixture was then heated (water-bath) for 30 minutes, allowed to stand at room temperature for 1 hour and poured into ice-cold water (1 l). The precipitate formed was filtered with suction, washed several times with water and dried (3.75 g). This was crystallized from acetic acid into yellow crystals of compound **3** (Table).

2-*o*-Chlorophenylbenzo[*c*]-*v*-triazolo[4,5-*a*]phenazine (**4**).

A mixture of the quinone **3** (0.31 g) and *o*-phenylenediamine (0.11 g) in acetic acid (5 ml) was heated under reflux for 3 minutes. After cooling, the precipitate was filtered with suction and recrystallized from acetic acid in pale brown crystals of compound **4** (Table).

2-*o*-Chlorophenyl-2*H*-naphtho[1,2-*d*]-*v*-triazole-4,5-quinone 4-Monosemicarbazone (**5a**).

A solution of the quinone **3** (3.1 g) and semicarbazide hydrochloride (1.1 g) in acetic acid (10 ml) was heated under reflux for 30 minutes. The reaction mixture was cooled and the product was filtered and recrystallized from butanol as yellow crystals of **5a** (Table).

2-*o*-Chlorophenyl-2*H*-naphtho[1,2-*d*]-*v*-triazole-4,5-quinone 4-Monothiosemicarbazone (**5b**).

A solution of the quinone **3** (3.1 g) and thiosemicarbazide (0.91 g) in acetic acid (10 ml) was heated under reflux for 20 minutes. The reaction mixture was cooled and the product **5b** was filtered and recrystallized from nitrobenzene as brown crystals (Table).

2-*o*-Chlorophenyl-6-hydroxybenzo[*f*]-*v*-triazolo[4,5-*h*]benzo[*e*]-*as*-triazine (**6a**).

The monosemicarbazone **5a** (2.0 g) and aqueous potassium hydroxide (100 ml, 5%) was heated under reflux for 1 hour. The reaction mixture was then cooled in ice and acidified with hydrochloric acid. The precipitate formed was filtered and recrystallized from acetic acid as golden yellow crystals of **6a** (Table).

2-*o*-Chlorophenyl-6-mercaptobenzo[*f*]-*v*-triazolo[4,5-*h*]benzo[*e*]-*as*-triazine (**6b**).

The monothiosemicarbazone **5b** (1.4 g) and aqueous potassium hydroxide (100 ml, 5%) was heated under reflux for 30 minutes. The reaction mixture was cooled and acidified with hydrochloric acid. The precipitate formed was filtered and recrystallized from dimethylformamide as dark red crystals of **6b** (Table).

2-*o*-Chlorophenyl-6-aminobenzo[*f*]-*v*-triazolo[4,5-*h*]benzo[*e*]-*as*-triazine (**6c**).

A mixture of the quinone **3** (3.1 g) and aminoguanidine bicarbonate (1.35 g) in acetic acid (10 ml) was heated under reflux for 3 hours. The reaction mixture was cooled and the product **6c** was filtered and recrystallized from pyridine into pale yellow crystals (Table).

2-*o*-Chlorophenyl-6-chlorobenzo[*f*]-*v*-triazolo[4,5-*h*]benzo[*e*]-*as*-triazine (**6d**).

A mixture of compound **6a** (3.5 g) and phosphorus oxychloride (5 ml) was heated at 140° for 1½ hours. The reaction mixture was cooled and poured over crushed ice. The precipitate formed was filtered, washed with water, then with aqueous sodium bicarbonate solution (50%), and again with water. It was then recrystallized from acetic acid into yellow crystals of compound **6d** (Table).

2-*o*-Chlorophenyl-6-arylaminobenzo[*f*]-*v*-triazolo[4,5-*h*]benzo[*e*]-*as*-triazines **7a-c**.

A mixture of compound **6d** (0.75 g) and the appropriate amine (1.5 g) was heated under reflux for 5 minutes. The reaction mixture was then cooled, washed with alcohol and filtered. Recrystallization from dimethylformamide afforded the products **7a-c** in yellow, orange and dark yellow crystals respectively (Table).

2-*o*-Chlorophenyl-6-hydrazinobenzo[*f*]-*v*-triazolo[4,5-*h*]benzo[*e*]-*as*-triazine (**7d**).

Method (i).

A mixture of the mercaptotriazine **6b** (3.0 g) and hydrazine hydrate (5 ml, 99%) was heated under reflux for 40 minutes. After cooling the reaction mixture was poured over water (25 ml). The precipitate was filtered with suction, washed well with water and recrystallized from pyridine in yellow crystals of compound **7d** (Table).

Method (ii).

A mixture of compound **6d** (1.0 g) and hydrazine hydrate (3 ml, 99%) was heated under reflux for 30 minutes. The reaction mixture was cooled and poured over water (20 ml). The precipitate formed was collected and recrystallized from pyridine as yellow crystals (yield *ca.* 74%) identical with compound **7d** obtained from method (i), mp and mixed mp with the compound obtained from method (i) showed no depression.

Action of Aromatic Aldehydes on Compound **7d**.

A mixture of compound **7d** (0.002 mole) and each of *p*-chlorobenzaldehyde, benzaldehyde, *p*-methoxybenzaldehyde and piperonal (0.002 mole) in ethanol (20 ml) was heated under reflux for 45 minutes. After cooling, the precipitate was filtered and recrystallized from dimethylformamide into orange crystals of **7e-h** respectively (Table).

6-*o*-Chlorophenylbenzo[*f*]-*v*-triazolo[4,5-*h*]-*s*-triazolo[4,3-*b*]benzo[*e*]-*as*-triazine (**8a**).

A mixture of compound **7d** (0.75 g) and formic acid (3 ml, 85%) was heated under reflux for 5 hours. The reaction mixture was then cooled and poured over crushed ice, and the precipitate was filtered with suction and recrystallized from dimethylformamide into yellow crystals of **8a** (Table).

6-*o*-Chlorophenyl-3-mercaptobenzo[*f*]-*v*-triazolo[4,5-*h*]-*s*-triazolo[4,3-*b*]-benzo[*e*]-*as*-triazine (**8b**).

To compound **7d** (0.75 g) was added pyridine (5 ml) followed by carbon disulfide (0.5 ml). The reaction mixture was heated under reflux for 1½ hours. It was then cooled, and the reddish brown precipitate was filtered and recrystallized from dimethylformamide into reddish brown crystals of **8b** (Table).

REFERENCES AND NOTES

[1] T. Zsolnai, *Biochem. Pharmacol.*, **11**, 995 (1962); *Chem. Abstr.*, **58**, 837g (1963).

[2] P. Mantegazza, R. Tommasini, R. Fusco and S. Rossi, *Arch. Int. Pharmacodyn.*, **95**, 123 (1953); *Chem. Abstr.*, **48**, 3548 (1954).

[3] E. L. Dalang and E. O. Stapley, *Appl. Microbiol.*, **7**, 276 (1959); *Chem. Abstr.*, **54**, 6871 (1960).

[4] M. Jauttelat, K. Ley and L. Eue, German Offen. 2,236,340 (Feb. 7, 1974); *Chem. Abstr.*, **80**, 108583h (1974).

[5] K. Dickore and L. Eue, German Offen. 1,965,739 (July 8, 1971); *Chem. Abstr.*, **75**, 129842d (1971).

[6] K. Wasti and M. M. Joullie, *Heterocycles*, **4**, 1341 (1976).

[7] K. Wasti and M. M. Joullie, *J. Chem. Soc., Perkin Trans. I.*, 2521 (1976).

[8] L. C. March, G. S. Bajwa, J. Lee, K. Wasti and M. M. Joullie, *J. Med. Chem.*, **19**, 845 (1976).

[9] A. K. Mansour, S. B. Awad and S. Antoun, *Z. Naturforsch.*, **29b**, 792 (1974).

[10] M. M. Eid, M. A. Badawy and Y. A. Ibrahim, *J. Heterocyclic, Chem.*, **20**, 1255 (1983).

[11] G. Charrier and A. Manfredi, *Gazz. Chim. Ital.*, **56**, 196 (1926); *Chem. Abstr.*, **20**, 2859 (1926).

[12] R. Meldola and M. O. Forster, *J. Chem. Soc.*, **59**, 678 (1891).