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The Reaction of Biguanides and Related Compounds. XI.[1] The Interaction of Ethylene Carbonates with Arylbiguanides and Related Compounds.

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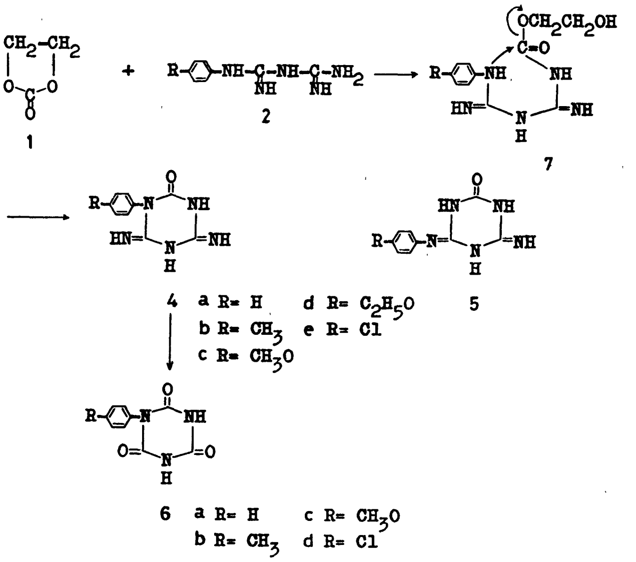
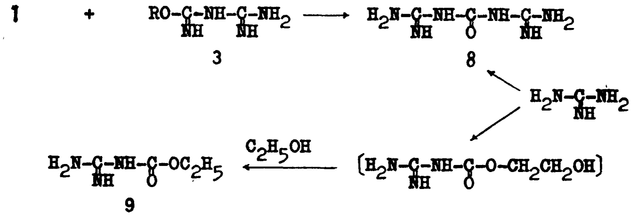
Synopsis. The treatment of arylbiguanides with ethylene carbonates afforded 1-aryl-4,6-diimino-2-oxo-hexahydro-*s*-triazines, which were then readily converted into 1-arylisocyanuric acid by hydrolysis with concentrated hydrochloric acid.

A number of previous workers have shown that the addition of carboxylic esters, ketones, and aldehydes to biguanides is followed by the immediate cyclization of the intermediates to amino-*s*-triazines.[2] In continuation of our investigation on the cyclization of systems containing carbonyl groups to biguanides and its homologues, we examined the behavior of ethylene carbonates (**1**) toward arylbiguanides (**2**) and *N*-amidino-*O*-alkylisoureas (**3**).

When **1a** and **2** were heated in ethanol or, preferably, allowed to stand in dimethylformamide (DMF), a product was yielded in a comparatively good yield. The same product was also obtained by treating **1b** with **2** under similar conditions. This result obviously indicates that the ethylene moiety originating from **1a** is not retained in the molecule of the product. The mass spectrum of the product exhibited a strong molecular ion peak corresponding to that of the condensation product of molecular equivalents of **1a** and **2**, with the elimination of ethylene glycol. The infrared (IR) spectrum showed the absorptions assignable to amino and imino groups in the regions of 3450 and 3260 cm^{-1} and that due to a carbonyl group near 1680 cm^{-1}. These results suggest that the products are 2-oxo-hexahydro-*s*-triazines, though two isomeric structures, 1-aryl-4,6-diimino-2-oxo-hexahydro-*s*-triazine (**4**) and 2-arylimino-4-imino-6-oxo-hexahydro-*s*-triazine (**5**), due to the orientation of the cyclization are possible. Although support for **4** was provided by observing the fragment-ion peak probably arising from the arylisocyanate ion formed by the decomposition of the molecular ion in the mass spectrum, a distinction between **4** and **5** on the basis of the results of elemental analyses and the spectral data alone is impossible. In order to elucidate the structure, the product was hydrolyzed with hydrochloric acid to give 1-arylisocyanuric acid



Scheme 1.



Scheme 2.

TABLE 1. 1-ARYL-4,6-DIIMINO-2-OXO-HEXAHYDRO-*s*-TRIAZINE (**4**)

Compd.	Yield (%)		Mp (°C)	Formula	Analysis % Found (Calcd)		
	in EtOH	in DMF			C	H	N
4a	70	74	>360	$C_9H_9ON_5$	52.86 (53.19)	4.61 (4.46)	34.43 (34.47)
4b	84	91	349—350	$C_{10}H_{11}ON_5$	55.06 (55.29)	5.45 (5.10)	31.98 (32.24)
4c	74	89	348—349	$C_{10}H_{11}O_2N_5$	51.82 (51.49)	5.08 (4.75)	29.79 (30.03)
4d	58	63	350—351	$C_{11}H_{13}O_2N_5$	53.02 (53.43)	5.40 (5.30)	28.23 (28.33)
4e	38	39	>360	$C_9H_8ON_5Cl$	45.85 (45.48)	3.54 (3.39)	29.44 (29.47)

Table 2. 1-arylisocyanuric acid (**6**)

Compd.	Yield (%)	Mp (°C)	Formula	Analysis % Found (Calcd) C	H	N
6a	35	307—308	$C_9H_7O_3N_3$	52.43	3.21	20.52
				(52.68)	(3.44)	(20.48)
6b	71	300—301	$C_{10}H_9O_3N_3$	54.86	4.36	18.59
				(54.79)	(4.14)	(19.17)
6c	30	269—270	$C_{10}H_9O_4N_3$	51.04	4.13	17.35
				(51.06)	(3.86)	(17.85)
6d	60	301—302	$C_9H_6O_3N_3Cl$	44.63	2.70	17.49
				(45.11)	(2.52)	(17.53)

(**6**).[3] The IR spectrum of **6** exhibited the characteristic three absorption bands assignable to the carbonyl groups in the region of 1700—1800 cm^{-1}, and the mass spectrum showed the molecular ion as the most abundant peak. Detailed data on **4** and **6** are summarized in Tables 1 and 2.

The formation of **4** probably proceeds step by step as follows: the initial addition of **2** to **1a** may occur theoretically at the central (N^3) or at the equivalent terminal nitrogen atom (N^5), of which only the latter case is capable of yielding *s*-triazine on cyclization. The N^3 atom is inactive, and the nucleophilic attack of this nitrogen is unknown. The interaction of the ester carbonyl group in the intermediate (**7**) would occur rapidly with the N^1 atom rather than with the N^2 atom or more **2**, giving **4**, but not **5** or a bis-compound. The formation of the acyl intermediate, **7**, in the reaction of **2** with carboxylic esters was suggested by Overberger[4] and Shapiro,[5] and elucidated by us.[6]

The reaction of **1a** with **3** is also expected to undergo cyclization to *s*-triazines. However, no formation of any of the *s*-triazines anticipated was observed. The heating of equimolar quantities of **1a** and **3** in ethanol unexpectedly gave *N,N′*-carbonyl-*bis*-guanidine (**8**), whose structure was established by a comparison of it with an authentic sample prepared from **1a** and guanidine.

The IR spectrum of **8** showed the strong absorption assignable to a carbonyl group at 1660 cm^{-1}, and the absorption pattern was quite similar to that of guanidine. Compound **8** would be formed by the reaction of **1a** with the guanidine formed by the decomposition of **3**. The facile decomposition of **3** to guanidine was practically observed. The heating of equimolar quantities of **1a** and guanidine in ethanol also gave a low yield of **8**, as had been expected. On the other hand, when **1a** was treated with one-half equivalent amount of guanidine, a mixture of **8** and ethyl guanidinocarboxylate (**9**)[7] was obtained in a low yield. Compound **9** would be formed by the ester exchange of an intermediate β-hydroxyethyl guanidinocarboxylate with the ethanol used as the solvent. The conversion of **9** to **8** was also observed upon heating with guanidine in ethanol.

Experimental

1-Aryl-4,6-diimino-2-oxo-hexahydro-s-triazine (4). General Procedure: 1) A mixture of arylbiguanide (4 mmol) and ethylene carbonate (4 mmol) in ethanol (20 ml) or in DMF (1 ml) was refluxed for 2 hr or allowed to stand for a few days at room temperature respectively. The precipitates thus deposited were collected by filtration upon cooling. Purification was carried out by neutralizing a solution of the precipitates in an aqueous sodium hydroxide solution with dilute hydrochloric acid. The detailed data are summarized in Table 1. 2) A solution of arylbiguanide (4 mmol) and propylene carbonate (4 mmol) in ethanol (20 ml) was heated for 2 hr under reflux. The precipitates thus deposited were collected by filtration while hot. The precipitates were identified with an authentic sample prepared by Procedure 1 by means of a mixed-melting-point determination and by a comparison of the IR spectra.

1-Arylisocyanuric Acid (6). General Procedure: A suspension of 1-aryl-4,6-diimino-2-oxo-hexahydro-*s*-triazine (2 mmol) in concentrated hydrochloric acid (10 ml) was heated for 12 hr under reflux. The suspended solid was gradually dissolved, and the precipitates were newly separated. The precipitates were collected by filtration while hot and washed with dilute hydrochloric acid. The detailed data are summarized in Table 2.

N,N′*-Carbonyl-bis-guanidine (8).* Into a solution of sodium ethoxide (0.34 g, 5 mmol) in ethanol (20 ml), we stirred *N*-amidino-*O*-alkylisourea hydrochloride (5 mmol). The precipitates were then filtered off, and ethylene carbonate (0.44 g, 5 mmol) was added to the filtrate. The mixture was heated for 2 hr, and the precipitates thus deposited were collected by filtration. Recrystallization from dilute ethanol gave a 40% yield of colorless prisms; mp>360 °C. Found: C, 21.99; H, 6.67; N, 50.69. Calcd for $C_3H_8ON_6H_2O$: C, 22.22; H, 6.22; N, 51.21. The same compound was also obtained in a 50% yield by the reaction of ethylene carbonate with an excess of guanidine and in a 70% yield by the treatment of guanidine with ethyl guanidinocarboxylate.

Ethyl Guanidinocarboxylate (9). A solution of guanidine (0.30 g, 5 mmol) and ethylene carbonate (0.88 g, 10 mmol) in ethanol (10 ml) was refluxed for 4 hr and then concentrated. The precipitates (0.02 g, 5.8%) of *N,N′*-carbonyl-bis-guanidine were filtered off, and the filtrate was evaporated by distillation and then allowed to stand overnight to give colorless prisms (0.05 g, 6.7%) melting at 93—95 °C.

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