Reaction of *N*-Cyanoformimidates with some Heterocyclic Compounds. A New Synthesis of 5-Azaadenine and Related Compounds (1)

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3-Amino-1,2,4-triazoles and 2-aminobenzimidazole were reacted with *N*-cyanoimidates to give 5-amino-1,2,4-triazolo[2,3-*a*]-1,3,5-triazines (5-azaadenines) and 4-aminobenzimidazo[1,2-*a*]-1,3,5-triazines, respectively. The structures of the compounds obtained were confirmed through the comparison with some of the possible isomers prepared by independant methods.

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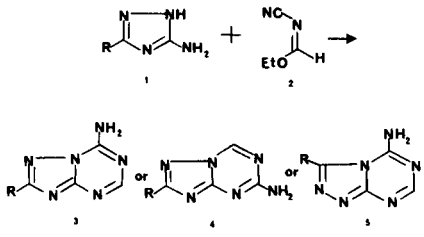
Ethyl *N*-cyanoformimidate (**2**) has been shown to interact with molecules incorporating an amidine moiety to give 1,3,5-triazine derivatives (3-8).

In connection with a research program in the synthesis of polyheterocyclic compounds (9-11), the synthesis and structure elucidation of 5-amino-1,2,4-triazolo[2,3-*a*]-1,3,5-triazines (5-azaadenines) (**3a-d**) and 4-aminobenzimidazo-[1,2-*a*]-1,3,5-triazines (**6a-c**) was attempted. 3-Amino-1,2,4-triazole and its 5-substituted derivatives (**1**) and 2-aminobenzimidazole (**5**) were chosen as model molecules having amidine structures.

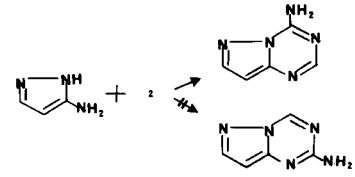
The reaction of 1,2,4-triazoles and *N*-cyanoformimidates in methanol gave compounds which were subjected to elemental analysis as well as ir, nmr and mass spectroscopy. The results corresponded to 5-amino-1,2,4-triazolo-[2,3-*a*]-1,3,5-triazines (**3**), 7-amino-1,2,4-triazolo[2,3-*a*]-1,3,5-triazines (**4**) or 5-amino-1,2,4-triazolo[4,3-*a*]-1,3,5-triazines (**5**) (Scheme I).

Scheme I



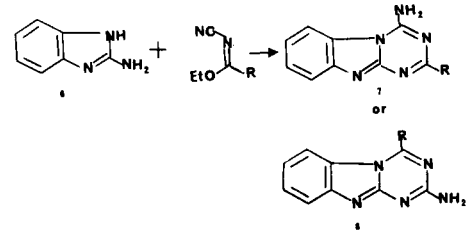
The compound obtained was found to be identical with 5-amino-1,2,4-triazolo[2,3-*a*]-1,3,5-triazine (5-azaadenine) (**3a**) prepared according to the method of Taylor and Hendess (12). Involvement of N2 of 1,2,4-triazole in the ring formation leading to the compounds **3** could be attributed to its greater basicity as a result of being adjacent to a nitrogen atom. Whereas, the N4 which would afford the compound **5** is deactivated by the neighboring unsaturated electron deficient carbon atom. Formation of compounds **3** *versus* compounds **4** is also in good agreement with the recent work of *Tam, et al.*, in a similar reaction with 3-aminopyrazole (8) (Scheme II).

Scheme II



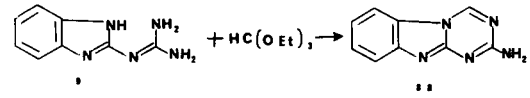
In a similar reaction, 2-aminobenzimidazole (**6**) and *N*-cyanoimidates (**2**) were reacted in refluxing 1,2-dimethoxyethane and gave a series of aminobenzimidazo[1,2-*a*]-1,3,5-triazines, which would have the structures **7** or their isomers **8**. (Scheme III).

Scheme III



The structure elucidation was achieved by the independant synthesis of the compounds **8a** and **8c** and comparison with the corresponding compounds obtained in the above reaction. The compound **8a** (R = H) was synthesized by the reaction of 2-guanylbenzimidazole (**9**) (12) with ethyl orthoformate (Scheme IV).

Scheme IV



The compound **8c** (R = Ph) was prepared according to the method of Capuano *et al.* (13).

The structures of the compounds prepared were confirmed by elemental analysis, nmr, ir and mass spectroscopy. Mass spectral data of the compounds prepared are reported in Table III.

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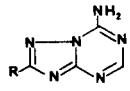
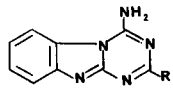
Table I



Compound No.	R	M.p. °C	Yield %	Formula	Analyses C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found
3a	H	320 dec (a)	93	$C_4H_4N_6$	35.29	35.08	2.94	2.91	61.76	62.01
3b	Me	276-278	70	$C_5H_6N_6$	40.00	40.21	4.00	3.96	56.00	56.36
3c	Et	219-223	66	$C_6H_8N_6$	43.90	44.15	4.87	4.90	51.21	51.26
3d	Ph	290-293	78	$C_{10}H_8N_6$	56.60	56.43	3.77	3.80	39.62	39.70

(a) Lit. (12) m.p. 320 dec.

Table II



Compound No.	R	M.p. °C	Yield %	Formula	Analyses C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found
7a	H	296-298 (a)	68	$C_9H_7N_5$	58.37	58.50	3.78	3.76	37.83	37.89
7b	Me	293-295 (b)	73	$C_{10}H_9N_5$	60.30	60.22	4.52	4.80	35.17	35.40
7c	Ph	> 300 (c)	71	$C_{15}H_{11}N_5$	68.96	68.74	4.21	4.11	26.81	27.03

(a) Ir (potassim bromide): ν max 3120, 1660, 1540 and 1210 cm^{-1}. (b) Nmr (trifluoroacetic acid): δ 7.65-8.22 (m, 4H, aromatics), 2.63 (s, 3H, $CH_3$8). (c) Ir (potassium bromide): ν max 3120, 1660, 1560, 1580 and 980 cm^{-1}.

Table III

Mass m/e (relative intensity)

Compound No.	
3a	M^+ 136 (100), M-CHN 109 (43), M-CHN_2 95 (65), M-C_2N_2 84 (50)
3b	M^+ 150 (100), M-CHN 123 (26), M-CH_2N_2 108 (33)
3c	M^+ 164 (100), M-N_2 136 (23), M-CH_2N_2 122 (55)
3d	M^+ 212 (100), M-CHN_2 171 (17), M-$C_4H_3N_6$ (C_6H_5), 77 (10)
7a	M^+ 185 (100), M-CHN 158 (27), M-CH_2N_2 143 (65)
7b	M^+ 199 (100), M-CN_2 159 (34)
7c	M^+ 261 (100), M-CH_2N_2 219 (34), M-C_6H_5CN 158 (87)
8a	M^+ 185 (100), M-CHN 158 (70), M-CH_2N_2 143 (22)
8c	M^+ 261 (100), M-CH_2N_2 219 (22), M-C_6H_5CN 158 (12)

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover apparatus and are uncorrected. Ir spectra were recorded using a Perkin-Elmer 267 spectrograph. Nmr and mass spectra were run on Varian T-60 and Ms-311 instruments.

5-Amino-1,2,4-triazolo[2,3-*a*]-1,3,5-triazine (5-Azaadenine) (**3a**).

A mixture of 1.76 g. (0.02 mole) of 2-amino-1,2,4-triazole (**1**) and 3.92 g. (0.04 mole) of ethyl *N*-cyanoformimidate (**2**) in 30 ml. of methanol was refluxed for 1 hour. After cooling, the white precipitate was filtered and recrystallized from water to give a white microcrystalline powder, 2.53 g. (93%) m.p. > 320° dec [lit. (10) m.p. > 320° dec]. The physical and spectroscopic properties of the compound **3** obtained were identical with those of a sample prepared by an independant method (10).

Compounds **3b-d** were prepared similarly. The physical properties of the compounds **3a-d** are listed in Tables I and III.

4-Aminobenzimidazo[1,2-*a*]-1,3,5-triazine (**7a**).

A mixture of 1.33 g. (0.01 mole) of 2-aminobenzimidazole (**6**) and 1.96 g. (0.02 mole) of ethyl cyanoformimidate in 15 ml. of dimethoxyethane was refluxed for ½ hour. After cooling, the white precipitate was filtered and recrystallized from dimethyl formamide to give 1.25 g. (68%) of **7a**. Compounds **7b** and **7c** were prepared similarly using methyl cyanoformimidate and phenyl cyanoformimidate respectively. The physical properties of compounds **7** are reported in Tables II and III.

2-Aminobenzimidazo[1,2-*a*]-1,3,5-triazine (**8a**).

A mixture of 1.75 g. (0.01 mole) 2-guanylbenzimidazole (13) and 5 ml. of triethyl orthoformate was refluxed for 3 hours. After cooling, the white precipitate was washed with ether and recrystallized from dimethylformamide to give 1.23 g. (67%) of **8a** ir (potassium bromide): ν max 3160, 1680, 1610, and 1180. For mass spectrum see Table II.

Anal. Calcd. for $C_9H_7N_5$: C, 58.37; H, 3.78; N, 37.83. Found: C, 58.42; H, 3.80; N, 38.01.

REFERENCES AND NOTES

(1) This work was partly presented at the 7th International Congress of Heterocyclic Chemistry, August 12-17, 1979, Tampa, Florida, USA.

(2) Research associate, Department of Chemistry, College of Pharmacy, Tehran University, Tehran, Iran.

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