Oxidative Cyclization of Methylglyoxal Bis(aroylhydrazones) to Substituted 1,2,3-Triazoles

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Bis(aroylhydrazones) of 1,2-dicarbonyl compounds have been known to undergo oxidation with iodine and yellow mercuric oxide to give cyclic products ascribed, at that time, 1,2,3,4-dihydrotetrazine structures (3,5). Later, however, these products were assigned 1-substituted amino-1,2,3-triazole structures on the basis of their ir and nmr spectral data (6-10).

Pursuing our study on the reaction of hydrazones (7-11), we ahve prepared a number of methylglyoxal bis-(aroylhydrazones) (I) and converted them by oxidative cyclization into 1-α-aroyloxyarylideneamino-4-methyl-1,2,3-triazoles (II).

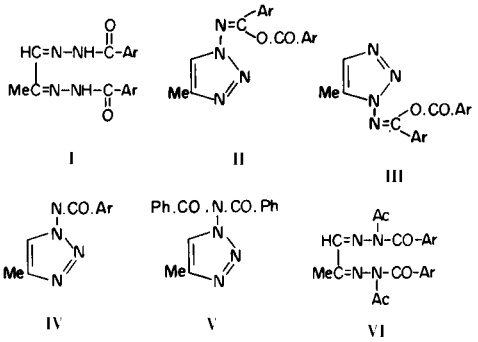
Methylglyoxal was condensed with two equivalents of aroylhydrazines to give the corresponding bis(aroylhydrazones) (I). Ir spectra of these compounds showed the characteristic amide-I bands of the aroylhydrazone residues at 1650-1673 cm^{-1} (see Table II). Their uv spectra showed two absorption maxima at 209-214 and 315-323 nm, which were only little affected by the substituent on the aroylhydrazone residue, and a third maximum at 225-255 nm which seems to be influenced by such a substitution. Unlike methylglyoxal bis(arylhydrazones) which are yellow to orange in color, methylglyoxal bis(aroylhydrazones) are colorless.

Oxidation of I with iodine and yellow mercuric oxide gave products (II) with two hydrogens less than the parent bis(hydrazones). Ir spectra of the oxidation products revealed strong C=N and ester absorption bands at 1635-1640 and 1735-1750 cm^{-1} respectively and no amide or NH bands.

On the basis of previous work, these products may be formulated as 1,4- (II) (7-10,12,13) or 1,5-disubstituted 1,2,3-triazoles (III). Curtin and Alexandrou (6) assigned a 1,5-disubstituted 1,2,3-triazole structure (III) for the oxidation product of methylglyoxal bis(benzoylhydrazone). However, there was no conclusive evidence that the oxidation product is the 1,5- and not acutally the 1,4-disubstituted 1,2,3-triazole.

Treatment of II with methanolic ammonia gave the expected 1-aroylamino-4-methyl-1,2,3-triazole (IV) through the alkaline hydrolysis of the enol ester group. Ir spectra of IV revealed the disappearance of the ester band of their precursors II with concomitant absorption at 1660-1695 cm^{-1} due to the newly formed amide function.

Thermal isomerization of II (Ar = Ph) by heating above its melting point afforded a product having the same physical constants as those recorded in literature (4) but is now assigned the structure of 1-(*N,N*-dibenzoylamino)-4-methyl-1,2,3-triazole (V). The isomerization occurs through a 1,3-migration of the enol benzoate group.



I II III IV V VI

We have also investigated the action of boiling acetic anhydride on the prepared methylglyoxal bis(aroylhydrazones) and in all cases we have obtained the corresponding bis(*N*-acetyl-*N*-aroylhydrazones) (VI).

Attempted benzoylation of the hydrazone iminoprotons of I with benzoyl chloride and pyridine either at room temperature or at 100° for several hours, failed giving the unchanged bis(hydrazones).

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Ir spectra were recorded with a Unicam SP-200 spectrophotometer for potassium bromide pellets and uv absorption spectra with a Unicam SP 800 spectrophotometer for ethanolic solutions. Homogeneity of the compounds were checked by tlc on silica gel plates (layer thickness 0.25 mm) in benzene-methanol of different ratios depending on the polarity of the compound. Spots were detected by spraying with 20% sulphuric acid followed by heating on a hot plate for few minutes.

Methylglyoxal Bis(aroylhydrazones) (I) (Table I).

A solution of methylglyoxal (1 g.) in methanol (10 ml.) was

TABLE I

Compound No.	R	M.p.	Calcd. C	H	N	Formula	Found C	H	N
			Methylglyoxal Bis(aroylhydrazones) (I)						
1	C_6H_4	253 (a)	64.4	5.4	17.6	$C_{17}H_{16}N_4O_2$	64.6	5.2	17.2
2	*m*-$CH_3C_6H_4$	247 (a)	67.8	6.0	16.7	$C_{19}H_{20}N_4O_2$	67.8	6.0	16.3
3	*p*-$CH_3C_6H_4$	264 (a)	67.8	6.0	16.7	$C_{19}H_{20}N_4O_2$	68.0	6.1	16.3
4	*p*-$CH_3OC_6H_4$	266 (a)	59.1	5.7	14.5	$C_{19}H_{20}N_4O_4.H_2O$	58.8	5.3	14.2
5	*m*-ClC_6H_4	254 (a)	54.1	3.7	14.8	$C_{17}H_{14}Cl_2N_4O_2$	54.5	3.8	14.9
6	*p*-ClC_6H_4	259 (a)	54.1	3.7	14.8	$C_{17}H_{14}Cl_2N_4O_2$	54.5	3.9	14.5
			1-α-Aroyloxyarylideneamino-4-methyl-1,2,3-triazoles (II)						
7	C_6H_4	124	66.7	4.6	18.3	$C_{17}H_{14}N_4O_2$	66.6	4.4	18.0
8	*m*-$CH_3C_6H_4$	106	68.2	5.4	16.8	$C_{19}H_{18}N_4O_2$	68.2	5.6	16.9
9	*p*-$CH_3C_6H_4$	146	68.2	5.4	16.8	$C_{19}H_{18}N_4O_2$	68.5	5.6	16.5
10	*p*-$CH_3OC_6H_4$	153	62.3	5.0	15.3	$C_{19}H_{18}N_4O_4$	62.5	4.8	15.3
11	*m*-ClC_6H_4	110	54.4	3.2	14.9	$C_{17}H_{12}Cl_2N_4O_2$	54.1	3.1	14.9
12	*p*-ClC_6H_4	208	54.4	3.2	14.9	$C_{17}H_{12}Cl_2N_4O_2$	54.7	3.3	15.2
			1-Aroylamino-4-methyl-1,2,3-triazoles (IV)						
13	C_6H_4	158	59.4	5.0	27.7	$C_{10}H_{10}N_4O$	59.6	5.0	27.5
14	*m*-$CH_3C_6H_4$	168	61.1	5.6	25.9	$C_{11}H_{12}N_4O$	61.1	5.6	25.9
15	*p*-$CH_3C_6H_4$	160	61.1	5.6	25.9	$C_{11}H_{12}N_4O$	61.4	5.3	26.0
16	*p*-$CH_3OC_6H_4$	220	56.9	5.2	24.1	$C_{11}H_{12}N_4O_2$	56.9	5.4	24.4
17	*m*-ClC_6H_4	120	50.7	3.8	23.8	$C_{10}H_9ClN_4O$	51.0	4.1	24.9
18	*p*-ClC_6H_4	159	50.7	3.8	23.8	$C_{10}H_9ClN_4O$	50.9	4.0	23.9
			Methylglyoxal Bis(*N*-acetyl-*N*-aroylhydrazones) (VI)						
19	C_6H_4	156	64.3	5.1	14.3	$C_{21}H_{20}N_4O_4$	64.3	5.3	14.3
20	*p*-$CH_3C_6H_4$	160	65.7	5.8	13.3	$C_{23}H_{24}N_4O_4$	65.8	5.5	13.6
21	*p*-$CH_3OC_6H_4$	168	61.0	5.4	12.4	$C_{23}H_{24}N_4O_4$	60.9	5.2	12.1
22	*m*-ClC_6H_4	141	52.5	4.3	11.7	$C_{21}H_{18}Cl_2N_4O_4.H_2O$	52.4	4.6	11.9
23	*p*-ClC_6H_4	219	54.7	3.9	12.1	$C_{21}H_{18}Cl_2N_4O_4$	54.7	3.9	12.1

(a) Melts with decomposition.

heated with a solution of the required amount of the appropriate aroylhydrazine in methanol (20 ml.) and a few drops of acetic acid and heated on a water-bath for 30 minutes. After cooling, the bis(hydrazone), which separated, was filtered off and crystallized from 1:1 benzene-ethanol mixture. The bis(hydrazones) are sparingly soluble in methanol and ethanol and insoluble in ether. They gave greenish-brown colorations with neutral ferric chloride solution and stable green copper complexes with cupric chloride.

1-α-Aroyloxyarylideneamino-4-methyl-1,2,3-triazoles (II) (Table I).

A solution of the methylglyoxal bis(aroylhydrazone) (I, 1 g.) in dry ether (100 ml.) was treated successively with mercuric oxide (1.5 g.), magnesium oxide (0.15 g.), and iodine (0.75 g.) and kept at room temperature for 72 hours. The ethereal solution was filtered and the inorganic residue was extracted repeatedly with chloroform. The ethereal solution and chloroform extract were washed with potassium iodide solution followed by sodium thiosulphate solution and water, and then dried (sodium sulfate). Evaporation of the solvents yielded the products which crystallized from dilute methanol.

1-Aroylamino-4-methyl-1,2,3-triazoles (IV) (Table I).

A solution of 1-α-aroyloxyarylideneamino-4-methyl-1,2,3-triazole (II) (1 g.) in methanol (100 ml.) was treated with 20% ammonia solution (10 ml.) and left at room temperature for 48 hours. The solution was evaporated and the residue was crystallized from methanol.

1-(*N*,*N*-Dibenzoylamino)-4-methyl-1,2,3-triazole (V).

1-α-Benzoyloxybenzylideneamino-4-methyl-1,2,3-triazole (II, Ar = Ph) (1 g.) in a dry test tube was heated at 140° for two hours. The melt was left to attain room temperature and then triturated with methanol (5 ml.). The crystalline product was filtered and recrystallized from methanol to give plates, m.p. 134-135° (yield, 82%), [lit. (6), m.p. 134°]; ν max (potassium bromide): 1730 (amide-I); λ max (ethanol): 242 nm (log ε, 4.2458).

Anal. Calcd. for $C_{17}H_{14}N_4O_2$: C, 66.7; H, 4.6; N, 18.3. Found: C, 66.5; H, 4.7; N, 18.1.

Methylglyoxal Bis(*N*-acetyl-*N*-aroylhydrazones) (VI) (Table I).

Methylglyoxal bis(aroylhydrazones) (I) (1 g.) was treated with

TABLE II

Infrared and Ultraviolet Absorption Data

Compound No.	λ max (Potassium bromide) cm^{-1}		λ max (Ethanol) nm			log ε		
	CONH	NH						
1	1673	3240	209	240	315	4.19	4.24	4.53
2	1660	3250	211	243	315	4.32	4.25	4.63
3	1665	3250	210	255	318	4.16	4.29	4.49
4	1660	3300	210	255	323	4.35	4.37	4.66
5	1650	3200	214	238	317	4.22	4.18	4.46
6	1660	3230	210	250	318	4.20	4.33	4.48
	CO.O							
7	1735		242	280		4.70	4.22	
8	1735		215	263		3.80	3.99	
9	1735		226	263		4.07	4.18	
10	1740		224	275		4.18	4.32	
11	1745		236	280		4.23	4.11	
12	1750		217	262		4.18	4.02	
	CONH							
13	1695	3110	237			3.89		
14	1695	3100	236			4.08		
15	1695	3150	245			4.07		
16	1675	3200	258			4.26		
17	1695	3200	235			3.95		
18	1660	3200	242			4.25		
	CO.N							
19	1680		205	269		4.07	5.31	
20	1670		233	293		4.27	4.38	
21	1670			270			4.52	
22	1680		215	280	300	4.38	4.39	4.36
23	1670		210	237	290	4.15	4.31	4.23

acetic anhydride (10 ml.) and refluxed for 2 hours. The mixture was poured onto crushed ice and the separated product was filtered, washed, and crystallized from methanol-water.

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