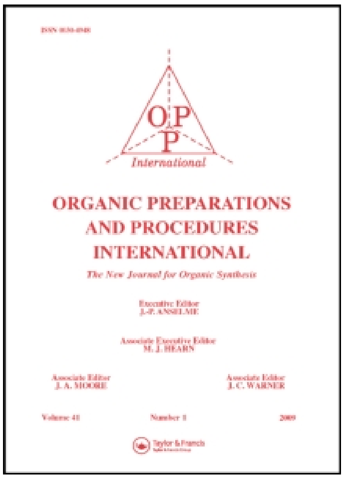

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

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To cite this Article Shaban, M. , Nassr, M. , Ashry, E. El and Mustafa, M.(1977) 'REACTIONS OF AROYLHYDRAZONES. III: OXIDATIVE CYCLIZATION OF CYCLOHEXANE-1,2-DIONE BIS(AROYLHYDRAZONES) TO SUBSTITUTED 1,2,3-TRIAZOLES', Organic Preparations and Procedures International, 9: 3, 117 — 124

To link to this Article: DOI: 10.1080/00304947709356867

URL: http://dx.doi.org/10.1080/00304947709356867

ORGANIC PREPARATIONS AND PROCEDURES INT. 9(3), 117-124 (1977)

REACTIONS OF AROYLHYDRAZONES. III[1]: OXIDATIVE CYCLIZATION OF CYCLOHEXANE-1,2-DIONE BIS(AROYLHYDRAZONES) TO SUBSTITUTED 1,2,3-TRIAZOLES

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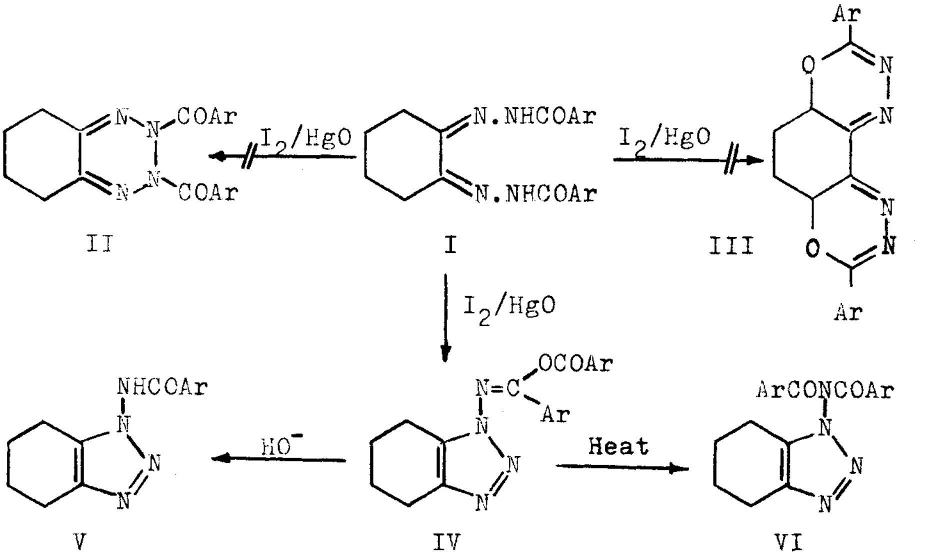
Oxidative cyclization of mono-, di-, and poly(aroylhydrazones) of carbonyl compounds with iodine and yellow mercuric oxide or with an alkaline solution of potassium hexacyanoferrate affords a convenient route for the synthesis of a variety of heterocyclic compounds. Thus, whereas aroyl-



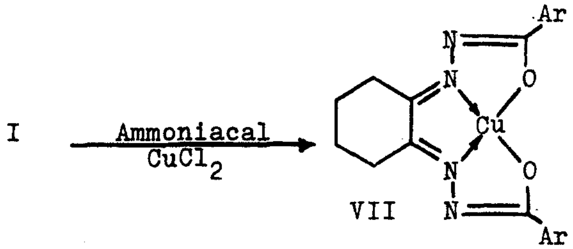
a) Ar = C_6H_5 b) Ar = *m*-MeC_6H_4 c) Ar = *p*-MeC_6H_4
d) Ar = *p*-$MeOC_6H_4$ e) Ar = *p*-ClC_6H_4 f) Ar = *p*-$O_2NC_6H_4$

hydrazones of aromatic aldehydes and aldehydo-sugar acetates[2-5] are invariably oxidized with these reagents to 1,3,4-oxadiazole derivatives, bis(aroylhydrazones) of 1,2-dicarbonyl compounds give either 1,3,4-oxadiazoles[4,5] or 1,2,3-triazole[6-9] derivatives.

Theoretically, bis(aroylhydrazones) of cyclohexane-1,2-dione (I) have the potentiality of being oxidatively cyclized to 1,2,3,4-tetrazine (II), 1,3,4-oxadiazine (III), or 1,2,3-triazole (IV) derivatives. In this paper, and as a continuation of our studies on the reactions of aroylhydrazones, we describe the results of the oxidative cyclization of I.

Condensation of cyclohexane-1,2-dione[10] with two equivalents of the required aroylhydrazine gave the corresponding cyclohexane-1,2-dione bis(aroylhydrazone) (I) in good yield. Ir spectra of I showed amide absorption bands at 1680-1650 cm^{-1} in addition to the phenyl, C=N, and NH absorptions at 710-675, 1600-1580, and 3500-3350 cm^{-1} respectively. Nmr of Ia showed no indication that either of the two hydrazono-protons are intramolecularly hydrogen bonded since they appear as an exchangeable two-proton singlet at δ 14.9 and not as two one-proton singlets at different chemical shifts like those of other bis(arylhydrazones)[11-14] and bis(aroylhydrazones)[9]. The two phenyl groups appeared as a 10-proton multiplet at δ 7.8-7.2, and the four methylene groups of the cyclohexane ring as 4-proton multiplets at δ 3.0-2.5 and 1.8-1.3. The mass spectrum of Ia showed the molecular ion peak M^+ at m/e 348 and fragments at m/e 330 (M^+-H_2O), 243 (M^+-COPh), 229 (M^+-NCOPh), 227 (M^+-H_2NCOPh), 215 (M^+-N_2COPh), 122 [$M^+-(H_2$NCOPh+COPh)], 121 ($PhCONH_2$), 119

$(PhCON)^+$, 105 $(COPh)^+$, 103 $(CNPh)^+$, and 77 $(Ph)^+$. The bis(hydrazones) precipitated stable cupric complexes when treated with ammoniacal cupric chloride. Preliminary studies indicated that the stablity of these complexes is due to the formation of tetradentate ligands as in VII similar to those of 1,2-dicarbonyl compounds bis(thiosemicarbazones)[15,16].



VII

The ir spectra of the copper complexes VII showed C=N and phenyl absorptions at 1600-1580 and 700-675 cm^{-1} respectively and no amide or NH absorptions.

Treatment of the bis-hydrazones I with iodine and yellow mercuric oxide in dry ether gave crystalline products, the elemental anaylses as well as mass and nmr spectra of which indicated the loss of the two hydrazono-protons. Thus, the mass spectrum of the oxidation product from Ia showed molecular ion peak M^+ at m/e 346, two units less than the parent bis-hydrazone. Ir spectra of the oxidation products revealed the absence of amide and NH absorptions but showed strong ester carbonyl absorptions at 1740-1735 cm^{-1}. These results would only reconcile with the 1,2,3-triazole enol ester structure IV and not with either of the 1,2,3,4-tetrazine II or 1,3,4-oxadiazine structure III. Accordingly, the oxidation products were assigned the structure of 1-α-aroyloxyarylideneamino-4,5,6,7-tetrahydrobenzo-1,2,3-triazoles (IV). In agreement with this assignment is the ready alkaline hydrolysis of IV to benzoic or substituted benzoic acids and 1-aroylamino-4,5,6,7-tetrahydrobenzo-1,2,3-triazoles (V). The latter compounds lacked the ester absorption and showed, instead, amide and NH absorption bands. When heated above its melting point, IVa underwent the expected[7] 1,3-acyl migration to give 1-dibenzoylamino-4,5,6,7-tetrahydrobenzo-1,2,3-triazole (VIa). The latter showed only CON absorption band at 1730 cm^{-1} and no ester or NH absorptions. From these results it is evident that I were oxidized similar to methylglyoxal[17], phenylglyoxal[18], and benzil bis(aroylhydrazones)[1] and dissimilar to glyoxal[5] and mesoxalaldehyde bis(aroylhydrazones)[5] which gave 1,3,4-oxadiazole derivatives. The difference in the oxidation products of these bis-hydrazones cannot be firmly rationalized now, yet examination of the molecular models showed that different <u>Z,E</u> isomers of the bis-hydrazones would cyclize to different products.

EXPERIMENTAL

Melting points were determined with a Kofler block and are uncorrected. The ir spectra were recorded on a Unicam SP200 spectrophotometer. The nmr spectra were determined at 60 MHz with a Varian T-60 spectrometer for solutions in deuterochloroform or deuteropyridine containing 1% tetramethylsilane as the internal standard. The mass spectra were performed on a Hitachi-Perkin-Elmer RMU-6 mass spectrometer. Microanalyses were determined in the Microanalyses Unit, Faculty of Science, Cairo University, Cairo, Egypt. Homogeneity of the products was checked by tlc on Silica Gel G plates (layer thickness 0.25 mm) and the spots were detected with iodine or by spraying with 20% (v/v) sulfuric acid followed by heating the chromatograms on a hot plate for a few minutes.

<u>Cyclohexane-1,2-dione bis(aroylhydrazones)</u> (I) (<u>TABLE 1</u>).- A solution of cyclohexane-1,2-dione[10] (1 g, 8.9 mmole) in methanol (20 ml) was treated with the required amount (18

mmole) of the appropriate aroylhydrazine in methanol (60 ml) and a few drops of acetic acid. The mixture was heated on a water-bath for 30 min and kept at room temperature for 16 h. The bis-hydrazones were collected by filtration, washed with methanol and ether, and crystallized from methanol or a mixture of 1:1 (v/v) benzene-methanol.

TABLE 1. Cyclohexane-1,2-dione bis(aroylhydrazones) (Ia-If)

				Anal. $\frac{\text{Found}}{\text{Calcd}}$			ν_{max} (cm^{-1})
Cpd No.	Yield %	mp. °C	Formula	C	H	N	CONH
Ia	78	220-222	$C_{20}H_{20}N_4O_2$	$\frac{68.7}{69.0}$	$\frac{5.7}{5.8}$	$\frac{15.7}{16.1}$	1650
Ib	72	208-209	$C_{22}H_{24}N_4O_2$	$\frac{70.2}{70.2}$	$\frac{6.6}{6.4}$	$\frac{15.4}{14.9}$	1660
Ic	76	223-224	$C_{22}H_{24}N_4O_2$	$\frac{69.9}{70.2}$	$\frac{6.4}{6.4}$	$\frac{14.5}{14.9}$	1660
Id	77	120-121	$C_{22}H_{24}N_4O_4$	$\frac{64.6}{64.7}$	$\frac{5.9}{5.9}$	$\frac{13.3}{13.7}$	1680
Ie	82	228-230	$C_{20}H_{18}N_4Cl_2O_2$	$\frac{57.7}{57.5}$	$\frac{4.4}{4.3}$	$\frac{13.0}{13.4}$	1680
If	79	252-254	$C_{20}H_{18}N_6O_6$	$\frac{54.7}{54.8}$	$\frac{4.0}{4.1}$	$\frac{18.9}{19.2}$	1680

1-α-Aroyloxyarylideneamino-4,5,6,7-tetrahydrobenzo-1,2,3-triazoles (IV) (TABLE 2).- A suspension of cyclohexane-1,2-dione bis(aroylhydrazone) (I, 2.4 mmole) in absolute ether (100 ml) was successively treated with yellow mercuric oxide (5 mmole), magnesium oxide (5 mmole), and iodine (5 mmole). After being kept at room temperature for 12 h with occasional shaking, the ethereal solution was filtered and the inorganic residue was extracted with chloroform (6 x 25 ml). The combined ether and chloroform solutions were washed with saturated solutions of potassium iodide (4 x 50 ml), sodium thiosulfate (4 x 50 ml), and water (2 x 50 ml), and dried (sodium sulfate). Evaporation of the solvents gave products which were crystallized from methanol.

TABLE 2. 1-o-Aroyloxyarylideneamino-4,5,6,7-tetrahydrobenzo-1,2,3-triazoles (IVa-IVf)

Cpd No.	Yield %	mp. °C	Formula	Anal. Found/Calcd C	H	N	ν_{max}(cm^{-1}) COO
IVa	64	161-163	$C_{20}H_{18}N_4O_2$	69.6 69.4	5.3 5.2	16.4 16.2	1740
IVb	59	158-159	$C_{22}H_{22}N_4O_2$	70.2 70.6	5.5 5.9	14.8 15.0	1735
IVc	67	156-158	$C_{22}H_{22}N_4O_2$	70.2 70.6	6.1 5.9	15.0 15.0	1740
IVd	65	153-155	$C_{22}H_{22}N_4O_4$	64.5 65.0	5.1 5.5	14.2 13.8	1740
IVe	71	179-180	$C_{20}H_{16}N_4Cl_2O_2$	57.9 57.9	4.0 3.9	13.7 13.5	1740
IVf	68	156-157	$C_{20}H_{16}N_6O_6$	55.2 55.1	4.2 3.7	19.0 19.3	1740

1-Aroylamino-4,5,6,7-tetrahydrobenzo-1,2,3-triazoles (V) (TABLE 3).- A solution of IV (3 mmole) in methanol (100 ml) was stirred with 20% ammonium hydroxide solution (15 ml) for 25 h at room temperature. The solution was evaporated to dryness and the residue was triturated with water (20 ml) and filtered. The products (V) were crystallized from methanol.

Acidification of the filtrate with dilute hydrochloric acid precipitated the corresponding benzoic acid identified by m.p. and mixed m.p.

TABLE 3. 1-Aroylamino-4,5,6,7-tetrahydrobenzo-1,2,3-triazoles (Va-Ve)

Cpd No.	Yield %	mp. °C	Formula	Anal. $\frac{\text{Found}}{\text{Calcd}}$ C	H	N	ν_{max}(cm^{-1}) CONH
Va	89	239-241	$C_{13}H_{14}N_4O$	$\frac{64.9}{64.9}$	$\frac{6.1}{5.8}$	$\frac{22.8}{23.1}$	1690
Vb	87	230-231	$C_{14}H_{16}N_4O$	$\frac{65.7}{65.6}$	$\frac{6.3}{6.3}$	$\frac{22.2}{21.9}$	1695
Vc	90	147-148	$C_{14}H_{16}N_4O$	$\frac{65.3}{65.6}$	$\frac{6.1}{6.3}$	$\frac{21.7}{21.9}$	1695
Vd	87	174-176	$C_{14}H_{16}N_4O_2$	$\frac{61.6}{61.8}$	$\frac{5.7}{5.9}$	$\frac{20.5}{20.6}$	1680
Ve	90	215-216	$C_{13}H_{13}N_4ClO$	$\frac{56.9}{56.4}$	$\frac{5.1}{4.7}$	$\frac{20.0}{20.3}$	1695

1-Dibenzoylamino-4,5,6,7-tetrahydrobenzo-1,2,3-triazole (VIa).— 1-α-Benzoyloxybenzylideneamino-4,5,6,7-tetrahydrobenzo-1,2,3-triazole (IVa, 1 g, 2.9 mmole) was heated at 180° for 2 h. The melt was brought to room tempearture and then crystallized from methanol to give 0.9 g (90%) of plates, m.p. 175°, $^{KBr}_{max}$ 1730 cm^{-1} (CON).

Anal. Calcd for $C_{20}H_{18}N_4O_2$: C, 69.4; H, 5.2; N, 16.2. Found: C, 69.2; H, 5.4; N, 15.9.

Acknowledgment.— The authors thank Dr. Vernon N. Reinhold, Arthur D. Little, Inc., Cambridge, Massachusetts, U.S.A. for making the mass spectral measurements available.

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(Received June 6, 1977)