Oxidation of 2-Arylglyoxal 1-Aroylhydrazones with Lead(IV) Acetate[1]; Preparation of Unsymmetrically Substituted Triacylhydrazines

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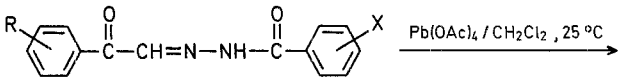
In the course of our work on the lead(IV) acetate oxidation of bis-aroylhydrazones and bis-semicarbazones of α-dicarbonyl compounds, which gives rise to 1,2,3-triazole derivatives[2], we studied the oxidation of mono-aroylhydrazones and, in particular, of 2-arylglyoxal 1-aroylhydrazones **(1)** with lead(IV) acetate and found that this reaction affords unsymmetrically substituted triacylhydrazines **(2)** and not the expected 1,3,4-oxadiazole derivatives **(3)**.



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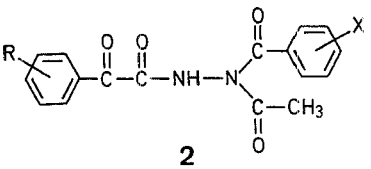

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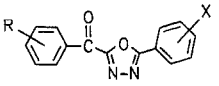

3

1,2	R	X
a	H	H
b	H	4-CH_3
c	H	4-NO_2
d	4-Cl	H
e	4-Cl	4-Cl
f	4-OCH_3	4-Cl

The 2-arylglyoxal 1-aroylhydrazones **(1)** were prepared from the corresponding arylglyoxals and benzoic hydrazides at room temperature; their structure was established by microanalyses and spectral data, especially, by their mass-spectrometric fragmentation pattern.

The main products of the oxidation of compounds **1** with lead(IV) acetate in dichloromethane at room temperature are the *N*-acetyl-*N*-aroyl-*N'*-arylglyoxyloylhydrazines **2**. Compounds **2** were thus obtained for the first time and in good

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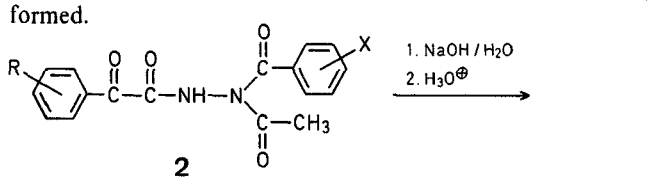
yields (40–70%). The oxadiazoles **3** were isolated only in two cases (**3a, b**) in < 1% yield and were identified by their mass spectra.

As in the case of *N*-acetyl-*N*-aryl-*N'*-aroylhydrazines[3], the acetyl group in compounds **2** is readily cleaved upon addition of aqueous 10% sodium hydroxide at room temperature, the corresponding *N*-aroyl-*N'*-arylglyoxyloylhydrazines (**4**) being formed.



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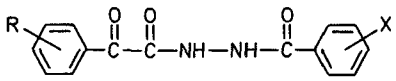


4

It has previously been shown[5,6,7] that the oxidation of aldehyde hydrazones with lead(IV) acetate leads to the formation of nitrilimines which cyclize to 1,3,4-oxadiazoles[5,8]. However, in the present case 1,3,4-oxadiazoles are only formed as by-products in negligible amounts and attempts to trap[5] the nitrilimines A failed. It is therefore assumed that the presence of the aroyl group Ar^1—CO adjacent to the carbenium center in A destabilizes the nitrilimine A and thus facilitates the nucleophilic attack by acetate anion with formation of hydrazonyl anion B which undergoes an acetyl [1,4]migration from O to N and thus rearranges to the triacylhydrazine **2**.

2-Arylglyoxal 1-Aroylhydrazones (1); General Procedure:
A mixture of arylglyoxal (2 equiv) and aroylhydrazine (1 equiv) in methanol (2500 ml for 1 mol of aroylhydrazine) is stirred at room temperature for 10–20 h. The precipitated hydrazone **1** is isolated by suction, washed with methanol, and recrystallized from methanol. An excess of arylglyoxal is always required to avoid the formation of the bis-aroylhydrazone.

Unsymmetrical Triacylhydrazines (2); General Procedure:
A solution of lead(IV) acetate (666 mg, 1.5 mmol) in dichloromethane (20 ml) is added to a stirred suspension of the 2-arylglyoxal 1-aroylhydrazone (**1**; 1 mmol) in dichloromethane (30 ml). An orange-red color appears immediately and after a while the mixture turns yellow. Stirring is continued at room temperature for 1 h and the mixture then poured into water (100 ml). The organic layer is washed with aqueous 10% sodium carbonate (20 ml) and with water (50 ml), dried with sodium sulfate, and evaporated in vacuo. Treatment of the oily residue with ether/petroleum ether causes crystallization of the product **2**.

From the oxidation mixture obtained from compounds **1a** and **1b**, the 1,3,4-oxadiazoles **3a** and **3b**, respectively, may be isolated in < 1% yield by column chromatography on silica gel using chloroform (+ 1% methanol) as eluent.

M.S. of **3a**: m/e = 250 (M^+), 222 $(M-28)^+$, 166 $(222-56)^+$, 145 $(M-105)^+$, 105 (C_6H_5—$\overset{+}{C}O$).

M.S. of **3b**: m/e = 264 (M^+), 236 $(M-28)^+$, 180 $(236-56)^+$, 159 $(M-105)^+$, 119 (4-CH_3—C_6H_4—$\overset{+}{C}O$), 105 (C_6H_5—$\overset{+}{C}O$).

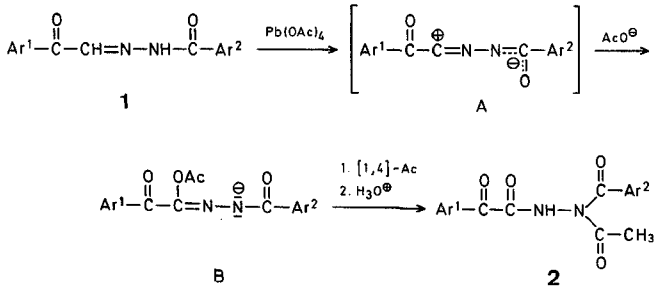
***N*-Aroyl-*N'*-arylglyoxyloylhydrazines (4); General Procedure:**
Aqueous 10% sodium hydroxide (10 ml, 25 mmol) is added to a solution of the triacylhydrazine (**2**; 2 mmol) in methanol (10 ml). The mixture is allowed to stand at room temperature for 20 min. A yellow precipitate is formed which is then acidified with dilute (5%) sulfuric acid. The resultant white solid product **4** is isolated by suction and recrystallized from methanol.

Table. Compounds **1**, **2**, and **4** prepared

	Compounds **1**			Compounds **2**			Compounds **4**		
	Yield [%]	m.p.[a] [°C]	Molecular formula[c]	Yield [%]	m.p. [°C] (solvent)	Molecular formula[c]	Yield [%]	m.p.[a] [°C]	Molecular formula[c]
a	75	166–167°	$C_{15}H_{12}N_2O_2$ (252.3)	60	oil	$C_{17}H_{14}N_2O_4$ (310.3)	60	141–142°	$C_{15}H_{12}N_2O_3$ (268.3)
b	70	163–165°	$C_{16}H_{14}N_2O_2$ (266.3)	54	89–91° ($CHCl_3$/PE)	$C_{18}H_{16}N_2O_4$ (324.3)	60	64–66°[b]	$C_{16}H_{14}N_2O_3 \cdot H_2O$ (300.3)
c	85	244–246°	$C_{15}H_{11}N_3O_4$ (297.3)	40	151–153° ($CHCl_3$/PE)	$C_{17}H_{13}N_3O_6$ (355.3)	50	203–206°	$C_{15}H_{11}N_3O_5$ (313.3)
d	76	190–193°	$C_{15}H_{11}ClN_2O_2$ (286.7)	80	124–126° (benzene/PE)	$C_{17}H_{13}ClN_2O_4$ (344.8)	43	144–146°[b]	$C_{15}H_{11}ClN_2O_3 \cdot H_2O$ (320.7)
e	73	220–222°	$C_{15}H_{10}Cl_2N_2O_2$ (321.2)	75	128–132° ($CHCl_3$/PE)	$C_{17}H_{12}Cl_2N_2O_4$ (379.2)	42	205–207°[b]	$C_{15}H_{10}Cl_2N_2O_3 \cdot H_2O$ (355.1)
f	90	183–186°	$C_{16}H_{13}ClN_2O_3$ (316.8)	40	117–119° (ether)	$C_{18}H_{15}ClN_2O_5$ (374.8)	50	178–179°	$C_{16}H_{13}ClN_2O_4$ (332.7)

[a] From methanol.
[b] Crystallized as monohydrate.
[c] The microanalyses showed the following maximum deviations from the calculated values: C, ±0.37; H, ±0.10; N, ±0.33. Exceptions: **4b**, H, −0.45; **4d**, C, +0.65. The spectrometric data (M.S., I.R., N.M.R.) of all products were in agreement with the proposed structures.

In the I.R. spectra, the triacylhydrazines **2** show a peak at ν = 3280–3300 cm^{-1} (NH) and two or three peaks at ν = 1660–1740 cm^{-1} (C=O). In the ^{1}H-N.M.R. spectrum, compounds **2** give signals at δ = 7.5–8.3 ppm (aromatic protons), a signal at δ = 2.5–2.6 ppm (acetyl group) and a signal at δ = 9.1–9.4 ppm (NH proton, exchangeable with D_2O). In the mass spectrum, the main peaks besides the molecular ion M^+ are the peaks corresponding to $(M^+ - CH_2{=}CO)$, $(M^+ - Ar^1{-}CO)$, $Ar^1{-}CO^+$, $Ar^2{-}CO^+$, and $H_3C{-}CO^+$. In addition, the structure of compound **2f** was fully established from an X-ray analysis[4].



1 **A** **B** **2**

This work is dedicated to the memory of Professor George Varvoglis.

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