REACTION OF ARYL- AND HETEROARYL BENZOYL- AND ACETYLHYDRAZONES WITH PHENYLISOCYANATE
SYNTHESIS OF SUBSTITUTED-2,3-DIHYDRO-1,3,4-OXADIAZOLES

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Abstract: Aryl benzoylhydrazones (1a-c) react readily with phenylisocyanate (2) at room temperature to give the corresponding substituted 2,3-dihydro-1,3,4-oxadiazoles (3a-c). On the other hand, the reaction of benzoylhydrazones of furan, thiophene and pyridine carbaldehydes gave 2,5-dioxo-1,5-diphenyl-1,3,4-triazapentane (4), and that of thiophene acetylhydrazone gave 2,5-dioxo-1-phenyl-1,3,4-triazahexane (5). Structure elucidation of these compounds was based on spectral data including IR, Ms and NMR.

Key Words: Oxadiazoles, Benzoylhydrazones, acetylhydrazones Phenylisocyanate, furan, thiophene, pyridine, aryl aldehydes.

Introduction
Azoles in general represent an important class of heterocycles that find many applications as antifungal and antibacterial agents [1]. Recently, some triazoles and oxadiazoles have been used in the preparation of dye sensitzed diods [2]. Some oxadiazole derivatives are used as herbicides [3].
REACTION OF ARYL- AND HETEROARYL…

Hydrazones of aryl aldehydes and ketones were found to react, in many cases, in different ways from that of the hydrazones of alkyl aldehydes and ketones. An example is the reaction of hydrazones of aliphatic ketones with nitrile oxides which gives the cycloaddition products 1,2,4-oxadiazolines [4]; while that of hydrazones of arylaldehydes with nitrile oxides gives acyclic nucleophilic addition adducts [5]. Also, the reaction of nitrilimines with methylhydrazones of aliphatic aldehydes and ketones gives the cyclic 1,2,4,5-tetrazines [6], while the same reaction with methylhydrazones of aryl aldehydes affords a mixture of ring-chain isomers [7].

The reaction of acetone and cycloalkanone hydrazones with phenylisocyanate was recently reported by one of our research group to give 1,3,4-oxadiazolines. The structure of the latter compounds was confirmed by spectral data and x-ray crystal structure analysis [8].

In continuation of our interest in the synthesis of different oxadiazole derivatives, and comparing the reaction of hydrazones of aryl- and aliphatic-aldehydes and ketones with different reagents, we now report the results of the reaction of acetophenone benzoylhydrazone 1a, benzoylhydrazones of aryl aldehydes 1b,c, benzoylhydrazones of 2-furan-, 2-thiophene- and 2-pyridine carbaldehydes 1d-f, and 2-thiophene acetylhydrazone 1g with phenylisocyanate.

**Results and discussion**

The reaction of the hydrazones 1a-g with phenylisocyanate 2 was carried out in chloroform under dry conditions at room temperature (Scheme 1). The small quantity of the precipitated diphenyl urea was removed by suction filtration and the solvent was evaporated. Trituration of the residual solid with ethanol gave the products 3a-c, 4 and 5.

2,3-Dihydro-1,3,4-oxadiazoles (3a-c) were obtained from the reaction of phenylisocyanate with arylhydrazones 1a-c. Assignment of the structure of these compounds was based on their spectral data including MS, IR and NMR.

On the other hand, the reaction of the hydrazones of heteroaryl aldehydes 1d-g gave the acyclic adducts 4 and 5 (Scheme 1). The assignment of structure 4 was based on its melting point [9] in addition to its spectral data. It is worth mentioning that compound 4 was obtained from the decomposition of the similar oxadiazoles derived from benzoylhydrazones of aliphatic ketones in the presence of trifluoroacetic anhydride [8]. This may suggest that, oxadiazoles were first formed before their decomposition to give compounds 4 and 5.
Adel M. Awadallah

Experimental
Melting points were determined on an Electrothermal Mel. Temp. apparatus and are uncorrected. IR spectra were obtained by using Perkin-Elmer 237 infrared spectrometer (KBr discs). $^1$H- and $^{13}$C NMR spectra were recorded on a Brucker 300 MHz instrument for solutions in CDCl3 or DMSO-d6 at 21 °C, using TMS as an internal reference. Chemical shifts are expressed in δ (ppm) downfield from TMS. Hydrazones 1a-g were prepared in good yields by Schiff base condensation between equimolar amounts of the corresponding aryl aldehyde or ketone with benzoyl- or acethyldrazides in refluxing ethanol.

Synthesis of the title compounds 3a-h
To a stirred solution of the respective hydrazone (1, 0.005 mol) in chloroform (30 mL) was dropwise added phenyl isocyanate (2, 0.006 mol) in chloroform (10 mL) at room temperature. Stirring was continued for 24
hours. A small quantity of a precipitated solid was filtered and the solvent was evaporated. The residual solid was triturated with ethanol and collected by suction filtration. Further purification was achieved by crystallization from chloroform / petroleum ether (40-60 °C). The yields were in the range of 60-80%. The following compounds were prepared utilizing this procedure.

3-Carbanilino-2-methyl-2,5-diphenyl-2,3-dihydro-1,3,4-oxadiazole (3a)
M. p. = 95 °C; yield 52 %; ¹H NMR (CDCl₃): 6.7-8.1 (m, 16 H, aromatics + NH), 2.5, (s, 3H, CH₃); ¹³C NMR: 153.04 (C=O), 150.07 (C=N), 131.53, 129.24, 128.97, 128.76, 128.49, 126.87, 125.18, 123.18, 119.23 (9 aromatic C-H), 139.97, 138.31, 124.74 (3 aromatic C) 100.97 (C2), 23.75 (CH₃); IR (cm⁻¹): 3288 (NH), 3050 (aromatic hydrogens), 2981 (aliphatic hydrogens), 1659 (C=O); M. Wt: 357 (C₂₂H₁₉N₃O₂).

3-Carbanilino-5-phenyl-2-(tolyl)-2,3-dihydro-1,3,4-oxadiazole (3b)
M. p. = 117 °C; yield 42 %; ¹H NMR (CDCl₃): 7.0-7.9 (m, 16 H, aromatics + NH + CH) 2.4, (s, 3H, CH₃); ¹³C NMR: 155.17 (C=O), 151.65 (C=N), 131.70, 129.54, 128.99, 128.76, 127.05, 126.67, 123.33, 119.15 (8 aromatic C-H), 140.07, 138.07, 134.41, 124.5 (4 aromatic C) 93.09 (C₂H), 21.43 (CH₃); IR (cm⁻¹): 3288 (NH), 3050 (aromatic hydrogens), 2981 (aliphatic hydrogens), 1659 (C=O); M. Wt: 357 (C₂₂H₁₉N₃O₂).

3-Carbanilino-2-(4-chlorophenyl)-5-phenyl-2,3-dihydro-1,3,4-oxadiazole (3c)
M. p. = 132 °C; yield 35 %; ¹H NMR (CDCl₃): 7.0-7.9 (m, 16 H, aromatics + NH + CH), ¹³C NMR: 155.20 (C=O), 151.73 (C=N), 131.88, 129.08, 129.03, 128.81, 128.14, 127.04, 123.56, 119.23 (8 aromatic C-H), 137.81, 135.93, 135.78, 124.18 (4 aromatic C) 92.23 (C₂H); IR (cm⁻¹): 3288 (NH), 3050 (aromatic hydrogens), 2981 (aliphatic hydrogens), 1659 (C=O); M. Wt: 377 (C₂₁H₁₆ClN₃O₂).

2,5-Dioxo-1,5-diphenyl-1,3,4-triazapentane (4)
Yields were in the range of 60 to 80 %. m. p = 208-210 °C (lit 210)[9]. ¹H NMR (DMSO-D₆): 10.3 (s, 1H, NH), 8.7 (s, 1H, NH), 8.2 (s, 1H, NH), 6.9 – 7.9 (m, 10 H, aromatics); ¹³C NMR: 166.9 (PhC=O), 156.2 (NHC=O), 140.2, 133.0, 132.3, 129.2, 128.9, 128.1, 122.4, 119.0 (Aromatic carbons) IR (cm⁻¹): 3300, 3272, 3140, (3N-H), 1677.0 (PhC=O), 1647.0 (NHC=O).

2,5-dioxo-1-phenyl-1,3,4-triazahexane (5).
Yield 65%. m. p = 156-158 °C (lit)[10]. ¹H NMR: 9.6 (s, 1H, NH), 8.7 (s, 1H, NH), 8.0 (s, 1H, NH), 6.9 – 7.4 (m, 5 H, aromatics); ¹³C NMR: 169.8 (CH₃C=O), 155.9 (NHC=O), 140.1, 129.1, 122.4, 119.0 (Aromatic carbons); 21.1 (CH₃); IR (cm⁻¹): 3300, 3272, 3140, (3N-H), 1677.0 (CH₃C=O), 1647.0 (NHC=O).
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References