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

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ملخص: تتفاعل بنزويل هيدرازوانات الألدهيدات والكيتونات الأروماتية (**1a-c**) بسهولة مع فينيل أيسوسيانات (**2**) عند درجة حرارة الغرفة لتعطي مركبات اوكساديازول المستبدلة (**3a-c**). بينما تتفاعل بنزويل هيدرازونات ألدهيدات الفيوران والثيوفين والبيريدين لتعطي المركب 2،5-ثنائي أكسو-1،5-ثنائي فينيل-1،3،4-ثلاثي أزا بنتان (**4**)، وكذلك يتفاعل أسيتل هيدرازون الثيوفين مع فينيل أيسوسيانات (**2**) ليعطي المركب 2،5-ثنائي أكسو-1-فينيل-1، 3،4-ثلاثي أزا هكسان (**5**)، وقد تم تحديد بنى المركبات الناتجة بناء على دراسة أطيافها المختلفة مثل طيف الأشعة تحت الحمراء وطيف الكتلة وأطياف الرنين النووي المغناطيسي.

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 theiophene 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 preparion of dye sensetized diods [2]. Some oxadiazole derivatives are used as herbicides [3].

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 structre of the later compounds was confirmed by spectral data and x-ray cystal structure analysis [8].

In continuation of our interst 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 phenylisocyante.

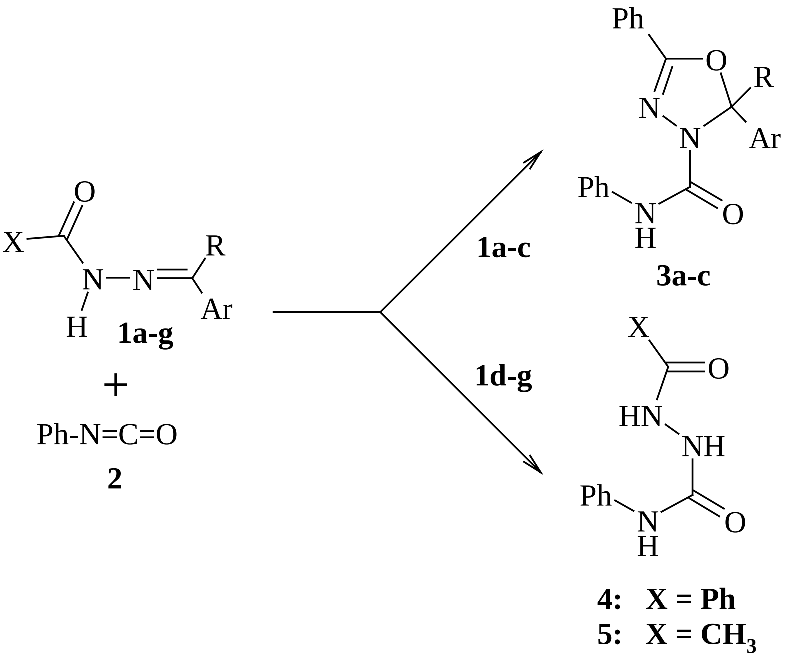
Results and discussion

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**.



	a	b	c	d	e	f	g
R	CH_3	H	H	H	H	H	H
Ar	Ph	4-Me-Ph	4-Cl-Ph	2-furyl	2-thienyl	2-pyridyl	2-thienyl
X	Ph	Ph	Ph	Ph	Ph	Ph	CH_3

Scheme 1

Experimental

Melting points were determined on an Electrothermal Mel. Temp. apparatus and are uncorrected. IR spectra were obtained by using Perkin-Elmer 237 infrared specrometer (KBr discs). ^{1}H- and ^{13}C NMR spectra were recorded on a Brucker 300 MHz instrument for solutions in $CDCl_3$ or DMSO-d_6 at 21 ^{o}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 acethydrazides 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 ºC). 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 ^{o}C; yield 52 %; ^{1}H NMR ($CDCl_3$): 6.7-8.1 (m, 16 H, aromatics + NH), 2.5, (s, 3H, CH_3); ^{13}C 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 (CH_3); IR (cm^{-1}): 3288 (NH), 3050 (aromatic hydrogens), 2981 (aliphatic hydrogens), 1659 (C=O); M. Wt: 357 ($C_{22}H_{19}N_3O_2$).

3-Carbanilino-5-phenyl-2-(tolyl)-2,3-dihydro-1,3,4-oxadiazole (3b)

M. p. = 117 ^{o}C; yield 42 %;^{1}H NMR ($CDCl_3$): 7.0-7.9 (m, 16 H, aromatics + NH + CH) 2.4, (s, 3H, CH_3);. ^{13}C 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, 124.50 (4 aromatic C) 93.09 (C_2H), 21.43 (CH_3); IR (cm^{-1}): 3288 (NH), 3050 (aromatic hydrogens), 2981 (aliphatic hydrogens), 1659 (C=O); M. Wt: 357 ($C_{22}H_{19}N_3O_2$)

3-Carbanilino-2-(4-chlorophenyl)-5-phenyl-2,3-dihydro-1,3,4-oxadiazole (3c)

M. p. = 132 ^{o}C; yield 35 %;^{1}H NMR ($CDCl_3$): 7.0-7.9 (m, 16 H, aromatics + NH + CH), ^{13}C 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 (C_2H); IR (cm^{-1}): 3288 (NH), 3050 (aromatic hydrogens), 2981 (aliphatic hydrogens), 1659 (C=O)
M. Wt: 377 ($C_{21}H_{16}ClN_3O_2$)

2,5-Dioxo-1,5-diphenyl-1,3,4-triazapentane (4)

Yields were in the range of 60 to 80 %. m. p = 208-210 ^{o}C (lit 210)[9]. ^{1}H NMR (DMSO-D_6): 10.3 (s, 1H, NH), 8.7 (s, 1H, NH), 8.2 (s, 1H, NH), 6.9 – 7.9 (m, 10 H, aromatics); ^{13}C 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 ^{o}C (lit)[10]. ^{1}H NMR: 9.6 (s, 1H, NH), 8.7 (s, 1H, NH), 8.0 (s, 1H, NH), 6.9 – 7.4 (m, 5 H, aromatics); ^{13}C NMR: 169.8 (CH_3C=O), 155.9 (NHC=O), 140.1, 129.1, 122.4, 119.0 (Aromatic carbons); 21.1 (CH_3); IR (cm^{-1}): 3300, 3272, 3140, (3N-H), 1677.0 (CH_3C=O), 1647.0 (NHC=O).

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