SYNTHESIS AND BIOLOGICAL ACTIVITY STUDY OF SOME HETEROCYCLES DERIVED FROM DIBENZALACETONE

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Abstract

Condensation of benzaldehyde with acetone in ethanolic alkaline solution leads to the formation of dibenzalacetone, which when treated with selected nucleophiles undergoes Michael addition to give a variety of heterocyclic compounds, these compounds have been characterized by physical and spectral methods, and also they have been screened for their anti bacterial activities.

Key words: Benzaldehyde, Dibenzalacetone, Heterocyclic compounds, Antibacterial activity.

Introduction

Condensation of aldehydes and / or ketones is a particular example of Claisen reaction, therefore when an ethanolic solution containing an aldehyde and / or a ketone is made alkaline with sodium hydroxide, rapid condensation occurs leads to the formation of α, β – unsaturated carbonyl compound which usually called chalcone [1, 2]. This reaction is very well known and documented and many researchers had studied and investigated this reaction thoroughly [3]. The chalcone then subjected to a variety of chemical reactions and were found to be useful in synthesis of a variety of heterocyclic compounds [4]. Due to the importance of the heterocyclic compounds obtained, as they exhibit diverse pharmacological activities [5-7], we have decided to synthesize many heterocycles derived from dibenzalacetone which is quite easily accessible[8,9], then examine the products obtained for their biological activities against certain Gram-positive and Gram-negative bacteria available and compare the results obtained with standard drug[10].

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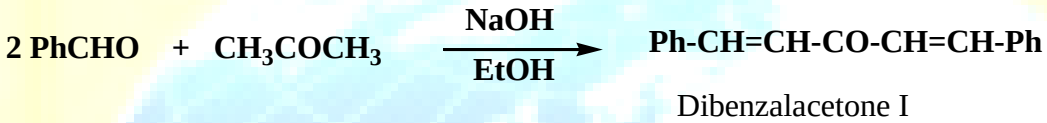
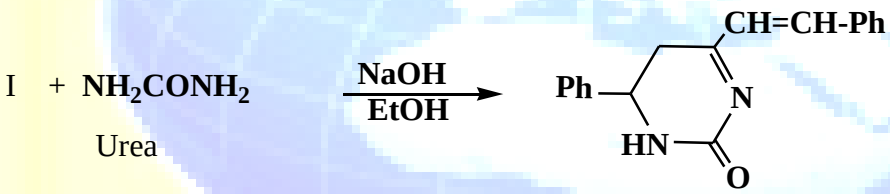
Material and Methods

All reagents and chemicals were of analytical grade they were used without further purification; melting points of the products were measured on Stuart apparatus and are uncorrected. IR spectra were recorded on FTIR-1615 of Perkin- Elmer spectrophotometer in KBr pellets. The ^{1}HNMR spectra were recorded on Brucker AMX – 300 spectrometer in d_6-DMSO, chemical shifts relative to TMS used as internal standard were obtained in δ-unit. The spectral analysis was carried out at Ain Shams University, Egypt.

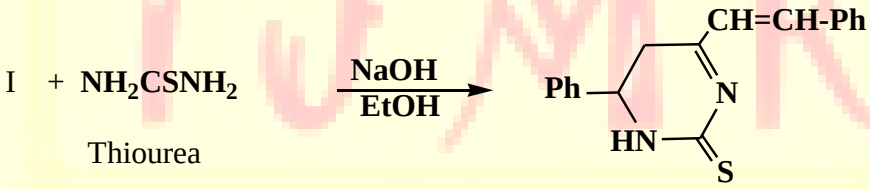
In the first step dibenzalacetone was prepared, Then five heterocyclic compounds were prepared by reaction of dibenzalacetone with urea, thiourea, 2, 4-dinitrophenylhydrazine, semicarbazide and hydroxylamine hydrochloride according to the scheme outlined below:



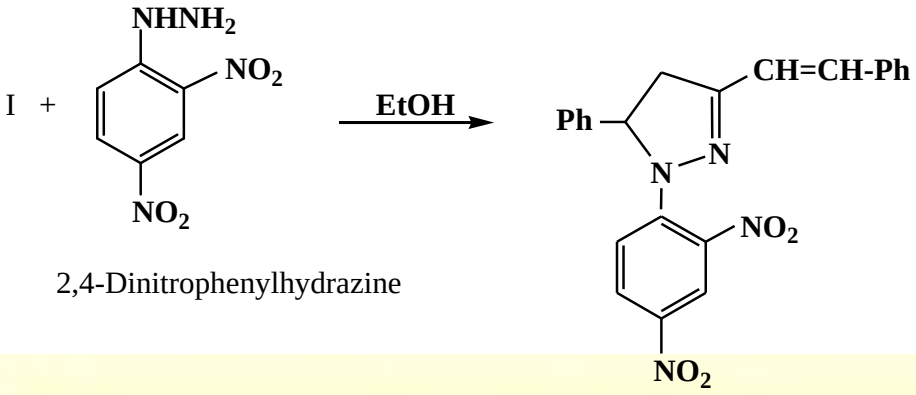
Dibenzalacetone I



4-(2-Phenylethylidene)-6-phenyl-1,5,6-trihydro-2-pyrimidone (II)

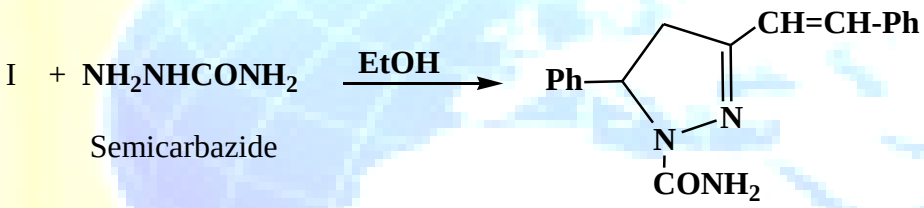


4-(2-Phenylethylidene)-6-phenyl-5,6-dihydro)pyrimidone-2(1H)thione (III)



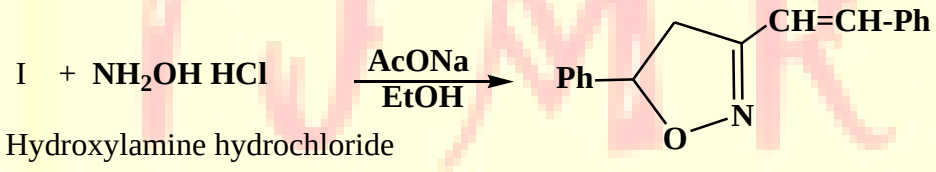
2,4-Dinitrophenylhydrazine

1-[(2,4-Dinitrophenyl)-3(-2-phenylethylidene)]-5-phenyl-4,5-dihydropyrazole (IV)



Semicarbazide

1-Carbamyl-3-(2-phenylethylidene)-5-phenyl-4,5-dihydropyrazole (V)



Hydroxylamine hydrochloride

3-(2-Phenylethylidene)-5-phenyl-4,5-dihydroisoxazole (VI)

Synthesis of dibenzalacetone (I)

Dissolve (0.02 mol) of benzaldehyde and (0.01 mol) of acetone in 10 ml of ethanol. Dilute 4 ml of aqueous sodium hydroxide solution with 15 ml of water and added to the former solution shake the mixture vigorously for about 15 minutes then allow to stand for another 15 minutes finally cool in ice water for 10 minutes. The dibenzalacetone separates as pale yellow crystals,

filter at the pump, wash well with water and drain thoroughly. Recrystallize from ethanol, the purity of the product was checked by TLC and its melting point was in agreement with the literature raule[8, 9]. (110 – 112 ^{0}C)

M .p. (109 – 111^{0}C), 78 % yield.

Synthesis of compound (II) and (III)

A mixture of compound (I) 0.02 mol, urea / thiourea (0.02 mol) were dissolved in ethanolic sodium hydroxide (10 mL) and stirred for 2 hours. The reaction mixture then poured into 250 mL of cold water with continuous stirring for one hour and kept if refrigerator overnight. The precipitated products obtained were filtered and washed with water, then recrystallized from ethanol.

Synthesis of compound (IV) and (V)

A mixture of compound (I) 0.02 mol, 2,4-dinitrophenylhydrazine / semicarbazide (0.02 mol) were dissolved in ethanol (10mL) and refluxed for 3 hours, then the mixture was poured into ice-water. The precipitate formed was filtered, washed and recrystallized.

Synthesis of compound (VI)

A mixture of compound (I) 0.02 mol, hydroxylamine hydrochloride (0.02 mol) and sodium acetate in ethanol (25 mL) was refluxed for 3 hours, and then the reaction mixture was poured into ice – water. The precipitate formed was filtered, washed then recrystallized.

Antimicrobial screening [10]

Compounds (II-VI) were screened for their activities against Gram-positive bacteria S. Aurens and Gram-negative E.Coli, standard drug (Ampolix) was used for comparison. The biological activities of these compounds have been evaluated by filter paper disk method in DMF, the inhibition zones of microbial growth were measured in mm at 25^{o}C. DMF alone showed no

inhibition zone. It is apparent from the data listed in table 3, that all compounds showed antibacterial activity comparable of the reference drug used.

Results and discussion

The scheme outlined above showed the successive steps carried out for preparation of compounds (I-VI), tables 1 and 2 showed the physical and spectral data respectively of all compounds obtained.

Table 1: Physical data of compounds (I-VI)

Compd. No.	Mol.formula	Mol. wt.	M.p ^{0}C	Yield %	Microanalysis (Found / Calc.)			
					C	H	N	S
I	$C_{17}H_{14}O$	234	160-1	78	87.17 (87.62)	6.86 (6.33)	---	---
II	$C_{18}H_{16}N_2O$	276	180-3	86	78.26 (78.43)	5.79 (5.56)	10.14 (10.52)	---
III	$C_{18}H_{16}N_2S$	292	174-6	56	73.97 (74.32)	5.47 (6.01)	9.58 (9.04)	10.95 (11.34)
IV	$C_{22}H_{18}N_4O_4$	402	122-4	70	65.67 (65.94)	4.47 (5.08)	13.93 (14.24)	---
V	$C_{18}H_{17}N_3O$	291	110-2	80	74.22 (74.64)	5.84 (6.13)	14.43 (14.73)	---
VI	$C_{17}H_{15}NO$	249	96-7	65	81.92 (82.28)	6.02 (6.46)	5.62 (5.29)	---

Table 2: Spectral data of compounds (I-VI)

Compound No.	IR υ cm^{-1}	^{1}HNMR δ ppm
I	1480 (C=C-Ar),1640 (C=C) 1700 (C=0)	4.6 (6,2H,2=CH-Ph); 7-1-7.4 (m,10H) Ar –H) 7.66 (d,2H,2=CH-Ph)
II	1485 (C=C-Ar);1625 (C=N) 1650 (C=C) 1710 (C=0);3300 (NH)	1.4-1.7 (d,2H,CH_2); 3.8(d,1H,CH); 6.06-6-4(d,2H,CH=CH); 7-175(m,10H,Ar-H); 8.0(S,1H,NH)
III	1479 (C=C-Ar);1624 (C=N),1645 (C=C) 1675 (C=S);3340 (NH) 1200 (C-N)	1.4-1.6 (d,2H,CH_2=CH); 3.7(d,1H,CH); 6.1-6.4(d,2H,CH=CH), 7.00-7.4(m,10H,,Ar-H); 8.0(S_1,1H,NH)
IV	1480 (C=C-Ar);1625 (C=N); 1650 (C=C);1520 (C=No_2)	1.4-1.7(d,CH_2); 3.8(d,CH); 6.1-6.5(d,CH=CH); 7.1-7.5(m-Ar-H)
V	1210 (C-N);1630 (C=N) 1650 (C=C);1710 (C=O); 3400 (NH_2)	1.4-1.7(d-CH_2); 3.9(d,CH); 5.6-6.00(d,CH=CH); 7.14-7.30(m,Ar-H)
VI	1100 (C-O);1640 (C=N);1650 (C=C)	1.4-1.7(d,CH_2); 3.8(d,CH); 5.8-6(d,CH=CH); 7.2-7.6(m,Ar-H)

Table 3: Antimicrobial activity of compounds (II-VI)

Compound No.	Zones of inhibition (mm)	
	S .Aurens	E . coli

II	28	28
III	16	30
IV	.....	28
V	38	36
VI	…….	22
Standared drugs	38	37

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References

1- A. T. Nielsen, W. J. Honlihan, Org. Reactions, 16, 1 (1968)

2-R. Kalirajan, S. U. Sivakuman, S. Jubie, B. Gowramma and B. Suresh, Int. J. Chem. Tech., 1,27(2009)

3- W. Foerst, Ed." Newer Methods of Prep. Org. Chem." 6, 48(1971)

4- H. O. House, " Modern Synthetic Reactions " (W. A. Benjamin, California, 2nd., Ed., (1972), pp 629-682.

5- Y. B. Vibhute and M. A. Bassen, Ind. J. Chem. 42B, 202(2003)

6- M. L. Edwards, D. M. Stemerick and P. S. Sunkara, J. Med. Chem., 33, 1948(1999)

7- U. Gupta, V. Sareen, V. Khatri and S. Chugh, Ind. J. Het. Chem., 14, 265(2005)

8- F. G. Mann and B. C. Saunders, " Practical Organic Chemistry ". Longman, UK, 4th Ed.,1994, p.231

9- Conrad, Dolliver, Org. Synthesis, 12, 22(1939); Dinwiddie etal, J. Org. Chem. 27, 327(1972), Merck Index, 9th Ed., 1976

10- P. R. Murray, E. J. Baron, M. A. Pfaller, F. C. Tenover and R. H. Yolken, " Manual of Clinical Microbiology", 6th Ed., 1995