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SYNTHESIS OF CERTAIN CYCLOPENTYL[b]PYRIDIN-5-ONES OF ANTICIPATED ANTI-INFLAMMATORY, ANTICOAGULANT AND ANTIMICROBIAL ACTIVITIES

Refat H. Omar; Makarem M. Said; Hosam El-Din A. Ahmed*, Adel H. Omar** and Ahmed B. Mahmoud***

Organic Chemistry Department, Faculty of Pharmacy, Cairo University,
*Organic Chemistry Department, Faculty of Pharmacy, Suez Canal University** Clinical Pharmacology Department, ***Microbiology Department, Faculty of Medicine, Menofia University, Egypt

Abstract:

The reaction of quinolinic anhydride **(2)** with α-(or γ-) picoline yielded 6-(2-pyridinyl)cyclopenty[b]pyridine-5,7-dione **(3)** or 6-(4-pyridinyl) analogue **4** Compounds **3** and **4** were changed into the chloro derivatives **5** and **6** respectively by using mixture of phosphorus pentachloride and phosphorus oxychloride . The chloro compounds (**5** and **6**) underwent nucleophilic substitution reactions with different amines to produce compound **7** and **8** respectively. The hydrazino derivatives 7_i and 8_i respectively were condensed with different aromatic aldehydes to produce **9** and **10** respectively.

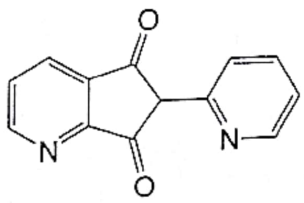
Compounds 8_g and 10_f which showed a significant antiinflammatory action compared to Indomethacine. Also compounds 8_h and 9_b were active as anticoagulant as phenindione. Finally, 9_f and 9_e showed antimicrobial activity especially against Staphlococcus aureus and Escherichica coli.

INTRODUCTION

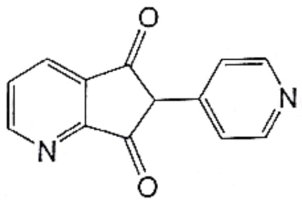
Pyridine containing compounds have been reported to exhibit antihypertensive[1], cardiotonic[2-4], antitumor[5], antiinflammatory, analgesic[6-8], antimicrobial[9-11] and anoxiolytic[12] activities. Also indanedione derivatives have antiinflammatory[13], antimicrobial[14], antiallergic and anticoagulant[15] activities. Thus, the present work involves the synthesis of new compounds containing pyridine moiety aiming to increase the anti-inflammatory, anticoagulant and antibacterial actions.

RESULTS AND DISCUSSION

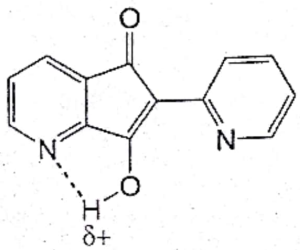
Quinolinic acid **(1)** and quinolinic anhydride **(2)** were prepared according to the directions of Holland and his associates[16]; Rotberg and Oskaja[17] respectively. Compound **2** was treated with α-or γ-picoline in presence of fused sodium acetate as a base adopting the reported procedure[18] to afford 6-(2- or 4-pyridinyl) cyclopentyl[b]pyridine-5,7-diones (**3** and **4**). In case of 2-picoline, the reaction time was more than that for 4-picoline because the latter is more acidic and easily deprotonated than 2-picoline[19]. The IR spectral data of compounds **(3 and 4)** indicated that each compound exists as an equilibrium mixture of two possible tautomeric forms **(3A-3B)** and **(4A-4B)**. The enolic OH stretching absorption is seen a broad shallow band at 3448 cm.



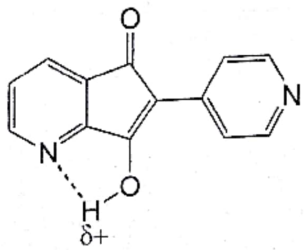
(3A)



(4A)



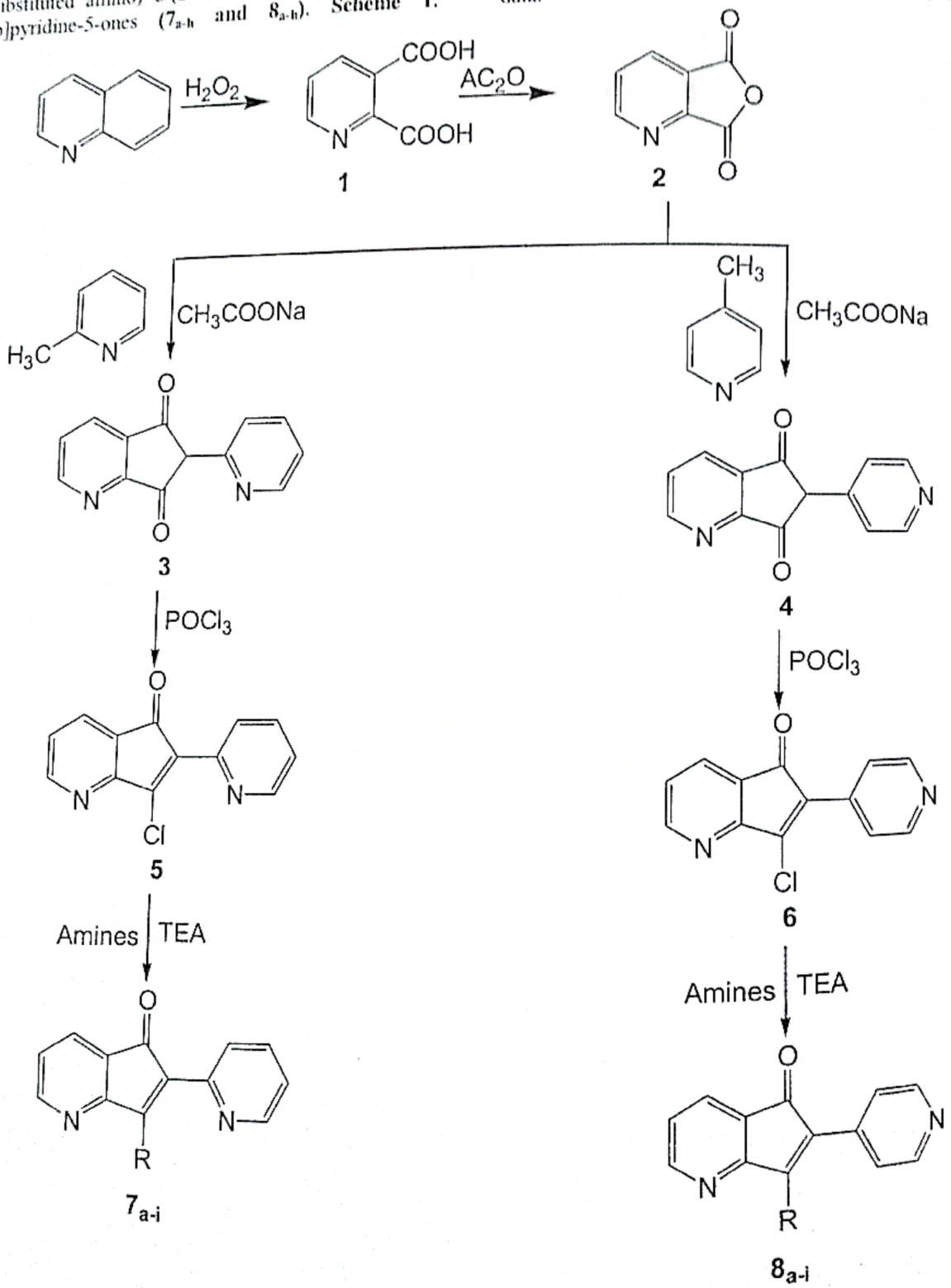
(3B)



(4B)

Access to the enolic forms (**3** and **4**) suggests their reaction with phosphorous oxychloride/ phosphorous pentachloride mixture adopting the reported method[20] to prepare the chloro derivatives **5** and **6**, respectively. The latter compounds were kept under ether for subsequent use due to high unstability, then, were refluxed in ethanol with different amines in presence of triethylamine for suitable time to afford 7-(N-substituted amino) 6-(2- or 4-pyridinyl)cyclopentyl-[b]pyridine-5-ones (7_{a-h} and 8_{a-h}). **Scheme 1.**

Furthermore, a second approach was applied to synthesize the hydrazine derivatives 7_i and 8_i through refluxing the chloro derivatives **5** and **6** with hydrazine hydrate (99%) in absolute ethanol for one hour. Finally, the latter compounds (7_i and 8_i) were condensed with different aromatic aldehydes producing 7-(N-arylidene hydrazone derivatives (**9 and 10) scheme 2**, All the new prepared structures were confirmed by elemental analysis and spectral data.



Scheme (II)

R = benzylamino, piperidinyl, phenylhydrazino, 2,4-dinitrophenylhydrazino, ethoxycarbonylmethylamino, cyclohexylamino, 4-phenylpiperazinyl, p-anisidinyl and hydrazine

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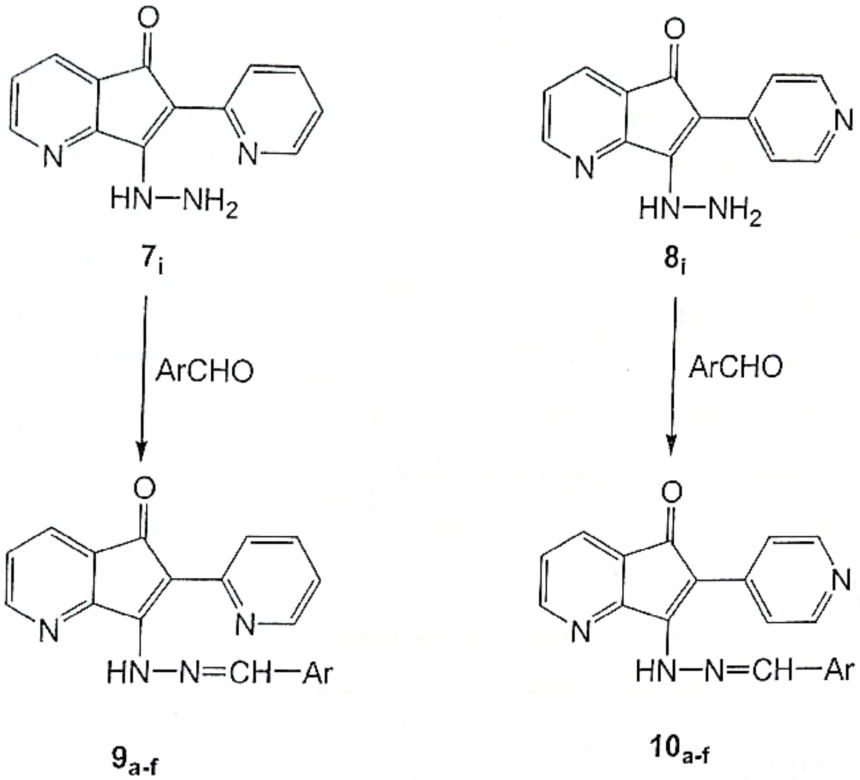

Ar= p-nitrophenyl, p-chlorophenyl, p-bromophenyl, p-fluorophenyl, m-fluorophenyl, o-fluorophenyl.

EXPERIMENTAL

Melting points were determined on a Griffin or a Stuart Scientific Apparatus and are uncorrected. IR Spectra were determined as KBr discs on Shimadzu IR 435 spectrophotometer and values are represented in cm^{-1}. ^1H NMR were carried out on Jeol FXQ-90 MHz, Varian 200 MHz and Jeol Ex-270 MHz, using tetramethylsilane (TMS) as an internal standard and chemical shift values are recorded in ppm on δ scale. Mass spectra were run on Hewlett packard 5988 spectrometer. Elemental analysis were carried out at Microanalytical center, Cairo University Egypt. Progress of the reactions was monitored by TLC using aluminum sheets recoated with UV fluorescent silica gel (Merck 60 F 254) and were visualized using UV lamp and I_2 vapor. The used developing system was benzene: chloroform: acetone [9 : 1.5 : 0.1].

6-(2 or 4-pyridinyl)-cyclopentyl [b] pyridine 5,7 dione (3 and 4):

To a mixture of quinolinic anhydride (0.013 mol), 2- or 4-picoline (0.104 mol) and anhydrous sodium acetate, (0.013 mol) was added and the mixture was heated under reflux for 14 hours and 10 hours for 2-picoline and 4-picoline, respectively. The reaction mixture was left overnight and the separated solid was washed with cold water for several times. The solid was air dried, then dried at 100°C for 2 hours. Crystallization from 80% aqueous acetic acid afforded a green crystalline solid **(3 or 4).** (Table 1). IR (cm^{-1}) for **3**: 1675 (CO), 3448 (OH), 1568 (C=C), 1639 (C=N); for **4**: 1675 (CO), 3448 (OH), 1568 (C=C), 1639 (C=N), ^{1}HNMR ($CDCl_3$) for **3**: δ 3.18 (s, 1H CH aliphatic), 7.19-7.23 (2d, 2H, 2-pyridyl), 7.48-7.51 (2t, 2H, 2- pyridyl) 8.23-8.27 (2d, 2H, Fused pyridine), 8.68 (t, 1H Fused pyridine) ppm; For **4**: 3.18 (s, 1H of CH aliphatic), 7.68-7.70 (2d, 2H, 4-pyridyl), 8.13-8.14 (2d, 2H, 4-pyridyl), 8.27-8.41 (2d, 2H, Fused pyridine), 8.44 (1t, 1H, Fused pyridine) ppm. EIMS (m/z) For **3** : 225 $(M+1)^+$, (8.7%); 224 $(M)^+$ (52.5%), 223 $(M-1)^+$ (16.2%); For **4** : 226 $(M+2)^+$ (8%), 225 $(M+1)^+$ (5.6%), 224 $(M)^+$ (36.3%).

Table 1: Physical data of compounds 3 & 4

Comp.	m.p. (°C)	Yield %	Molecular formula (mol. wt.)	Analysis calcd (found)		
				C	H	N
3	185	20	$C_{13}H_8N_2O_2$ 224	69.64 (69.51)	3.57 (3.47)	12.50 (12.31)
4	180	25	$C_{13}H_8N_2O_2$ 224	69.64 (70.01)	3.57 (3.91)	12.50 (12.40)

7-Chloro-6-(2- or 4-pyridinyl)-cyclopentyl[b]pyridin-5-one (5 and 6).

A mixture of phosphorous pentachloride (0.01 mol) and phosphorus oxychloride (0.03 mol) was added to compound 3 or 4 (0.01 mol), the reaction mixture was heated at 110-120°C for one hour and excess acid chlorides were removed by distillation under reduced pressure. The residue was cooled, washed with dry ether and kept under ether for subsequent reactions without purification.

7-(N–substitutedamino)-6-(2- or 4-pyridinyl)-cyclopentyl[b]pyridin-5-ones (7a-h and 8 a-h):

A mixture of compound (5 or 6) (0.01 mol) the appropriate amine (0.01 mol), triethylamine (0.01 mol) and absolute ethanol (15 ml) was heated under reflux for suitable time. The mixture was cooled, filtered and the precipitate was crystallized from the suitable solvent (table 2) ^{1}HNMR ($CDCl_3$) of 7e : 3.16-3.94 (2t, 8H, $4CH_2$ of piprazine), 6.31-6.41 (m, 5H, ArH), 6.51-6.91 (m, 4H, 2-Pyridyl), 7.01-7.61 (m, 3H, Fused Pyridine) ppm; For 8e; 3.26-4,10 (2t, 8H, $4CH_2$ of piprazine), 6.42-6.71 (m, 5H, ArH), 6.7-7.10 (m, 4H, 4-pyridy), 74.0- 7.41 (m, 3H, fused pyridine) ppm.; EIMS (m/z) For 7a: 290 $(M-1)^+$ (7.66%); for 7 h: 303 $(M)^+$ (0.3%); for 7d: 404 $(M)^+$ (48%); For 8c: 315 $(M+1)^+$ (1.88%), 314 $(M)^+$ (81%); For 8b : 313 $(M)^+$ (7.24%), 313 $(M-1)^+$ (2.14%).

Table (2) : Physical data of compounds 7a-h & 8a-h:

Comp. No.	R	m.p(°C) Cryst. Solvent	Yield (%) reaction time (hr)	IR (cm^{-1})		Molecular formula (mol. wt.)	Analysis Calcd. (Found)		
				NH	CO		C	H	N
7a	7-piperidino	220-3 Ethanol	52 1	-	1617	$C_{18}H_{17}N_3O$ (291)	74.20 (74.6)	5.80 (6.1)	14.40 (14.1)
7b	7-benzylamino	210-4 Ethanol	72 1	3444	1797	$C_{20}H_{15}N_3O$ (313)	76.60 (76.5)	4.70 (4.5)	13.40 (13.1)
7c	7-Phenyl hydrazino	150-4 Ehanol	84 0.45	3828	1613	$C_{19}H_{14}N_4O$ (314)	72.60 (72.9)	4.40 (4.7)	17.80 (17.6)
7d	7-(2,4 dinitro phenylhdrazino)	155-5 Ethanol	82 1.30	3477	1627	$C_{19}H_{12}N_6O_5$ (404)	56.40 (56.5)	2.90 (3.1)	20.70 (20.2)
7e	7-phenyl piprazino	245-6 Ethanol	92 1	-	1600	$C_{23}H_{20}N_4O$ (368)	75.00 (75.2)	5.40 (5.8)	15.20 (15.1)
7f	7-p-anisidino	137-3 Ethanol	36.6 1.30	3053	1703	$C_{20}H_5N_3O_2$ (329)	72.90 (72.5)	4.50 (4.2)	12.70 (13.1)
7g	7-cyclohexylamino	260 Ethanol	20 1	3426	1676	$C_{19}H_{18}N_3O$ (305)	74.74 (75.1)	6.22 (5.6)	13.77 (13.4)
7h	7-(ethoxycarbonyl methyl amino)	260 Methanol	76 2	3420	1798	$C_{16}H_{13}N_3O_3$ (295)	65.00 (64.7)	4.40 (3.9)	14.20 (14.1)
8a	7-piperidino	215 Ethanol	49 1	-	1595	$C_{18}H_{17}N_3O$ (291)	74.20 (74.3)	5.80 (5.9)	14.40 (14.2)
8b	7-benzyl amino	209 Ethanol	75 1	3428	1798	$C_{20}H_{15}N_3O$ (313)	76.60 (76.8)	4.70 (4.9)	13.40 (13.1)
8c	7-phenyl hydrazino	150-4 Ethanol	84 1	3828	1613	$C_{19}H_{14}N_4O$ (314)	72.60 (73.1)	4.40 (4.8)	17.80 (17.4)
8d	7-(2,4 dinitro phenylhydrazino	155-5 Ethanol	82 1	3477	1627	$C_{19}H_{12}N_6O_5$ (404)	56.40 (56.8)	2.90 (3.2)	20.70 (20.3)
8e	7-phenyl piperazino	245-6 Ethanol	92 1	-	1600	$C_{23}H_{20}N_4O$ (368)	75.00 (75.3)	5.40 (5.6)	15.20 (15.2)
8f	7-p anisidino	137-3 Ethanol	36.6 1	3053	1703	$C_{20}H_5N_3O_2$ (329)	72.90 (73.1)	45.00 (4.54)	12.70 (12.5)
8g	7-p cycohexylamino	260 Ethanol	20 1	3426	1676	$C_{19}H_{18}N_3O$ (305)	74.74 (75.2)	6.22 (6.1)	13.77 (13.7)
8h	7-(ethoxycarbonyl methyl amino)	260 Methanol	76 1	3420	1798	$C_{16}H_{13}N_3O_3$ (295)	65.00 (64.9)	4.40 (4.3)	14.20 (14.1)

7-hydrazino-6-(2-or 4 pyridinyl)-cyclopentyl[b]-pyridin-5-one(7i and 8i):

To a compound **5** or **6** (0.01 mol) in absolute ethanol (15 ml) and hydrazine hydrate (99%) (0.01 mol) dropwise with stirring, then the mixture was heated cender reflux for one hour, cooled and filtered. The separated solid was washed with ethanol, air dried and dried at 80°C for one hour. Crystallization from ethanol affords a yellow crystalline precipitate **7i** or **8i** (Table 3). IR (cm^{-1}) For **7i**: 3164-3058 ($NH-NH_2$), 1675 (co) 1598 (C=N), 1476 (C=C); For 10: 3165-3059 ($NH-NH_2$), 1676 (CO), 1598 (C=N), 1476 (C=C); ^{1}HNMR ($CDCl_3$): For **7i**: 1.84 (s, NH, D_2O exchangeable.), 7.15-7.21 (2d, 2H, 2-pyridyl), 8.34 (d, 1H, fused pyridine), 8.51-8.54 (d, 1H, Fused pyridine), 8.71 (t, 1H, fused pyridine), 10.95 (s, NH, D_2O exchangeable) ppm.; For **8i**: 2.11 (s, H, NH_2, D_2O exchangeable), 7.25-7.26 (2d, 2H, 4-pyridyl), 7.27-7.31 (2d, 2H, 4-pyridyl), 8.33 (d, 1H, fused pyridine), 8.36 (d, 1H, fused pyridine), 8.76 (t. 1H, fused pyridine), 11.19 (s, NH, D_2O exchangeable) ppm; EIMS (m/z): For **7i**: 240 $(M+2)^+$ (1.3%), 239 $(M+1)^+$ (15.03%), 238 (M^+) (100%).; For **8i**: 240 $(M+2)^+$ (1.27%), 239 $(M+1)^+$ (15. 44%), 238 (M^+) (100%).

Table 3: Physical data of compound **7i & 8i**

Comp.	m.p (°c)	Yield %	Molecular formula (mol. Wt.)	Analysis calcd (found)		
				C	H	N
7i	193	70	$C_{13}H_{10}N_4O$ 238	65.54 (65.41)	4.20 (4.1)	23.52 (23.71)
8i	196	65	$C_{13}H_{10}N_4O$ 238	65.54 (65.21)	4.20 (3.61)	23.52 (23.10)

7-(5-Arylidenehydrazino)-6-(2- or 4-pyridinyl)-cyclopenty[b]pyridin-5-ones (9a-f & 10a-f):

A mixture of compound **7i** or **8i** (0.01 mol), the appropriate aromatic aldehydes (0.01 mol) and ethanol (15 ml, 95%) was heated under reflux for appropriate time. The mixture was cooled, filtered and the solid was crystallized from a suitable solvent (Table 4). ^{1}HNMR ($CDCl_3$): For **9d**: 1.67 (s, H, NH, D_2O exchangeable of hydrazino), 7.09 (s, 1H of olefinic carbon), 8.16 (it, 1H, fused pyridine), 7.27-7.40 (2d, 2H, fused pyridine), 7.47-7.97 (2d, 2H, 2-pyridyl), 7.27-7.29 (2t, 2H, 2-pyridyl) ppm. For **12f**: 1.66 (s, 1H, NH, D_2O exchangeable of hydrazino), 7.08 (s, 1H, of olefinic carbon), 7.14-7.18 (2d, 2H, fused pyridine), , 7.19-7.23 (4d, 4H, 4-pyridyl), 8.13 (it, 1H, fused pyridine) ppm. EIMS (m/z): For **9d**, 342 (M^+) (2.98%); For **10d**: 342 (M^+) (25%).

Table 4: Physical data of compounds 9a-f and 10a-f

Comp. No.	R	m.p(°C) Cryst. Solvent	Yield (%) reaction time (hr)	IR (cm^{-1})		Molecular formula (mol.wt.)	Analysis Calcd. (Found)		
				NH	CO		C	H	N
9a	p-nitrobenzylidene	286-3 Methylene chloride	50 1	3448	1650	$C_{20}H_{13}N_5O_3$ (371)	64.60 (64.4)	3.50 (3.3)	18.80 (18.5)
9b	p-chlorobenzylidene	210-4 Ethanol	18 4	3449	1624	$C_{20}H_{13}ClN_4O$ (360.5)	66.50 (66.4)	3.80 (3.4)	15.50 (15.6)
9c	p-bromobenzylidene	220-5 Ethanol	90 1	3448	1677	$C_{20}H_{13}BrN_4O$ (405)	59.70 (59.2)	3.70 (3.5)	13.80 (13.5)
9d	o-flurobenzylidene	115-4 Ethanol	99 4	3400	1610	$C_{20}H_{13}FN_4O$ (344)	59.70 (59.3)	3.70 (4.1)	16.20 (16.6)
9e	m-flurobenzylidene	222-4 Ethanol	46 4	3420	1677	$C_{20}H_{13}FN_4O$ (344)	59.70 (59.7)	3.70 (3.6)	16.20 (16.1)
9f	p-flurobenzylidene	215-4 Chloroform, per ether	20 1	3043	1626	$C_{20}H_{13}FN_4O$ (344)	59.70 (59.9)	3.70 (3.6)	16.20 (16.4)
10a	p-nitrobenzylidene	293-4 Methylene chloride	44 1	3422	1678	$C_{20}H_{13}N_5O_3$ (371)	64.61 (64.2)	3.50 (3.1)	18.80 (18.2)
10b	p-chlorobezylidene	270-4 Ethanol	20 2	3448	1623	$C_{20}H_{13}ClN_4O$ (360.5)	66.50 (66.5)	3.80 (3.3)	15.50 (15.1)
10c	p-bromobenzylidene	270-4 Ethanol	84 4	3164	1678	$C_{20}H_{13}BrN_4O$ (405)	59.70 (59.7)	3.70 (3.6)	13.80 (13.4)
10d	o-flurobenzylidene	112-6 Ethanol	95 1	3400	1650	$C_{20}H_{13}FN_4O$ (344)	59.70 (59.6)	3.70 (4.1)	16.20 (16.1)
10e	m-flurobenzylidene	225-6 Ethanol	50 4	3100	1690	$C_{20}H_{13}FN_4O$ (344)	59.70 (59.6)	3.70 (4.1)	16.20 (16.5)
10f	p-flurobenzylidene	210-3 Chloroform	25 1	3047	1624	$C_{20}H_{13}FN_4O$ (344)	59.70 (60.1)	3.70 (3.4)	16.20 (16.1)

Evaluation of antiinflammatory activity:

Inflammation was induced in rats according to the method described by Winter et al.[21]. Group of 6 rats weighing 100-120 gm were given orally the test compounds in a single dose of 9.6 mg/kg.

One hour later, the animals were injected with 0.1 ml of 1% carrageenan solution in normal saline into the subplanter tissue of right hind paw. A control group was also used and it was given the same volume of distilled water as in the test groups. Another group of rats was treated with indomethacine in a dose of 2 mg/kg orally as a reference anti-inflammatory drug. The percentage of inhibition was calculated using the following formula:

$$\text{Percentage inhibition} = 100\ (1 - \frac{a - x}{b - y})$$

Where (x) and (a) are the mean foot volume of rats before and after the administration of carrageenan respectively in the test of treated group. Whereas (y) and (b) are the mean foot volume of rats before and after the administration of carrageenan in the control group.

RESULTS

The results show that compound **8g** is the most active anti-inflammatory agent ($P<0.001$), while compound **10f** is also active ($P<0.01$). Compounds **3,7b, 8b, 8c, 9e** are less active ($P<0.05$). The rest of compounds did not show any significant anti-inflammatory activity. The results are listed in table 5.

Table 5: Antiinflammatory effect of the test compounds.

Test compound	Volume of Paw (ml) after carrageen an Mean ± S.E.		Total increase in paw after 4 hr Mean ± S.E	% of inhibition
	O hr	4.0 hr		
Control	2.04±0.02	3.23±0.02	1.19±0.09	0
Indomethacine	208±0.03	2.43±0.02	0.35±0.07***	71
Compound 3	2.08±0.02	3.00±0.03	0.92±0.06*	23
Compound 4	2.02±0.02	3.14±0.04	1.12±0.08	6
Compound 7b	2.09±0.03	3.00±0.03	0.91±0.07*	24
Compound 7c	2.02±0.02	3.00±0.03	0.98±0.08	18
Compound 7d	2.03±0.02	3.02±0.04	0.99±0.08	17
Compound 7f	2.09±0.03	3.11±0.03	1.02±0.07	14
Compound 8b	2.05±0.03	2.09±0.03	0.85±0.07*	29
Compound 8c	2.05±0.03	2.99±0.02	0.94±0.06*	21
Compound 8d	2.04±0.02	3.3±0.04	1.26±0.08	-6
Compound 8f	2.03±0.02	3.17±0.04	1.14±0.10	4
Compound 8g	2.08±0.02	2.50±0.02	042±0.07***	65
Compound 8h	2.08±0.03	3.37±0.04	1.29±0.09	-8
Compound 8i	2.04±0.02	3.33±0.02	1.29±0.09	-8
Compound 9a	2.08±0.03	3.11±0.03	1.03±0.08	13
Compound 9b	2.08±0.02	3.12±0.03	1.10±0.07	8
Compound 9c	2.4±0.02	2.97±0.03	0.93±0.06*	18
Compound 9f	2.03±0.03	3.18±0.04	1.15±0.10	3
Compound 10b	2.08±0.04	3.16±0.04	1.10±0.04	7
Compound 10d	2.08±0.03	3.15±0.03	1.07±0.08	10
Compound 10f	2.09±0.02	2.84±0.03	0.75±0.07**	37

* P<0.05. ** P<0.01 and *** P<0.001

Anticoagulant activity:

In this experiment, groups of 6 rats weighing 100-120 gm were given orally the test compounds in a single dose of 9.6 mg/kg according to Paget and Barmes[22]. Another group of 6 rats was kept as a control groups. Also a group of 6 rats was given phenindione (Dindivan) in the same previous dose, as standard anticoagulant-drug. After 24 hrs, 1.8ml of each blood sample withdrawn from retro-orbital vein of each rat using a capillary pipett, mixed with 0.2ml heparin and centrifuged at 3000 rpm for 15 min to obtain plasma. The obtained plasma was used for determination of prothrombin time (PT) according to the method of Dacie and Lewis[23]. International Normalised Ratio (INR) is calculated.

Results

The result show that compounds **8h, 9b** are active anticoagulant (as phenindione group) (P<0.01) while compounds **7b, 7c, 8d, 8i, 10b, 10d** and **10f** are less active (P<0.05). The rest of the test compounds did not show any significant anticoagulant activity. The results are listed in table 6.

Antimicrobial activity:

The anti-microbial screening of the test compounds **9d, 9e, 9f, 10d, 10e, 10f** against gram positive bacteria (*Staphylococcus aureus*), gram negative bacteria (*Escherichia coli*) was carried out using the disc diffusion method[24]. Whatman N 0.1 filter paper disc of 5 mm diameter were sterilized by autoclaving for 15 min at 121°C. The sterile discs were impregnated with different compounds (500 µg/disc). Agar plates were surface inoculated uniformly from the broth culture of the tested microorganism. The impregnated disc were placed on the medium suitably spaced apart and the plates were incubated at 5°C for 1 hr to permit good diffusion and then transferred to an incubator at 37°C for 24hrs, then examined for the inhibition zones caused by various compounds on the tested microorganisms. The activities listed in table 7 are expressed by the terms moderately active (++), slightly active (+) and not active (-).

Results

As a regard, the antimicrobial activity compound **9f** is the most active against *Staphlococcus aureus* and compound **9e** is the most active against *Escherichia coli*.

Table 6: Anticoagulant effect of the test compounds.

Test Compounds		Prothrombin time (sec) Mean + S.E.	I.N.R.
Control		11.25±0.39	-
Phendione		14.53±0.61	1.26
Compound	3	12.64±0.53	1.10
Compound	4	11.92±0.58	1.03
Compound	7b	13.53±0.55*	1.17
Compound	7c	12.98±0.41*	1.13
Compound	7d	12.68±0.58	1.10
Compound	7f	12.12±0.43	1.05
Compound	7i	12.13±0.52	1.05
Compound	8b	13.1±0.69	1.14
Compound	8c	12.99±0.85	1.13
Compound	8d	13.35±0.48*	1.16
Compound	8e	13.09±0.59	1.14
Compound	8f	13.16±0.77	1.14
Compound	9g	12.61±0.49	1.10
Compound	8h	13.63±0.51**	1.18
Compound	8i	13.19±0.54	1.14
Compound	9a	12.98±0.49	1.13
Compound	9b	14.11±0.68**	1.22
Compound	9c	12.13±0.52	1.05
Compound	9e	13.2±.53*	1.15
Compound	10f	12.13±0.52	1.05
Compound	10b	13.22±0.49*	1.15
Compound	10d	13.91±0.68*	1.21
Compound	10f	13.71±0.69*	1.19

* P<0.05 and **P<0.01

Table 7: **Antibacterial screening of the test compounds**

Comp. No.	*Staphlococcus aureus*	*Escherichia coli*
9d	+	-
9e	-	++
9f	++	-
10d	-	-
10e	-	+
10f	-	-

++ = moderately active
+ = slightly active
- = not active

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تشييد بعض مشتقات سيكلوبنتيل (ب) بيريدين-٥- أونات وتقييمها كمضادات للالتهابات والتجلط والميكروبات

رفعت حسين عمر- مكارم محمد سعيد - [*] حسام الدين عبد الحميد أحمد-
[**] عادل حسين عمر - [***] أحمد بكر محمود

قسم الكيمياء العضوية – كلية الصيدلة – جامعة القاهرة

[*] قسم الكيمياء العضوية – كلية الصيدلة – جامعة قناة السويس

[**] قسم الفارما كولوجى و [***] الميكروبيولوجى – كلية الطب – جامعة المنوفية - مصر

قد تم تفاعل كينولينيك انهيدرايد (٢) مع ألفا أو جاما بيكولين لتحضير ٦-(٢- بيريدينيل) سيكلوبنتيل [٣،٢ب] بيريدين ٥، ٧ دايون (٣) أو ٦-(٤-بيريدينيل) المماثل ٤. وقد تحولت المركبات الأخيرة ٣ أو ٤الى مشتقات الكلورو ٥ أو ٦ على التوالى . بالإضافة الى أن مشتقات الكلورو قد عوملت مع أمينات مختلفة لتحضير ٧ أو ٨ على الترتيب ومن جهة أخرى فقد تفاعل المركب ٥ أو ٦ مع هيدرازين هيدرات لتكوين ٩ أو ١٠الذى تم تكاثفهما مع الالدهيدات العطرية المختلفة لتحضير المركبات ١١ أو ١٢ على التوالى . وقد تم مسح البيولوجى لعديد من مشتقات سيكلو بنتل بيريدين -٥- أونات مثل ضد الالتهابات والتجلط والميكروبات . فالمركبات ٨ج و١٢ف قد أظهروا تأثير واضح ضد الألتهابات مقارنة بالاندوميثاثين. والمركبات ٨هـ و١١ب لهم فاعلية مماثلة ضد التجلوط مثل فينيندايون. أخيرا المركبات ١١ف و١١ى قد تأثير مضاد للبكتريا خاصة ضد ميكروب الاستاف أوريوس وايشيرشيا كولاى على الترتيب.