Journal of Al-Nahrain University Vol. 8(2), December, 2005, pp.1-6 Science

Synthesis of New 4-Aminoantipyrine Derivatives

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Abstract

Refluxing of 4-aminoantipyrine with propargyl chloride or 3-chloro propinyl chloride in the presence of triethylamine gave the 4-(amino-2-propinyl) antipyrine (2) or 4-[(aminopropinyl)-3-chloro)] antipyrine (5) respectively in good yield. When compound (2) was refluxed with secondary amines and paraformaldehyde in the presence of cuprous chloride, the corresponding Mannich Bases (4-10) were achieved, while the reaction of compound (5) with secondary amines in boiling ethanol gave the 4-(amino propinyl 3-alkyl/aryl amino) antipyrine (11-16) in quantitative yields. The intended compounds were identified by their IR, UV spectra and C.H.N. analyses data.

Introduction

In continuation of our research program directed towards the synthesis of novel heterocycles with potential biological applications [1-5], a new series of antipyrine systems linked to 1,3,4-oxadiazole, mercapto-1,3,4-oxadiazole, hydrazide and amide derivatives [6] has been prepared. A number of compounds containing antipyrine nucleus have been found to posses fungicical [7,8], herbicidal [9], antiinflammatory [10] and bactericidal [11,12] activities.

The above observations promoted us to synthesize a new series of antipyrine systems having the potentially biological active moieties.

Experimental

Melting points were determined on Gallen-Kamp MFB-600 melting point apparatus. IR spectra were recorded on a Pye-Unicam SP3-100 as KBr discs and films. The UV spectra were performed on a Hitachi/UV-2000 spectrophotometer. Elemental analyses of compounds were carried out on C.H.N. analyzer type 1160 (Carlo-Erba).

Preparation of 4-(amino-2-propynyl) antipyrine (2) [13]

To a stirring solution of compound (1) (0.01 mole) and triethyl amine (0.01 mole) in ethanol (25 ml), propargyl chloride (0.02 mole) was added drop-wise. The mixture was refluxed for (3 hrs) on a water bath. The excess of ethanol was removed under vacuum. The product was collected and recrystallized from chloroform (tables 1,4,7).

Preparation of Mannich bases (4-10) [14]

To a stirring solution of compound (2) (0.001 mole) and cuprous chloride (0.12 gm) in dioxane (50 ml) which was heated for few minutes, paraformaldehyde (0.001 mole) and secondary amine (0.005 mole) were added. The mixture was refluxed for (2 hrs) at (90 °C). After cooling, the formed precipitate was filtered off and recrystallized from ethanol (tables 1,4,7,8).

Preparation of 4-(amino propynyl-3-chloro) antipyrine (5) [15]

To a stirring solution of compound (1) (0.01 mole) in dry benzene (35 ml) and triethyl amine (3 ml), a solution of β-chloro propinyl chloride (0.02 mole) in dry benzene (20 ml) was added drop-wise. The mixture was refluxed for (2 hrs) on a water bath. After that the excess of benzene was distilled off, the precipitate collected, washed with 2% $NaHCO_3$, then with distilled water and recrystallized from ethanol (tables 3,5,6,7,8).

Preparation of 4-(amino propynyl-3-alkyl/aryl) antipyrine (11-16) [15]

To a stirring solution of compound (5) (0.01 mole) in ethanol (20 ml), secondary amine (0.03 mole) was added drop wise. The mixture was refluxed for (6 hrs). Excess of ethanol and secondary amine was distilled off, the product was collected, washed with 3% $NaHCO_3$, then with distilled water and recrystallized from ethanol (tables 3,6,7,8).

Results and Discussion

For the target compounds, the reaction sequence outlined in scheme (1) was followed: -

The 4-(amino-2-propynyl) antipyrine (2) have been smoothly prepared from the corresponding 4-amino antipyrine (1) with propargyl chloride and triethyl amine in ethanol. The infrared spectrum of the compound (2) clearly shows the main characteristics bands at 3240 cm^{-1} of (≡CH) stretching vibration, at 2100 cm^{-1} of (C≡C) stretching vibration and at 3200 cm^{-1} of (NH) stretching vibration [16].

Treatment of the synthesized acetylenic compound (2) under Mannich condition with morpholine, piperidine, dicyclohexylamine, N-

ISSN: 1814-5922

methyl aniline, piperazine, pyrrolidine and diethylamine yielded their corresponding Mannich bases (4-10).

The IR spectrum of compound (5) shows the disappearance of the band at 3240 cm^{-1} which has been assigned to (≡ CH) and the appearance of (C-N) stretching vibration at 1290 cm^{-1} which are good indications for the formation of Mannich bases [9,9]. The physical properties of compounds (4-10) are listed in table (2) and their structures have been confirmed on the bases of their UV and IR spectra (tables 4,5).

On the other hand, we investigated the reaction of 4-amino antipyrine (1) with β-chloro propinyl chloride and diethyl amine in refluxing dry benzene, 4-(aminopropinyl-3-chloro) antipyrine (3) was formed. The infrared spectrum of compound (3) shows the following characteristics absorption bands at 3200 cm^{-1} of (NH) stretching vibration, at 1680 cm^{-1} of (C=O) stretching vibration and at 690 cm^{-1} of (C-Cl) function.

Subsequent reaction of compound (3) with different secondary amines in refluxing ethanol for (6 hrs) and 4-(aminopropinyl-3-alkyl/aryl) antipyrine derivatives (11-16) were obtained.

The IR spectrum of compounds (11-16) show disappearance of the band at 690 cm^{-1}, which has been belonged to (C-Cl) function, and the appearance of (C-N) stretching vibration at 1110-1310 cm^{-1}.

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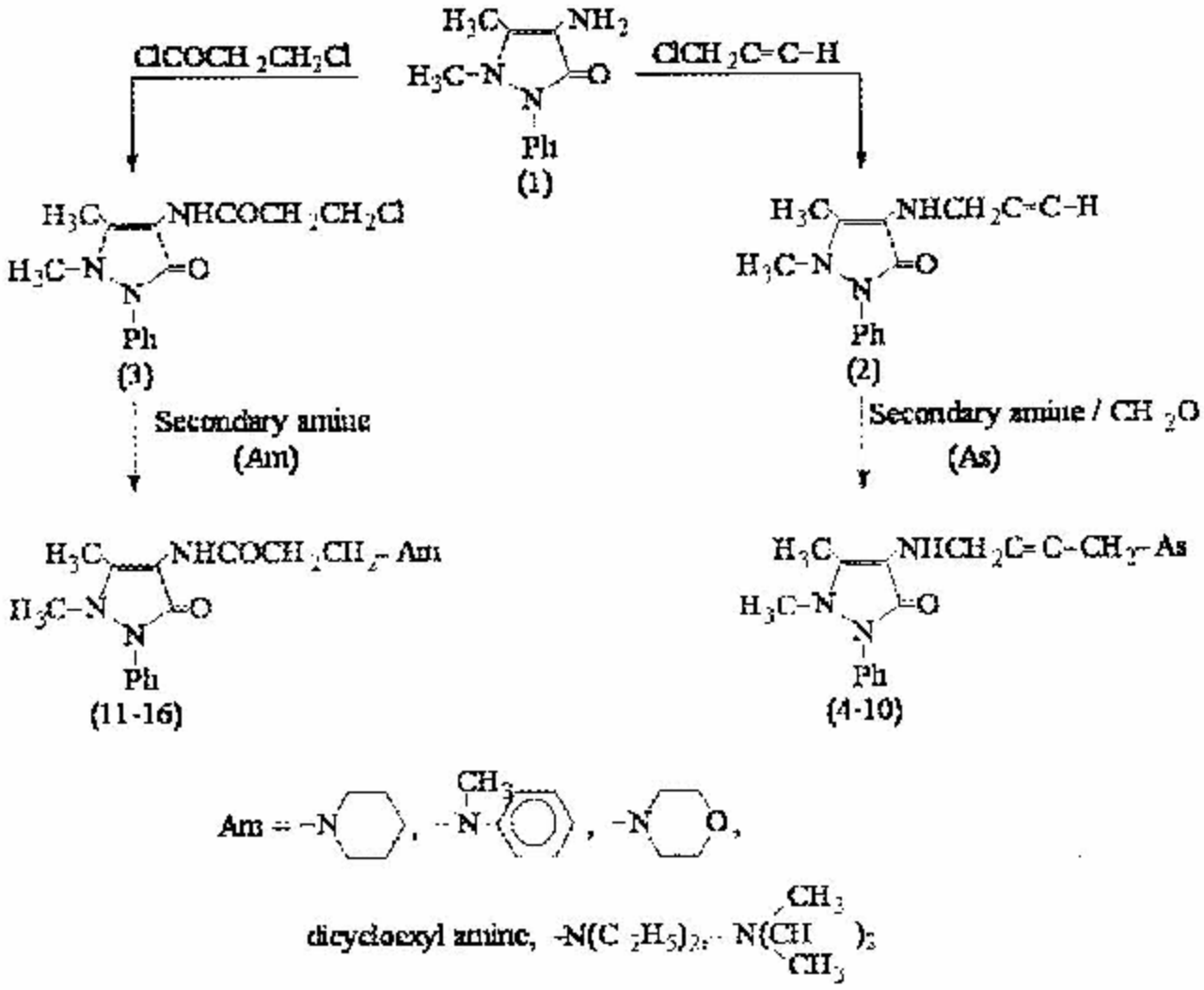
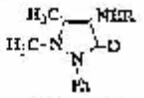

ClCOCH 2CH2Cl
ClCH 2C≡C–H
(1)
(3)
(2)
Secondary amine
(Am)
Secondary amine / CH 2O
(As)
(11-16)
(4-10)
Am = –N , –N , –N O,
dicyclohexyl amine, –N(C 2H5)2, –N( )2
As = –N , –N , –N O, dicyclohexyl amine,
–N N , –N , –N(CH3)2

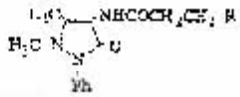
Scheme 1

Table (1): Physical properties of compound (2)



Comp. No.	-R	M.P. (°C)	Yield (%)	Purification solvent	Molecular formula
2	$-CH_2$ Cl	85-87	71	Chloroform	$C_{11}H_{11}N_3O$

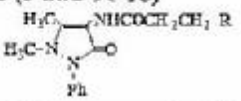
Table (2): Physical properties of Schiff bases (3-10)



Comp. No.	-R	M.P. (°C)	Yield (%)	Purification solvent*	Molecular formula
4		Oily	80	Chloroform	$C_{18}H_{22}N_4O_2$
5		Oily	88	Chloroform	$C_{20}H_{26}N_4O$
6		Oily	72	Chloroform	$C_{25}H_{36}N_4O$
7		Oily	84	Chloroform	$C_{22}H_{24}N_4O$
8		Oily	68	Chloroform	$C_{19}H_{29}N_5O$
9		Oily	79	Chloroform	$C_{20}H_{24}N_4O$
10		Oily	67	Chloroform	$C_{19}H_{24}N_4O$

* By column chromatography

Table (3): Physical properties of compounds (3 and 11-16)



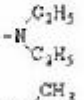
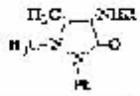
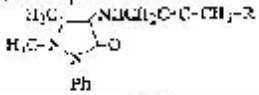
Comp. No.	-R	M.P. (°C)	Yield (%)	Purification solvent	Molecular formula
3	-Cl	156-158	87	Ethanol	$C_{14}H_{13}N_3O_2Cl$
11		181-183	63	Ethanol	$C_{19}H_{25}N_4O_2$
12		188-190	62	Ethanol	$C_{21}H_{19}N_4O_2$
13		182-184	63	Ethanol	$C_{19}H_{26}N_4O_2$
14		218-220	67	Ethanol	$C_{28}H_{32}N_4O_2$
15		190-192	59	Ethanol	$C_{18}H_{26}N_4O_2$
16		170-172	54	Ethanol	$C_{20}H_{30}N_4O_2$

Table (4): IR Spectral data of compounds (2)



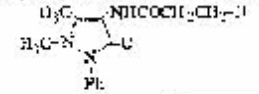
Comp. No.	R	υ(C-H) (cm^{-1}) aromatic	υ(C-H) (cm^{-1}) aliphatic	υ(C-H) (cm^{-1}) acetyl	υ(N-H) (cm^{-1})	υ(C=C) (cm^{-1})	υ(C-Cl) (cm^{-1})	υ(C=O) (cm^{-1})
2	$-CH_2C-CH$	3000	2820	3240	3200	2120	700	1640

Table (5): IR Spectral data of compounds (4-10)



Comp. No.	-R	υ(N-H) (cm^{-1})	υ(C-H) (cm^{-1}) aromatic	υ(C-H) (cm^{-1}) aliphatic	υ(C=O) (cm^{-1})	υ(C=C) (cm^{-1}) aromatic	Others (cm^{-1})
4		3200	3050	2900	1660	1590	υC-O 1200
5		3210	3000	2930	1670	1600	υC-N 1245
6		3210	3010	2960	1650	1580	υC-N 1290
7		3200	3010	2900	1680	1600	υC-N 1290
8		3240	-	2910	1650	1580	υC-N 1300
9		3200	3000	2930	1670	1600	υC-N 1350
10		3200	3000	2900	1680	1600	υC-N 1280

Table (6): IR Spectral data of compounds (3 and 11-16)



Comp. No.	-R	υ(N-H) (cm^{-1})	υ(C-H) (cm^{-1}) aromatic	υ(C-H) (cm^{-1}) aliphatic	υ(C=O) (cm^{-1})	υ(C=C) (cm^{-1})	Others (cm^{-1})
3	-Cl	3200	3000	-	1680	1600	υC-Cl 690
11		3180	3000	2840	1660	1580	υC-N 1280
12		3200	3050	2900	1680	1600	υC-N 1310
13		3200	3050	2870	1660	1580	υC-N 1280 υC-O 1110
14		3200	-	2860	1670	1590	υC-N 1260
15		3210	3020	-	1670	1610	υC-N 1240
16		3220	3000	2920	1670	1590	υC-N 1295

Table (7): UV Spectral data of some synthesized compounds

Comp. No.	λ_{max} EtOH (95%)
2	248.5, 269.5, 295.5, 392.5
4	317.5, 250, 269.5, 317.5, 392
5	312, 248, 270.5, 266
6	248.5, 270, 319.5, 382
7	318.5, 248, 275.5, 386
8	249, 274, 311, 385
9	319.5, 249, 271.5, 386
10	299.5, 261
3	248, 271.5, 292.5, 333
11	248, 274.5, 297, 323
12	219.5, 219.5, 259
13	248.5, 275, 293.5
14	249, 270, 298
15	248, 297
16	248.5, 269.5, 295.5, 392.5

Table (8): C.H.N analysis of some synthesized compounds

Comp. No.	C.H.N analysis % calculated (found %)		
	C %	H %	N %
3	69.86 (69.55)	5.74 (6.90)	17.15 (17.06)
4	42.56 (41.29)	4.09 (4.20)	9.65 (10.48)
15	50.20 (49.89)	6.04 (6.18)	13.01 (12.85)

الخلاصة

إن عملية ترميم الصور أو إزالة التشوه هي العملية التي يتم بواسطتها تقدير الصورة المثالية من تلك الحاوية على ضوضاء و تشوه والناتجة من تأثيرات عوامل عدة مختلفة مثل الحركة النسبية بين الجسم والكاميرا، اضطرابات الغلاف الجوي و الزيغ البصرية .

في هذا البحث ، تمت معالجة ترميم الصور المشوهة بتأثير اضطرابات الغلاف الجوي الملتقطة بواسطة الأقمار الصناعية باستخدام مرشحات الترميم الخطية غير المقيدة التي تعطي الحل بخطوة واحدة وبدون تكرار كالمرشح العكسي ومرشح وينر.