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Synthesis and Characterization of Some Spiro Pyrrolidine Compounds

Attallah M. Sheat[1], Mohammed S. Hussein*[2], Salih A.Abood[3]
[1]*Department of Chemistry, College of Science, University of Mosul, Iraq*
*[2]*Department of Chemistry, Faculty of Science, University of Zakho, Iraq*
[3]*Department of Biology, College of Science, University of Mosul, Iraq*
Email*[2]:mohammed.huseein@uoz.edu.krd

Abstract **- The present work includes the preparation of series of 2-Arylidine-1-tetralone (1-4) by reaction of 1-tetralone with some substituted benzaldehydes. Then the preparation of Schiff bases by reaction of benzyl amine with substituted benzaldehydes (5-9). The condensation of 2-Arylidine-1-tetralone (1-4) with Schiff base (5-9) in a strong medium to afford the new pyrrolidine [3] spiro [2`]-1`-tetralone (10-29). The structures of products were identified by physical and spectroscopic methods.**

Keywords **- pyrrolidine, spiro compounds, Schiff bases.**

I. INTRODUCTION

Among the various nitrogen-containing heterocycles, pyrrolidines have become important synthetic targets, as they constitute classes of compounds with significant biological activity [1]such as analgesic potency [2], antibacterial [3], dipeptidyl-4 peptidase inhibitors [4], histamine H3-receptor ligands [5], antimicrobial [6], and antitumor [7]. Some pyrrolidines also act as potent H3-antagonists [8].

The value of the pyrrolidines and their N-substituted analogues is not limited to the use of these compounds, but they can also be used as precursors for building other important compounds [9]. The same applies for the synthesis of Spiro compounds, which have cyclic structure fused at a central carbon, has drawn considerable attention of chemists as have their highly pronounced biological properties [10,11]. Spiropyrrolidine have acquired a prominent place owing to their presence in many pharmacologically relevant alkaloids, as typified by rhyncophylline, corynoxeine, mitraphylline, horsifiline, and spirotryprostatins[12]. Some of them are potential antileukaemic and anticonvulsant agents [13]. Also, they possess antiviral and local anaesthetic activities [14]. Many spiropyrolidine derivatives have been synthesized in our work by the 1,3-anionic cycloaddition of series of 2-Arylidine-1-tetralone with Schiff bases, of various substituted benzaldehydes, in a strong medium.

II. EXPERIMENTAL SETUP

Melting points were measured on Electrothermal 9300 (uncorrected). FTIR spectra were recovered using KBr disk Fourier-Transform, Tensor Co. Brucker, 2003, Germany. UV spectra were performed on Shimadzu UV-VIS Recording UN-160 Spectrophotometer using chloroform as a solvent. 1HNMR spectra were obtained from Brucker (400 MHz) Swiss, using CDCl3, as solvent, TMS as internal standard.

A. Preparation of chalcones (General procedure) [15]:

To an ice cooled mixture of aromatic aldehyde (0.01 mol) and 1-tetralone (0.01 mol) in 5 ml of absolute ethanol, add slowly with stirring 10 ml of 4% alcoholic potassium hydroxide solution in a period of 15 minutes. The stirring was continued for additional 3 hours, after completion of addition. The formed precipitate was then filtered off, washed with small amount of cold ethanol and recrystallized from ethanol to give the products (1-4). The names, some physical properties and spectral data were illustrated in table I.

B. Preparation of Schiff base (5-9) (General procedure) [16]:

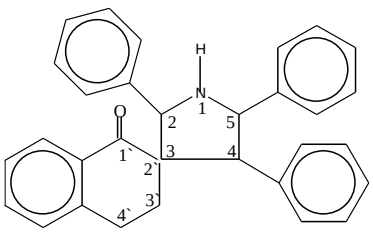
In a beaker 100ml, a (0.01 mol) of benzylamine, (0.01 mol) of aromatic aldehyde and (10 ml) of n-butanol were heated at (100^{o}C) for (10 min), cooled, the liquid products were purified by distillation. The names, some physical properties and spectral data were illustrated in table II.

C. Preparation of pyrrolidine (10-29) (General procedure) [17]:

In a 50 ml round-bottomed flask dissolve (0.001mol) of chalcone in 10ml) DMSO and (0.001 mol) of Schiff base was added, the mixture was magnetically stirred at room temperature for (10 min), then add (3) ml of (50%) sodium hydroxide solution dropwise. The stirring was continued for (3-4) hr at room temperature. Ice water was then added to the reaction mixture, the separated precipitates were washed with water until the filtrate became clear and neutral. The solid product was then dried and recrystallized from ethanol to give the products (10-29). The names, some physical properties and spectral data were illustrated in tables III & IV.

III.RESULTS AND DISSCUSION

Schiff bases [N-Arylidine benzylamine (5-9)] were added to [2-Arylidine-1-tetralone (1-4)] via 1,3-anonionic cycloaddition under strong basic conditions to afford the corresponding substituted spiro pyrrolidines [pyrrolidines [3] spiro[2`]-1`-tetralone (10-29)]. The product 10 is selected as a representative model in discussing the spectral data.



2,4,5-Triphenyl pyrrolidine [3] spiro[2`]-1`-tetralone (10)

The FT-IR spectrum [18], (Table 3), manifests a strong absorption band at (1670cm-1) corresponds to stretching vibration of carbonyl group compared with corresponding 2-benzylidine-1-tetralone (1) (1661cm-1) (Table I). This difference may be attributed to the absence of the conjugation. Another absorption band appeared at (1492cm-1) related to the bending vibration of N-H. the broad absorption band at (3446cm-1) is due to stretching vibration of N-H.

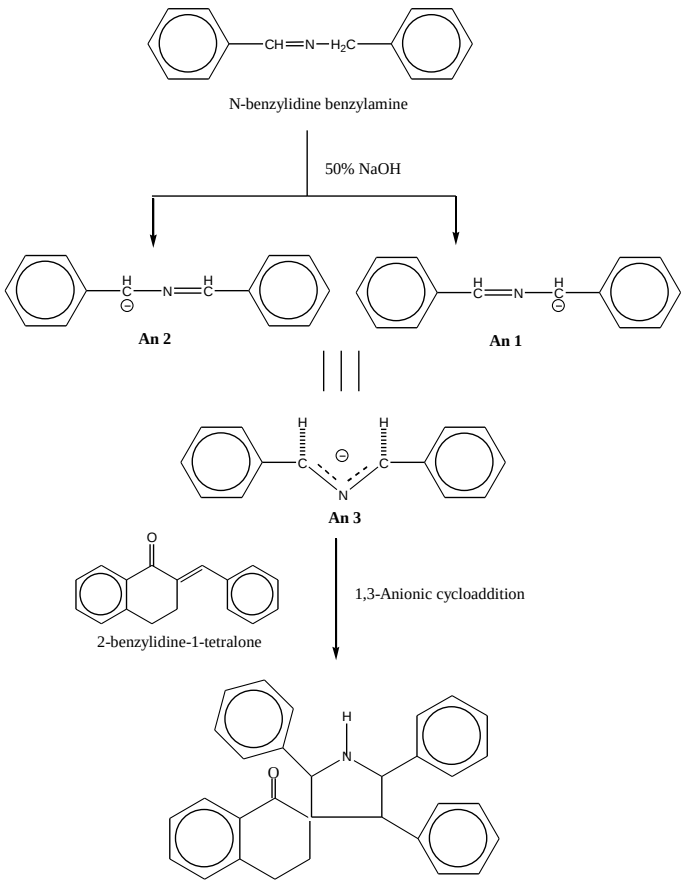
The U.V. spectrum [19,20], Table (3), shows a maximum absorption at wavelength= (258nm) which indicated a blue shift with respect to wave length of 2-benzylidine-1-tetralone (1) at (304nm).

The ^{1}H-NMR spectrum [21] shows a broad singlet signal resonates at δ (2.2) ppm (1H) related to N-H. A singlet signal at δ (5.8) ppm (1H) related to the methine proton at C-2. A doublet signal at δ (4.7) ppm (1H) attributed to the methine proton at C-4, another doublet signal is also shows at δ (5.1) ppm (1H) corresponds to the methine proton at C-5.

One triplet signal is resonating at δ (1.9) ppm (2H) attributed to methylene protons at C-3`, another triplet signal at δ (2.6) ppm (2H) attributed to methylene proton at C-4`. The aromatic protons are resonating as multiplet signal at δ (7-7.9) ppm (19H).

The suggested mechanism for the 1,3-anionic cycloaddition of N-benzylidine benzyl amine (5) to 2-benzylidine-1-tetralone (1) (as shown is scheme A) is initiated by the abstraction of the more acidic proton (benzylic) rather than the olefinic proton. Delocalization of the negative charge of An1 and An2 affording the resonance hybrid An3 (Scheme A) which in turn may attack the C=C of 2-benzylidine-1-tetralone via 1,3-anionic cycloaddition, which is analogous to the

synchronous cyclo addition of 2-azaalyllitium to stiblene[22] to afford final product (10).



2,4,5-Triphenyl pyrrolidine[3]spiro[2`]-1`-tetralone
Scheme (A)

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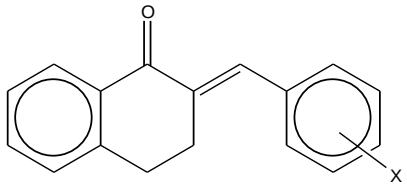
Table I

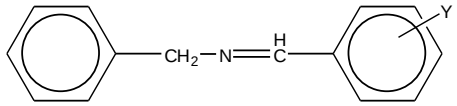
Names, some physical properties and spectra data of 2-Arylidine -1-tetralone (1-4)



Comp. No.	**X**	**m.p. (°C)**	**Yield (%)**	**Names of chlacones**	**U.V. $CHCl_3$ nm**	**FTIR (KBr) □ □cm^{-1}**		
						C=O	**C···C**	**C=C**
1	H	106-107	84	2-Benzylidine-1-tetralone	304	1660	1604	1589
2	2-Cl	60	80	2(*o*-Chlorobenzylidine)-1-tetralone	286	1661	1604	-
3	3,4-O-CH_2-O	126	78	2-(3,4-dioxymethylene benzylidine)-1-tetralone	352	1661	1602	1584
4	4-MeO	96	82	2(*p*-Methoxybenzylidine)-1-tetralone	340	1662	1600	-

Table II

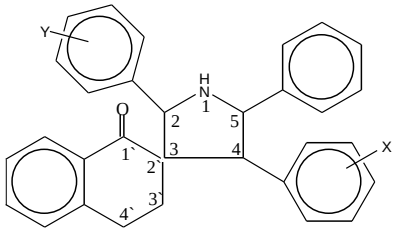
Names and some physical properties of prepared Schiffbases (5-9)



Comp. No.	**Name of Schiff bases**	**Y**	**b.p. (°C)**	**Yield (%)**	**Colour**	**U.V. $CHCl_3$ nm**	**FTIR (KBr) υ cm^{-1}**
5	N-Benzylidine benzylamine	H	276	76	Yellow	300	1645
6	N-(*o*-Chlorobenzylidine) benzylamine	2-Cl	-	72	Colorless	298	1655
7	N-(*p*-Bromobenzylidine) benzylamine	4-Br	262	80	Red	300	1658
8	N-(*p*-Methoxybenzylidine) benzylamine	4-OMe	200	68	Pale yellow	302	1653
9	N-(*p*-Chlorobenzylidine) benzylamine	4-Cl	122	83	Yellow	301	1658

Table III

Names and some physical properties and spectra data of spiro pyrrolidine (10-29)

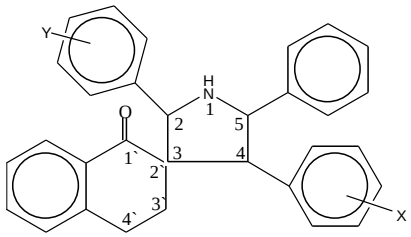


Comp. No.	X	Y	m.p. (°C)	Yield%	Names of spiro pyrrolidines	U.V. $CHCl_3$nm	FTIR (KBr) υ cm^{-1}			C⎓C Arom
							C=O	N-H Stret.	N-H Bend.	
10	H	H	140	80	2,4,5-Triphenyl pyrrolidine [3]spiro[2`]-1`-tetralone	252	1670	3339	1492	1598
11	H	2-Cl	125	77	2-(o-Chlorophenyl)-4,5-diphenyl pyrrolidine[3]spiro-[2`]-1`-tetralone	250	1672	3346	1488	1600
12	H	4-Br	75	85	2-(p-Bromophenyl))-4,5-diphenyl pyrrolidine[3]spiro-[2`]-1`-tetralone	258	1675	3446	1488	1601
13	H	4-OMe	58	69	2-(p-Methoxyphenyl))-4,5-diphenyl pyrrolidine[3]spiro-[2`]-1`-tetralone	258	1671	3324	1493	1601
14	H	4-Cl	78	75	2-(p-Chlorophenyl))-4,5-diphenyl pyrrolidine[3]spiro-[2`]-1`-tetralone	252	1674	3330	1490	1599
15	2-Cl	H	100	74	2,5-Diphenyl-4-(o-chlorophenyl) pyrrolidine [3]spiro[2`]-1`-tetralone	250	1670	3443	1492	1598
16	2-Cl	2-Cl	104	78	2,4-Di(o-chlorophenyl)-5-phenyl pyrrolidine [3]spiro[2`]-1`-tetralone	248	1667	3323	1488	1598
17	2-Cl	4-Br	112	88	2-(p-Bromophenyl)-4-(o-chlorophenyl)-5-phenyl pyrrolidine[3]spiro[2`]-1`-tetralone	244	1673	3320	1485	1599
18	2-Cl	4-OMe	106	82	2-(p-Methoxyphenyl)-4-(o-chlorophenyl)-5-phenyl pyrrolidine [3]spiro[2`]-1`-tetralone	250	1670	3320	1489	1598
19	2-Cl	4-Cl	115	80	2-(p-chlorophenyl)-4-(o-chlorophenyl)-5-phenyl pyrrolidine [3]spiro[2`]-1`-tetralone	254	1671	3326	1486	1599
20	3,4-O-CH_2-O	H	65	78	2,5-Diphenyl-4-(3,4-dioxymethylene phenyl) pyrrolidine[3]spiro[2`]-1`-tetralone	248	1671	3442	1488	1600
21	3,4-O-CH_2-O	2-Cl	62	66	2-(o-Chlorophenyl) -4-(3,4-dioxymethylene phenyl)-5-phenyl pyrrolidine [3]spiro[2`]-1`-tetralone	246	1672	3443	1488	1599
22	3,4-	4-Br	70	78	2-(p-Bromophenyl) -4-(3,4-	244	1674	3334	1487	1599

	O-CH_2-O				dioxymethylene phenyl))-5-phenyl pyrrolidine [3]spiro[2`]-1`-tetralone					
23	3,4-O-CH_2-O	4-OMe	75	70	2-(p-methylphenyl) -4-(3,4-dioxymethylene phenyl))-5-phenyl pyrrolidine [3]spiro[2`]-1`-tetralone	246	1671	3440	1487	1600
24	3,4-O-CH_2-O	4-Cl	66	81	2-(p-chlorophenyl) -4-(3,4-dioxymethylene phenyl))-5-phenyl pyrrolidine [3]spiro[2`]-1`-tetralone	250	1675	3417	1486	1599
25	4-OMe	H	60	68	2,5-Diphenyl-4-(p-methoxyphenyl) pyrrolidine [3]spiro[2`]-1`-tetralone	248	1672	3440	1490	1600
26	4-OMe	2-Cl	64	77	2-(o-Chlorophenyl) -4-(p-methoxy phenyl)-5-phenyl pyrrolidine [3]spiro[2`]-1`-tetralone	252	1670	3326	1492	1600
27	4-OMe	4-Br	80	90	2-(p-Bromoophenyl) -4-(p-methoxy phenyl)-5-phenyl pyrrolidine [3]spiro[2`]-1`-tetralone	246	1671	3382	1491	1600
28	4-OMe	4-OMe	74	84	2,4-Di(methoxyphenyl)-5-phenyl pyrrolidine [3]spiro[2`]-1`-tetralone	250	1672	3336	1492	1600
29	4-OMe	4-Cl	71	88	2-(p-Chlorophenyl) -4-(p-methoxy phenyl)-5-phenyl pyrrolidine [3]spiro[2`]-1`-tetralone	252	1673	3346	1490	1600

Table IV

^{1}HNMR spectra data of spiro pyrrolidines (10, 12)



Prod. No.	**X**	**Y**	**Proton N-H**	**Proton of Cppm**					
				C-2	**C-4**	**C-5**	**C-3`**	**C-4`**	**Aro. Pro.**
10	H	H	2.2 broad	5.8 Singlet(1H)	4.7 doublet(1H)	5.1 doublet(1H)	1.9 Triplet(2H)	2.4 Triplet(2H)	7-7.9 multiplet(19H)
12	H	Br	2.2 broad	5.8 singlet(1H)	4.7 doublet(1H)	5.1 doublet(1H)	1.9 Triplet(2H)	2.4 Triplet(2H)	7-7.9 multiplet(18H)