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Science Journal of University of Zakho

Vol. 6, No. 4, pp. 155 –159, Dec.-2018

p-ISSN: 2410-7549
e-ISSN: 2414-6943

SYNTHESIS AND SPECTRAL CHARACTERIZATION OF SOME NEW SUBSTITUTED BIS-SPIROCYCLOHEXANONES DERIVED FROM ACETONE

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Received: Jul. 2018 / Accepted: Nov., 2018 / Published: Dec., 2018 ***https://doi.org/10.25271/sjuoz.2018.6.4.548***

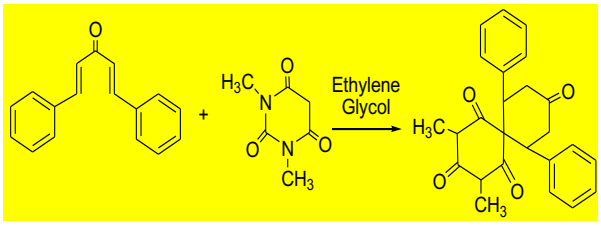
ABSTRACT:

Diarylidene acetones (DAA) (1-5) had been prepared by the condensation of acetone with substituted benzaldehydes via Claisen-Schmidt reaction, DAA's brought to condense with anthrone to afford the title compounds (6-10) through Michael addition. The structures of the products were suggested in the light of spectral data (UV, IR, 1H&13C-NMR).

KEYWORDS: Anthrone, spirocyclohexanones, Michael addition.

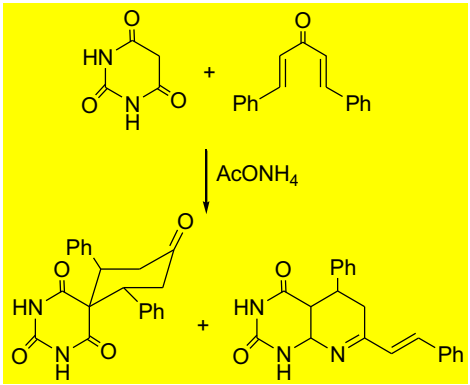
1. INTRODUCTION

Baeyer in 1900 was first used the name (Spirocyclane) (Rios, 2012).The quaternary carbon center and the presence of two fused rings cause a complexity of these ring structures. Natural Compounds that isolated from different plant sources are found to contain many Spiro cyclic structures (Smith and Baxendale, 2015). Spiro compounds have generated considerable interest in recent years due to their pharmacological activities (Ghandi et al, 2009; Raj and Raghnathan, 2003). Many Spiro compounds have been found to show anticancer, narcotic, anti-inflammatory and analgesic properties (Dandia et al, 2006; Sebahar and Williams, 2000; Ma and Hecht, 2004; Kang et al, 2002; Ding et al, 2005). Spiro compounds can be prepared by various methods (Jayashankaran et al, 2005; Khan et al, 2003; Marti and Carreira, 2005; Pearson, 2002; Ungureanu et al, 2001). But the reaction of dibenzalacetone with a compound having active methylene group yielding double Michael adduct would be an interesting subject of investigation. Aggarwal and co-worker carried out the reaction of dibenzylidene acetone and N,N-dimethyl barbituric acid in ethylene glycol (Aggarwal and Vij, 2014).



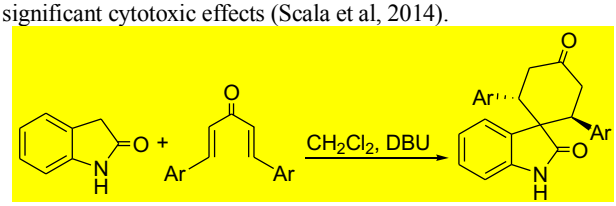
The reaction of dibenzylidene acetone and N,N-sub. barbituric acid.

Treatment of barbituric acid with dibenzylidene acetone in presence of ammonium acetate as a basic medium afforded a mixture of products (Assy et al, 2015).



The reaction of dibenzylidene acetone and barbituric acid.

Spiro[cyclohexanone-oxindoles] have been synthesized and evaluated in vitro for their antiproliferative effects against the protozoan Leishmania infantum. Interestingly, they appear able to kill L. infantum promastigotes and amastigotes, without significant cytotoxic effects (Scala et al, 2014).



Synthesis of spiro[cyclohexanone-oxindoles].

Wang and co-worker have developed a methodology for the construction of spiro[cyclohexanone-oxindoles] through cascade [5+1] Michael/Michael addition reactions between divinyl ketones and N-unprotected oxindoles catalyzed by combinations of cinchona-based chiral primary amines and α-amino acid derivatives. The final products were obtained with good diastereoselectivities and enantioselectivities (Wu et al, 2012).

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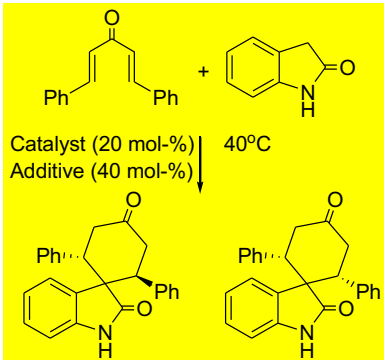


The reaction between divinyl ketones and N-unprotected oxindoles catalyzed by combinations of cinchona-based chiral primary amines and α-amino acid derivatives..

It had been witnessed in the last decade a growth of RCM (Rearranged Claisen-Michael) reaction as one of the powerful synthetic tools in organic synthesis (Grubbs and O'Leary, 2015). Its use in the synthesis of Spiro systems,however,was under-exploration. It was found that there are very few reports on the synthesis of Spiro cyclic compounds based on RCM reaction. It was conceived that a combination of Claisen rearrangement and RCM reaction-based methodology developed (Srikrishna and Vasantha Lakshmi, 2005).

In the present work a new class of Spiro compounds, bis-spirocyclohexanone with different substituted aryl group, are prepared by Michael reaction of diarylidene acetones with active methylene compound (Anthrone). The products of these reactions are of interest in terms of their stereochemistry and as starting materials for the synthesis of compounds with expected biological activity.

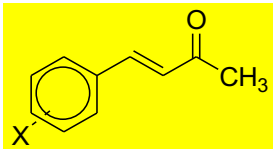
2. EXPERIMENTAL

2.1 Materials

Melting points were measured on Gallenkamp and uncorrected. UV-spectra were displayed using UV-visible spectrophotometer (1650-PC). IR spectra were recorded on FT-IR-600 Fourier-Transform infrared spectrophotometer.^{1}H-NMRspectra were recorded by Bruker spectrometer (400 MHz), using TMS as an internal standard and $CDCl_3$ / D_6-DMSO as solvents.^{13}C-NMR spectra were taken on Bruker spectrometer (75.5 MHz).

Condensation of acetone with benzaldehyde and substituted benzaldehydes

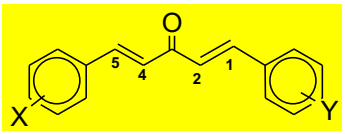
The steps of the original procedure had been followed to get arylidene acetones compared with the authentic samples showing a good agreement of their physical properties and spectral data. m.p. =38-40 °C, UV ($CHCl_3$ λmax.= 292nm), IR(KBr, ν cm^{-1}): 1666(C=O), 1612 (C=C), 1450 (C⋯C).



Structure of Arylidene acetone.

Condensation of arylidene acetones with different benzaldehydes (Al-Hamdany et al, 2014).

To a cold stirred mixture of the substituted benzaldehydes (0.03mole) and arylidene acetone (0.03 mole) in 50 ml absolute ethanol, 1 gm of potassium hydroxide was added in small portion to the mixture in a period of 15 min. The Stirring was continued for additional 1 h. at room temperature. The resulting precipitate was then filtered off, washed with a little amount of cold ethanol and recrystallized from ethanol to get a solid product(1,3-dibenzylidene acetone). Some physical properties and spectral data were illustrated in Tables (I, III, IV and V).



Structure of 1,3-Diarylidene acetone.

Table 1. Some physical properties of 1,3-diarylidene acetones

Comp. No.	X	Y	Name of compound	Color	m.p. (°C)	Yield (%)
1	H	H	1,5-diphenylpenta-1,4-dien-3-one	Yellow	99-100	50
2	2-Cl	4-Br	1-(4-bromophenyl)-5-(2-chlorophenyl) penta-1,4-dien-3-one	Pale Yellow	174-175	25
3	4-Br	4-MeO	1-(4-methoxyphenyl)-5-(4-bromophenyl) penta-1,4- dien-3-one	Yellow	178-180	50
4	H	3-NO_2	1-(3-nitrophenyl)-5-phenylpenta-1,4-dien-3-one	Pale Yellow	130-132	90
5	4-Br	4-Br	1,5-bis(4-bromopheny l)penta-1,4-dien-3-one	Pale Yellow	180-181	50

Condensation of Anthrone with DAA (Hussein, 2016).

A mixture of DAA (0.01 mole) and anthrone (0.01 mole) was magnetically stirred in the presence of 3ml of 50% NaOH in absolute ethanol. The stirring was continued for 2 hrs. at 50 °C in 10 ml DMSO. Some physical properties and spectral data were illustrated in Tables (II, VI, VII, and VIII).

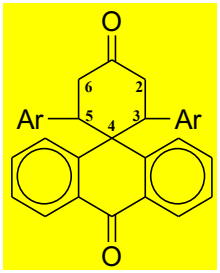


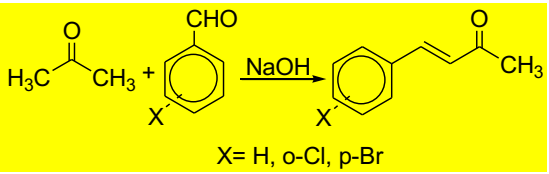
Fig. 7. Structure of final product (substituted Bis-spirocyclohexanones).

Table 2. Some physical properties of spirocyclohexanones

Comp No.	X	Y	Name of compound	Color	m.p. (°C)	Yield (%)
6	H	H	3,5-Diarylcyclohexanone Spiro [4,9'] anthrone	Pale paige	143-146	60
7	2-Cl	4-Br	3-(4-Bromophenyl)-5-(2-chlorophenyl cyclohexanone[4]Spiro[9] anthrone	Pale orange	133-134	40
8	4-Br	4-MeO	3-(4-bromophenyl)-5(4-methoxyphenyl cyclohexanone[4]Spiro[9] anthrone	Dark paige	166-167	11
9	H	3-NO_2	3-(phenyl)-5- (3-nitro phenyl)cyclohexanone [4] Spiro[9] anthrone	Brown	170-172	75
10	4-Br	4-Br	3,5-Di(4-Bromophenyl)-cyclohexanone Spiro [4,9'] anthrone	Paige	137-139	14

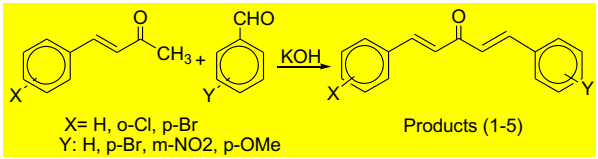
3. RESULTS AND DISSCUTION

The acidic protons of acetone had been used to get a condensation product by the addition of one mole of benzaldehyde or substituted benzaldehydes to afford arylidene acetone as shown below (Fig. 8):



The Condensation of Aceton with Benzaldehyde.

The condensation of arylidene acetones with another mole of the same or different substituted benzaldehydes gave diarylidene acetones DAA(1-5) as shown on (Fig. 9):



The Condensation of Arylidene Acetones with Benzaldehydes.

The spectral data (FTIR, U.V., ^{1}H-NMR and ^{13}C-NMR) of DAA compounds, which prepared from the condensation between Arylidene Acetones with Benzaldehydes, were consistent with the structures of (1-5), Tables (III, IV and V).

Table 3. spectral data (ftir, uv) of 1,3-diarylidene acetones

Comp. No.	U.V. $CHCl_3$ nm	FTIR (KBr) cm^{-1}		
		C=O	*C...C*	*C=C*
1	320	1651	1446	1626
2	340	1653	1490	1618
3	336	1650	1510	1593
4	318	1668	1589	1624
5	334	1649	1487	1624

Table 4. spectral data (^{13}C-NMR) of 1,3-diarylidene acetones

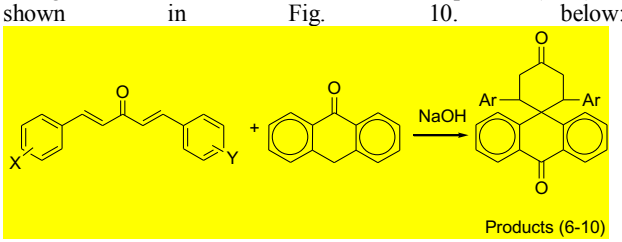
Comp. No.	^{13}C-NMR δ ppm			
	C-2, C-4	*C-1, C-5*	*C=O*	*Ar-C*
1	131	152	188	127-129
2	130	151	188	127-132
3	130	152	188	115-132
4	132	153	188	126-130
5	131	151	188	122

Table 5. spectral data (1h-NMR) of 1,3-diarylidene acetones

Comp. No.	^{1}H-NMR δ ppm				
	H-2	*H-4*	*H-1*	*H-5*	*Ar-H*
1	6.7d (1H)	7.1d (1H)	7.99d (1H)	7.7d (1H)	7.2-7.4m (10H)
2	6.7d (1H)	7.1d (1H)	8.1d (1H)	7.8d (1H)	7.2-7.4m (8H)
3	7.1d (2H)		7.7d (2H)		6.8-7.5m (8H)
4	7.1d (1H)	7.4d (1H)	7.7d (1H)	7.8d (1H)	7.2-8.3m (8H)

Comp. No.	^{1}H-NMR δ ppm				
	H-2	*H-4*	*H-1*	*H-5*	*Ar-H*
5	7.1d (2H)		7.7d (2H)		7.3-7.4m (8H)

The prepared DAA's (1-5) had been condensed with anthrone in a strong basic medium to afford the title compounds (6-10) as shown in Fig. 10. below:



Michael Condensation of Anthron with DAA.

The FT-IR spectrum of products (spiro cyclohexanone 6-10) manifests a strong absorption band at (1715cm^{-1}) corresponds to stretching vibration of carbonyl group compared with corresponding 1,3-diarylidene acetones compounds (1653cm^{-1}) (Table III). This difference may be attributed to the absence of the conjugation and cyclization. Another absorption band appeared at (1606cm^{-1}) related to the stretching vibration of aromatic ring. The U.V spectra showed wavelengths at maximum absorption (λmax) 332-386 nm (Table VI).

The ^{1}H-NMR for compound (6) as a representative model for the series showed a doublet signal for 4H resonates at δ 2.7 ppm for H-2 & H-6, while a triplet signal displayed at δ 3.6 attributed to 2H of H-3 and H-5. The aromatic 18H seemed as a multiplet signal at a range of δ 7.13 -7.87. ^{13}C-NMR showed a signal at δ 45 for C-2 and C-6, δ 40 for C-3 and C-5, δ 56 for C-4. but a signal at δ 190 related to C=O of anthrone, finally δ 212 belongs to C=O of C-1, Tables (VII and VIII).

Table 5. spectral data (ftir, uv) of spirocyclohexanones

Comp. No.	U.V. $CHCl_3$ nm	FTIR (KBr) cm^{-1}	
		C=O	*C...C*
6	332	1639	1601
7	386	1715	1606
8	340	1637,1710	1616
9	344	1637	1616
10	382	1637 1710	1618

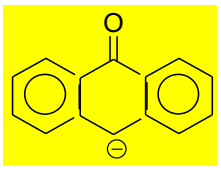
Table 6. spectral data (^{13}C-NMR) of spirocyclohexanones

Comp. No.	^{13}C-NMR δ ppm				
	C-2 , C-6	*C-3 , C-5*	*C-4*	*C=O of Anthrone*	*C=O of Cyclohexanone*
6	45	40	56	190	212
7	44 46	41 36	58	191	213
8	44	40	54	188	210
9	44	39	56	192	211
10	45	41	57	190	212

Table 7. spectral data (^{1}h-NMR) of spirocyclohexanones

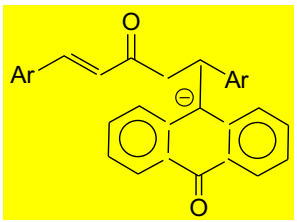
Comp. No.	^{1}H-NMR δ ppm		
	H-2 , H-6	*H-3 , H-5*	*Ar-H*
6	2.7d (4H)	3.6t (2H)	7.1-7.8m (18H)
7	2.6d (4H)	3.5t (2H)	7.1-7.9m (16H)
8	2.5d (4H)	3.6t (2H)	6.8-7.9m (16H)
9	2.6d (4H)	3.4t (2H)	7.2-7.9m (17H)
10	2.7d (4H)	3.7t (2H)	7.1-7.9m (16H)

The suggested mechanism for the reaction of (DAA) and anthrone described in fig. 13. It may follow the formation of the anion, fig. 11, which may in turn attack the α, β unsaturated system of the (DAA) through two stages:

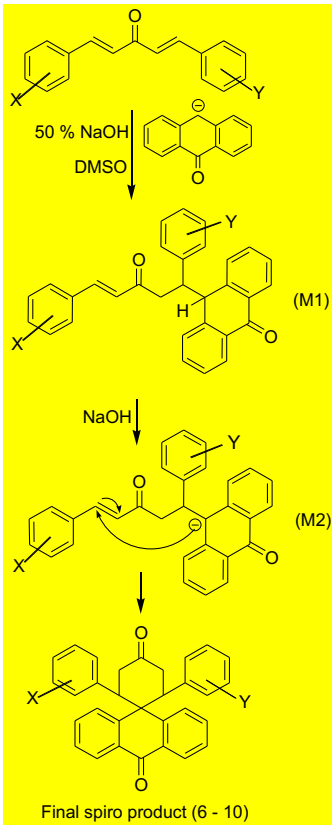


Structure of the first anion.

The anion may attack the β – carbon via Michael addition to afford M1, which may lose another acidic proton under the strong basic conditions to afford the second anion, fig. 12, which in turn may attack the β' – carbon via intramolecular Michael addition to produce the expected final spiro product.



Structure of the second anion.



The suggested mechanism for the reaction of (DAA) and anthrone to produce the expected final spiro product.

4. CONCLUSION

The two acidic protons of anthrone were the basis of the reaction, i.e. under strong basic conditions these protons will be abstracted to afford the corresponding carbanions which act as nucleophiles added as intermolecular Michael addition to DAA's to give the Spiro products.

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Science Journal of University of Zakho

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p-ISSN: 2410-7549
e-ISSN: 2414-6943