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New Conjugated Systems Derived from Piperazine-2,5-dione

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ABSTRACT. The preparation of mono arylidene and both symmetrical and unsymmetrical bis-arylidene derivatives of piperazine-2,5-dione is described. The use of 1,4 diacetyl piperazine-2,5-dione make it possible to prepare unsymmetrical bis-arylidene. The introduction of Dicyanomethylene moiety in the para position of one of the arylidene groups gave remarkable deepening in the colour of the resulting compound **11.**

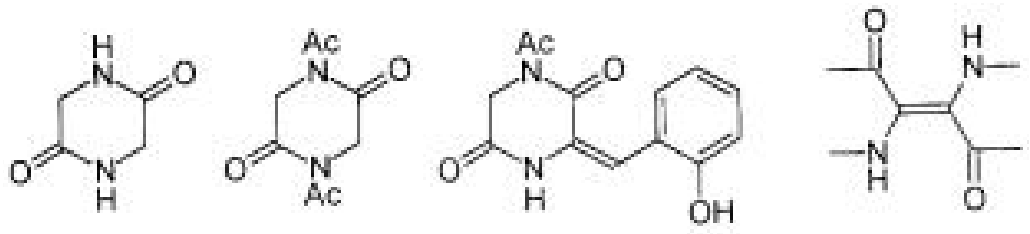
Introduction

The chemistry of piperazine-2,5-dione **1** is of great interest since many natural products possess its ring system[1-3]. Derivatives of **1** are useful in peptide synthesis[4], in synthesis of pyrazines[5-6], and in Diels-Alder reactions as 4π components[7]. Recent study showed that 3-salicylidene (piperazine-2,5-dione) **3** was supposed to be the most promising precursor for the synthesis of spiro[benzofuran-2(3H)3'-piperazine]-3',6'-dione as main skeleton of aspirochlorine[8-9].

The structural similarity of derivative **3** to the chromophore of indigo **4,** led us to assume that if the arylidene (piperazine-2,5-dione) could be obtained with donor-acceptor substituents, then merostabilization of the excited state[10] should occur to give deeply coloured compounds that might be novel dyestuffs. This paper deals with the synthesis of mono and bis-arylidene derivatives possessing donor and acceptors substituents.

Results and Discussion

Piperazine-2,5-dione **1** was prepared by self-condensation of glycine according to the literature method[4]. 1,4-diacetylpiperazine-2,5-dione **2** was prepared by treating compound **1** with acetyl chloride at room temperature[11].

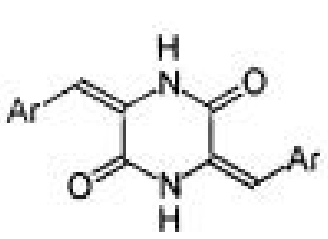


1 2 3 4

Symmetrical Bis-arylidene Derivatives

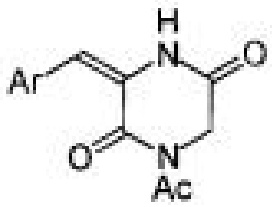
Condensation of compound **1** with two equivalents of thiophene-3-carboxaldehyde and indole-3-carboxaldehyde afforded the corresponding bis-arylidenes **5** and **6** respectively.

Compound **5** showed an NH absorption at 3266 cm^{-1}, a band at 1683 cm^{-1} for the carbonyl group and 1625 cm^{-1} for C = C (See Table 2).



5 ; Ar= 3-thienyl

6; Ar = 3-indolyl



7; Ar = 3-C_4H_3S

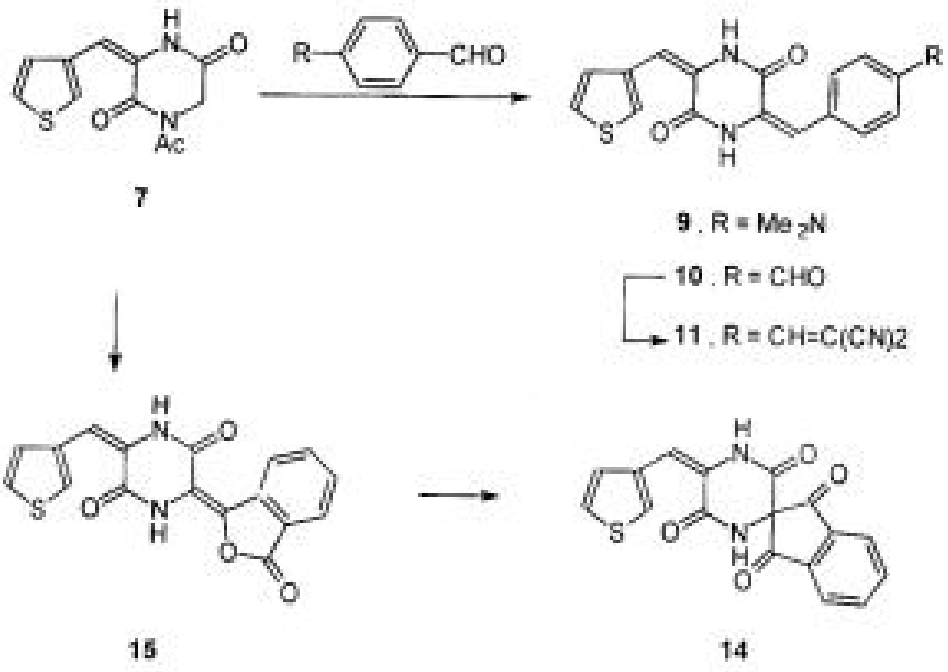
8; Ar = 4-$Me_2NC_6H_4$

Mono Arylidene and Unsymmetrical Bis-arylidene Derivatives

Condensation of piperazine-2,5-dione **1** with aromatic aldehyde always afforded symmetrical bis-arylidene derivative. However condensation using 1,4-diacetylpiperazine-2,5-dione **5** with aldehydes could be controlled to occur stepwise. Two novel monoarylidene **7** and **8** were synthesized from the reaction of equal molar quantity of **2** and the appropriate aldehyde.

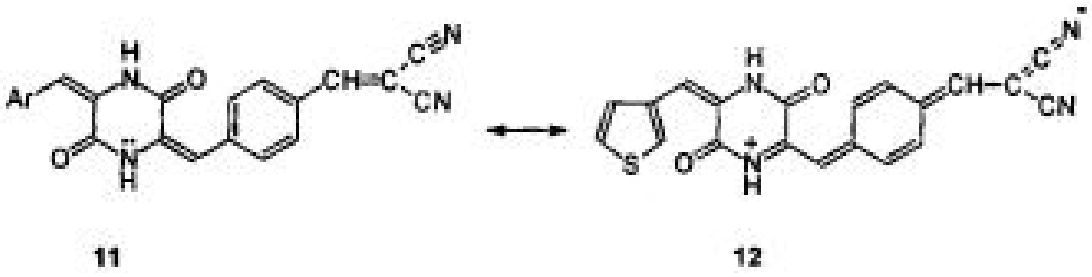
The H^1-NMR spectrum of compound **7** showed a singlet at δ 4.5 ppm attributed to the methylene signal indicative of mono arylidene derivative. Its ir spectrum showed an NH absorption band at 3255 cm^{-1} and broad bands at 1693 cm^{-1} and 1661 cm^{-1} for the two C = O groups.

The unsymmetrical diaryldene derivatives were prepared from the mono arylidene derivatives **7** and **8** as shown in Scheme 1.



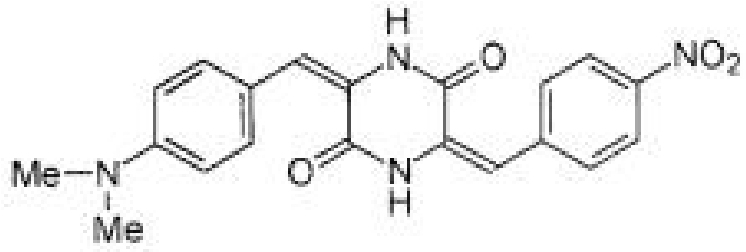
SCHEME 1

Compound **10** was synthesized by condensing one equivalent of compound **7** with the equivalent amount of terphthaldehyde in dimethylformamide at room temperature. Its ir spectrum showed an absorption band at 1705 cm^{-1} for the aldehydic C = O group of the free aldehyde. Compound **10** was readily undergo knovenagel condensation with active methylene compounds readily. Thus the treatment of the aldehyde derivative **10** with malononitrile using piperidene as a base to afford the red dicyanomethylene adduct **11** in good yield (Scheme 1). The ir spectrum of the later showed a CN absorption band at 2197 cm^{-1}. The introduction of the powerful electron withdrawing group CH = $C(CN)_2$ into the para position of the phenyl group in compound **11** gave a remarkable deepening in colour when compared with the yellow compound **10.** This deepening in colour is believed to be due to the stabilization of half of the molecule brought about by the hybrid resonance **12** (Scheme 2).



SCHEME 2

To get a clear insight of this colour change we synthesized two other bis arylidene derivatives **13** and **14** which both contains a donor group on one arylidene and an acceptor on the other one. Compound **14** was prepared from the mono arylidene **7** and phthalic anhydride in good yield. The formation of the 1,3-dione derivative **14** is believed to be via the intermediate **15.** The structure of compound **14** was followed from its ir spectrum which showed an absorption for the carbonyl groups of the 1,3-diketone moiety at 1670 cm^{-1} which expected to appear at wavenumber greater than 1750 cm^{-1} for compound **15.**



13

Experimental

Melting points were recorded on a Thomas-Hoover capillary melting apparatus without correction. IR spectra were taken as KBr disk on a Nicolet Magna 520 FT IR spectrometer, ^1H NMR were recorded solution in $CDCl_3$ on a Brucker DPX 400 MHz spectrometer using TMS as internal standard. Microanlyses were carried out using a Perkin Elmer 240B Analyzer.

The following compound were prepared by the literature methods reported previously: Piperazine-2,5-dione **1,** m.p. > 300ºC [lit.[4] m.p. > 300ºC]; 1,4-diacetylpiperazine-2,5-dione **2,** m.p. 98-100ºC [lit.[11] m.p. 99-100.5ºC].

3,6-di(3-thienylidene) piperazine-2,5-dione 5 and 3,6-di(3-indolylidene) piperazine-2,5-dione 6

A mixture of piperazine-2,5-dione **1** (0.01), the appropriate aldehyde (0.02 mol) and anhydrous acetate (0.04 mole) in acetic anhydride (15 ml) was refluxed for 5 hours. The mixture was cooled and washed with water, filter and washed with small amount of ether (see Tables 1 & 2).

1-Acetyl-3-(3-thienylidene) piperazine-2,5-dione 7 and 1-acetyl-3-(4-dimethyl aminobenzylidene) piperazine-2,5-dione 8

A mixture of 1,4-diacetylpiperazine-2,5-dione **2** (0.01 mol), the appropriate aldehyde (0.01 mole) and triethylamine (0.01 mole) was stirred at room tem-

perature for 12 hr. The resulting precipitate was filtered off and washed with water. Recrystallization from ethanol gave the pure monosubstituted derivatives **7** and **8** (see Tables 1 & 2).

TABLE 1. Physical and analytical data of synthesized compounds.

Comp. d no.	Yield (%)	M.P. (C)	Colour of crystals	Molecular formula	Calculated (%)			Found (%)		
					C	H	N	C	H	N
5	73	> 340	Yellow	$C_{14}H_{10}N_2O_2S_2$	55.63	3.31	9.27	55.11	3.52	10.12
6	85	> 340	Yellow	$C_{22}H_{14}N_4O_2$	72.13	3.83	15.3	71.88	3.94	15.5
7	86	> 320	White	$C_{11}H_{10}N_2O_3S$	52.80	4.00	11.2	52.65	3.85	11.1
8	80	> 320	White	$C_{15}H_{17}N_3O_3$	62.72	5.92	14.6	62.54	6.11	14.8
9	92	> 320	White	$C_{18}H_{17}N_3O_2S$	63.71	5.01	12.4	63.66	5.33	12.11
10	89	> 300	Yellow	$C_{17}H_{12}N_2O_3S$	62.96	3.70	8.64	62.75	3.86	8.75
11	87	> 340	Dark Red	$C_{20}H_{12}N_4O_2S$	64.52	3.22	15.05	64.32	3.42	15.38
12	94	> 340	White	$C_{20}H_{18}N_4O_4$	63.49	4.76	14.82	63.22	4.85	14.95
13	92	> 340	White	$C_{18}H_{10}N_2O_4S$	61.71	2.86	8.00	61.52	2.98	7.81

TABLE 2. IR and ^{1}H-NMR data of synthesized compounds.

Comd. no.	δ			ν_{max} / cm^{-1}			
	NH	Ar-H + – CH = C –	Other	NH	C = O	C = C	Other
5	10.34	6.70 - 7.90		3266	1683	1625	
6	10.84	7.10 - 8.40		3220	1702, 1665	1640	
7	11.11	6.82 - 7.61	4.5 (s, 2H, CH_2), 2.43 (s, 3H, CH_3CO)	3255	1693, 1661	1625	
8	10.34	7.00 - 7.55	4.42 (s, 2H, CH_2), 3.01 (s, 6H, $(CH_3)_2N$, 2.49 (s,3H, CH_3CO)	3320	1693, 1651	1609	
9	10.72	6.88 - 7.60	3.07 (S, 6H, $(CH_3)_2H$	3200	1683	1611	
10	11.85	6.95 - 7.60	9.80 (S, 1H, CHO)	3165	1694, 1682	1612	1705 (C = O)
11	10.72	6.81 - 7.90	8.3 (s, 1H, $CH = C(CN)_2$	3193	1688	1605	2197 (CN)
13	10.89	6.82 - 8.60	3.1 (s, 6H, $(CH_3)_2N$)	3225	1698, 1645		
14	10.85	6.66 - 8.20		3205	1670	1603	1695 (C = O)

General procedure for the preparation of unsymmetrical bis-arylidenes

3-(3-thienylmethylidene)-6-(4-Dimethylaminobenzylidene) piperazine-2,5-dione 9, 3-(3-thienylmethylidene)-6-(4-formylbenzylidene) piperazine-2,5-dione 10, and 3-(3-thienylmethylidene)-6-(1,3-dioxo-2-indanylidene) piperazine-2,5-dione 14

A solution of 1-acetyl-3-(3-thienylmethylidene) piperazine-2,5-dione 7 (0.01 mole), aldehyde (0.01 moles) and triethylamine (0.01 mole) in 25 ml of dimethylformamide was stirred at 25ºC for 12 hr. The precipitate was filtered and washed with water and small amount of cooled ethanol (10 ml). The pure samples were obtained after recrystallization from dimethylformamide (see Tables 1 & 2).

3-(4-Dimethylaminobenzylidene)-6-(4-nitrobenzylidene) piperazine-2,5-dione 13

This compound was prepared from 1-acetyl-3-(4-dimethylaminobenzylidene)-piperazine2,5-dione **8** (1.0 mmole) and 4-nitrobenzaldehyde (1.0 mmole) using the same general procedure mentioned above (see Tables 1 & 2).

3-(3-thienylmethylidene)-6-[4-(1,1-dicyanovinyl) benzylidene] piperazine-2,5-dione 11

Piperidine was added dropwise to a warm solution of the aldehyde **10** (0.5 g, 1.5 mmole) and malononitrile (0.1 g, 1.5 mmole) in ethanol (20 ml). A deepening in the colour of the solution was observed. The reaction mixture was refluxed for 3 hr, then cooled. A dark red solid was precipitated, filtered, and washed with cold ethanol and dried (see Tables 1 & 2).

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أنظمـة مقترحـة جديدة مشتقـة من بـبرازين-٢ و ٥-ثنائي أون

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جـــــدة - المملكة العربية السعودية

المستخلص . تم في هذا البحث تحضير مشتقات أريليدين الأحادية والثنائية المتجانسة وغير المتجانسة المشتقة من ببرازين-٢ و ٥-ثنائي أون ١ . استخدام مركب ١ و ٤-ثنائي أسيتايل ببرازين٢ جعل عملية التكاثف بين الألدهيد المستخدم وبينه تتم على خطوات بحيث تم التحكم في إضـافـة جـزيء واحـد فـقط ثـم بعـد ذلك تم التكاثف بين المركب الأحادي الأريلدين وبين الألدهيدات المختلفة عنه لتعطي مركبًا غير متماثل بالنسبة للاستبدال . وقد وجد أن استخدام ألدهيدات تحتوي على مجاميع ساحبة للإلكترونات يؤدي إلى تكوين مشتقات أغمق في اللون . وكذلك وجد أن استخدام المجموعة الساحبة القوية ثنائي سيانو الميثيلين في الموضع بارا في الألدهيد المستخدم للتكاثف نتج عنه تكوين مركب أحمر غامق .