Microwave Assisted Synthesis of Triphenodioxazines: A Novel and Convenient Approach

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Summary: A novel and economical method for the synthesis of triphenodioxazines is described. The method involves the oxidative cyclisation of the intermediates 2,5-bis-(arylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-dione in 95-97% sulphuric acid under microwave heating.

Introduction

Triphenodioxazines [TPDOs] have many applications in different fields of life, notably in the dyeing of many different materials [1-3]. These dyes have widespread use in dyeing a variety of fibres, such as textiles [4-5], leathers and papers [6-7]. They are also used in polymer based industry as dyes [8-9], and as polymer photo-stabilizers [10]. Their use as laser [11] and as fluorescent dyes are well documented [12]. TPDOs are also being used as components of printing inks [13], electrophotographic toners and developers, power coating materials and cosmetics [14]. Moreover, their use in optical recording systems and in optoelectronic devices such as optical computing, sensor protection and dynamic holography has also been reported [15].

The basic chemistry for the preparation of TPDOs involves either a cyclocondensation of *o*-aminophenol with *p*-chloranil or an oxidative cyclisation of 2,5-bis-(arylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-dione (*p*-benzoquinoes) intermediates. The cyclocondensation reactions may further be divided into two types i.e. direct and indirect methods. In the direct method, two equivalents of an *o*-aminophenol are condensed with one equivalent of *p*-chloranil in the presence of a base to neutralize the HCl generated during the condensation reaction. Such reactions usually work well in alcohol or water-alcohol mixtures or simply in aqueous medium [16-17]. In the indirect method, one equivalent of an *o*-aminophenol is condensed with *p*-chloranil to produce a l,2,4-trichloro-3H-aryloxazin-3-one intermediate, which on further condensation with another equivalent of an *o*-aminophenol gives symmetrical or unsymmetrical TPDO compounds [18]. On the other hand, oxidative cyclisations include the ring closure of the *p*-benzoquinones intermediates to form TPDOs. The advantage of this approach is the ready availability of anilines than the corresponding aminophenols. The ring closures of the intermediate *p*-benzoquinones normally require the use of very high boiling solvents such as nitrobenzene, chloronaphthalens or *o*-dichlorobenzene along with benzoyl chloride or *p*-toluenesulfonyl chloride [19-20]. In the patent literature persulfates, halogens, peroxides and oleum have also been used to accomplish the cyclisation of the intermediate *p*-benzoquinones [21-23]. Some alternative conventional methods employ concentrated sulfuric acid with additional oxidizing agent under reflux to obtain the cyclised product [24-25]. The percentage yields of many of these reactions are low accompanying a number of side products. Furthermore, the reaction times are lengthy and involve severe heating. Some improved and more modern methods include the use of hypervalent iodine reagents as oxidising agents [26]. As all of the oxidative cyclisations required heating, these could perhaps be much improved by the application of microwaves.

Results and Discussion

2,5-Bis(arylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-diones were prepared by the condensation of *p*-substituted anilines with *p*-chloranil using the reported methods [5, 27-28] with little modification. Acetone water mixture has been employed to partially solubilise the aromatic amines especially *p*-toluidine and *p*-anisidine (Scheme 1, Table-1).

For cyclisation of the intermediates **1-3**, microwave energy proved useful. The cyclisation step has been accomplished within 15-20 minutes under microwave conditions. In some of the reported methods conc. H_2SO_4 was used for cyclising the intermediates to TPDOs but the procedure involved

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heating the intermediate under reflux at higher temperature for much longer periods ranging from 9-12 hours and the percentage yield was also poor. Some other reported procedures used additional oxidizing agents with conc. H_2SO_4, and the reaction times were also longer [29-30]. In comparison to this microwave method provides the cyclised product within a very short time (Scheme 2) and has the potential to be used in flow injections methods to scale up the reaction. The novel microwave method routinely provides 70-75% (Table-2) of the isolated and purified yields of TPDOs **4-6**.

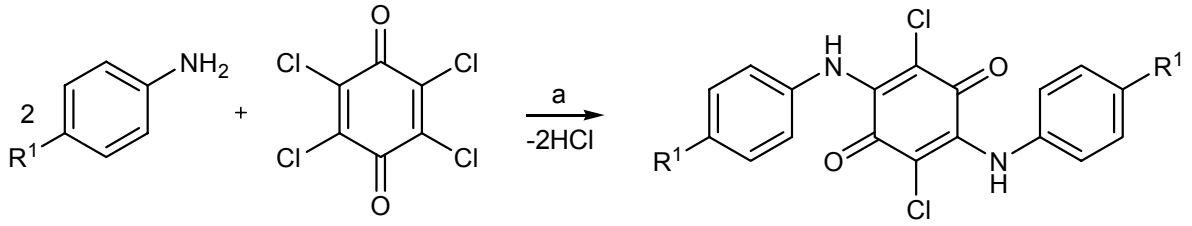
Table-1: Experimental conditions and isolated Percentage yields of 2,5-bis-(arylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-diones (1-3).

Sr. #	R^1	Reaction time (h)	Temp. (°C)	Isolated yield (%)
1	$-NH_2$	3.0	60	84
2	$-OCH_3$	3.0	55	87
3	$-CH_3$	4.0	55	86

Table-2: Experimental conditions and isolated percentage yields of 6,13-dichloro-3,10-disubstituted triphenodioxazines (4-6).

Sr. #	R^1	Reaction time (min)	Temp. (°C)	Isolated yield (%)
4	$-NH_2$	16	120	62
5	$-OCH_3$	15	120	73
6	$-CH_3$	20	120	71
7	$-NO_2$	50	120	--

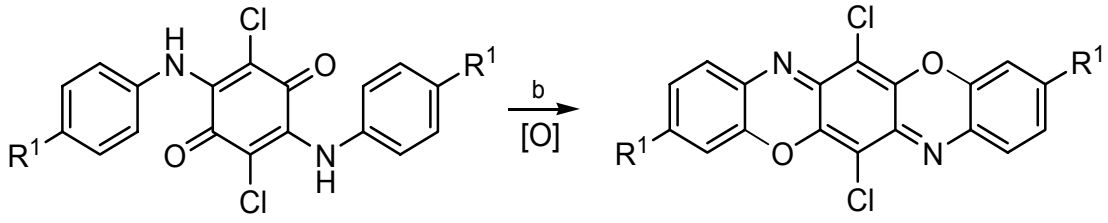
The yield was however 62% when intermediate **1** was cyclised to corresponding diaminotriphenodioxazine **4**. This may be explained by the presence of different reaction moieties in the structure **1**. These different functionalities may be involved in cyclisation, condensation and other substitution reactions. The electronic effects of the substituents at para position of the substituted *p*-benzoquinones had a great influence on the cyclisation process. Electron donating groups favoured the cyclisation whereas when electron withdrawing group like $-NO_2$ was used, no cyclisation was observed even when the microwave heating was continued for 50 minutes. The same effects are reported in literature [26]. With strong electron donating group like $-OCH_3$, the reaction was faster and completed within 15 minutes. So concluding the discussion we report herein a new microwave method for the preparation of triphenodioxazines [TPDOs] **4-6**. This new method has reduced the time of reaction from many hours to just 15 minutes and is highly economical as the oxidative cyclisation step is accomplished without any further addition of oxidizing agents in conc. H_2SO_4.



Aromatic amine *p*-Chloranil

R^1= NH_2: **1**; R^1= OCH_3: **2**; R^1= CH_3: **3**

Scheme 1: Preparation of 2,5-Bis(arylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-diones **1-3**. (a) water, of water.acetone mixture, Sodium bicarbonate, 60 °C.



R^1= NH_2: **1**; R^1= OCH_3: **2**; R^1= CH_3: **3**

R^1= NH_2: **4**; R^1= OCH_3: **5**; R^1= CH_3: **6**

Scheme 2: Preparation of 6,13-dichloro-2,9-disubstituted triphenodioxazines **4-6**. (b) 97% conc.H_2SO_4, Microwave irradiation, 50 W, 120 °C, 15-20min.

Experimental

General Information

All reagents were purchased from Aldrich and were used as received. The microwave instrument used was a CEM DISCOVERY having temperature control and pressure adjustment facilities. Melting points were determined using a Kofler hot stage apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker 400 MHz spectrometer. All NMR measurements were carried out at room temperature and chemical shifts are reported as ppm on the delta scale downfield from tetramethylsilane (TMS: δ = 0.00). Coupling constants (*J*) are reported in Hz. UV-Vis spectra were measured using a JASCO-v-570 spectrophotometer. Infrared spectra were recorded from KBr discs using a Nicolet Impact-410 FTIR spectrophotometer. The mass spectra were obtained using a VG Platform II Quadrupole spectrometer operating in the electron impact (EI, 70 eV) or atmospheric pressure chemical ionization (ApcI) modes, as stated. High resolution mass spectrometric data was obtained using the ionization modes specified. Elemental analyses were obtained using a Perkin Elmer 2400 Elemental Microanalyser.

A- Preparation of 2,5-bis-(arylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-diones (1-3)

2,5-Bis(4-aminophenylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-dione (1)

An aqueous suspension of *p*-chloranil (4.5 g, 18.5 mmol) and sodium bicarbonate (3.2 g, 38.1 mmol) in small portions was added to a stirred solution of *p*-phenylenediamine (4.0 g, 37.0 mmol) in water (40 ml) at ambient temperature and the stirring was continued for one hour. The temperature of the reaction mixture was slowly increased to 60°C and maintained for further two hours with stirring. The progress of the reaction was monitored by tlc [ethylacetate-hexanes (3ml : 7ml) and 2 drops of methanol]. The reaction mixture was then cooled and the resulting precipitates were filtered, washed extensively with water followed by ethanol and dried under vacuum. 2,5-B*is*(4-aminophenylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-dione **1** was obtained as a brown solid (6.05 g, 84%). A sample for analyses was purified by using silica gel column chromatography (2:3 EtOAc-hexane). Brown solid, m.p. > 300°C, ν_{max} (KBr)/cm^{-1} 3380, 3252, 1651, 1575, 1514, 1490, 1434, 1329, 1291, 1256, 1197, 1170, 1084, 1016, 890, 833, 757, 701, 650, 616, δ_H (DMSO-d_6) 5.98 (br. s, -NH_2), 6.71 (d, 4H, *J* = 8.5 Hz), 6.95 (d, 4H, *J* = 8.5 Hz), 9.57 (s, 2H, 2 x NH), Calc. for $C_{18}H_{14}Cl_2N_4O_2$: C, 55.54, H, 3.63, N, 14.39. Found: C, 55.54, H, 3.61, N, 14.32.

2,5-Bis(4-methoxyphenylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-dione (2)

An aqueous suspension of *p*-chloranil (4.5 g, 18.5 mmol) and sodium bicarbonate (3.2 g, 38.1 mmol) in small portions was added to a stirred solution of *p*-anisidine (4.56 g, 37.0 mmol) in water : acetone mixture (20ml : 20ml) at 45°C and the stirring was continued for one hour at this temperature. The temperature of the reaction mixture was slowly increased to 55°C and maintained for further two hours with stirring. The progress of the reaction was monitored by tlc [ethylacetate-hexanes (4ml : 6ml) and 2 drops of methanol]. The reaction mixture was cooled and the resulting precipitates were filtered, washed with water and ethanol and dried under vacuum. 2,5-B*is*(4-methoxyphenylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-dione **2** was obtained as a brown solid (6.75 g, 87%). A sample for analyses was purified by silica gel column chromatography (2:3 EtOAc-hexane). Brown solid, m.p. 296°C (decomp.), ν_{max} (KBr)/cm^{-1} 3221, 3013, 1651, 1609, 1568, 1510, 1486, 1417, 1322, 1306, 1244, 1195, 1171, 1112, 1032, 1012, 948, 894, 827, 800, 755, 737, 710, 696, 649, 622, δ_H (DMSO-d_6) 3.76 (s, 6H, 2 x OMe), 6.90 (d, 4H, *J* = 8.3 Hz), 7.11 (d, 4H, *J* = 8.3 Hz), 9.62 (s, 2H, 2 x NH), m/z (EI) 418 (M^+, (^{35}Cl), 64%), 386 (57), 350 (41), 250 (7), 174 (22), 146 (8), 108 (45), 84 (15), Calc. for $C_{20}H_{16}Cl_2N_2O_4$: C, 57.30, H, 3.85, N, 6.68. Found: C, 57.21, H, 3.84, N, 6.66.

2,5-Bis(p-tolylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-dione (3)

An aqueous suspension of *p*-chloranil (4.5 g, 18.5 mmol) and sodium bicarbonate (3.2 g, 38.1 mmol) in small portion was added to a stirred solution of *p*-toluidine (3.97 g, 37.0 mmol) in water : acetone mixture (20ml : 20ml) at 45°C and the stirring was continued for two hours. The temperature of the reaction mixture was slowly increased to 55°C and maintained for further two hours with stirring. The progress of the reaction was monitored by tlc [ethylacetate-hexanes (4ml : 6ml) and 2 drops of methanol]. The reaction mixture was cooled and the resulting precipitates were isolated by suction filtration. The residue was washed extensively with water followed by ethanol and dried under vacuum. 2,5-B*is*(*p*-tolylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-dione **3** was obtained as a green solid (6.17 g, 86 %). A sample

for analyses was purified by using silica gel column chromatography (2:3 EtOAc-hexane). Green solid, m.p. > 300°C, ν_{max} (KBr)/cm^{-1} 3232, 1648, 1610, 1561, 1510, 1475, 1404, 1322, 1307, 1248, 1198, 1172, 1109, 1034, 1020, 944, 890, 820, 800, 760, 739, 710, 695, 650, 628, δ_H (DMSO-d_6) 3.34 (s, 6H, 2 x Me), 7.05 (d, 4H, *J* = 8.2 Hz), 7.15 (d, 4H, *J* = 8.2 Hz), 9.63 (s, 2H, 2 x NH), m/z 388 (M^+, (^{35}Cl), 100%), 371 (17), 355 (51), 336 (9), 315 (38), 267 (32), 192 (17), 158 (19), 127 (78), 106 (23), 84 (53), Calc. for $C_{20}H_{16}Cl_2N_2O_2$: C, 62.03, H, 4.16, N, 7.23. Found: C, 61.90, H, 4.15, N, 7.21.

B- General procedure for the preparation of triphenodioxazines [TPDOs (4-6)]

The benzoquinoe intermediates 1-3 (0.32 mmol) in concentrated H_2SO_4 (97%, 2.5ml) were subjected to microwave irradiation at 120°C at 50 W Power for a period of 15 minutes. The reaction contents were cooled and poured into crushed ice (10g). The resulting precipitates were filtered under suction and washed with water until the filtrate showed no acidity. Analytically pure samples were obtained by dissolving a small quantity of a crude product in DMF and eluting the sample with 6 : 4 ethylacetate : petroleum ether on a silica gel column as reported in literature [26]. However the composition of eluting mixture was changed to get the better results. The products were further recrystallized from DMF. The percentage yield of the isolated and purified triphenodioxazine compounds are given in the Table-2.

2,9-diamino-6,13-dichlorotriphenodioxazine (4):

The compound **4** was prepared from the oxidative cyclisation of the intermediate 1 (0.32 mmol, 125 mg) under microwave heating using the general method B. Wine red powder, yield (62%, 76.7 mg), m.p. > 300°C, λ_{max}(DMF)/nm 560, ν_{max} (KBr)/cm^{-1} 3345, 3219, 2364, 2342, 1529, 1445, 1318, 1271, 1242, 1208, 1130, 1024, 898, 873, 778, 620, δ_H (DMSO-d_6) 6.02 (br. s, 4H, 2 x NH_2), 6.62 (d, 2H, *J* = 2.3 Hz), 6.68 (dd, 2H, *J* = 8.6, 2.3 Hz), 7.41 (d, 2H, *J* = 8.6 Hz), Calc. for $C_{20}H_{10}Cl_2N_4O_2$: C, 56.12, H, 2.62, N, 14.54. Found: C, 55.93, H, 2.61, N, 14.19.

6,13-dichloro-2,9-dimethoxytriphenodioxazine (5)

The compound **5** was prepared from the oxidative cyclisation of the intermediate **2** (0.32 mmol, 134 mg) under microwave heating using the general method B. Purple solid, yield (73%, 96.9 mg), m.p. > 300°C, λ_{max}(DMF)/nm 540.5, ν_{max} (KBr)/cm^{-1} 3040, 2980, 2936, 1630, 1609, 1600, 1560, 1548, 1480, 1440, 1250, 1220, 1150, 1115, 1100, 1049, 1020, 850, 830, 725, 700, 690, δ_H (DMSO-d_6) 3.83 (s, 6H, 2 x OMe), 7.10 (d, 2H, *J* = 2.4 Hz), 7.20 (dd, 2H, *J* = 8.7, 2.4 Hz), 7.58 (d, 2H, *J* = 8.7 Hz), Calc. for $C_{20}H_{12}Cl_2N_2O_4$: C, 57.85, H, 2.91, N, 6.75. Found: C, 57.67, H, 2.90, N, 6.73.

6,13-Dichloro-2,9-dimethyltriphenodioxazine (6)

The compound **6** was prepared from the oxidative cyclisation of the intermediate **3** (0.32 mmol, 124 mg) under microwave heating using the general method B. Red solid, yield (71%, 87.1 mg), m.p. > 300°C, λ_{max}(DMF)/nm 532, ν_{max} (KBr)/cm^{-1} 3030, 2980, 1625, 1570, 1550, 1480, 1440, 1409, 1290, 1245, 1150, 1120, 1110, 1085, 1070, 1020, 850, 830, 792, 730, 700 , δ_H (DMSO-d_6) 2.40 (s, 6H, 2 x Me), 6.99 (d, 2H, *J* = 2.2 Hz), 7.08 (dd, 2H, *J* = 8.4, 2.2 Hz), 7.46 (d, 2H, *J* = 8.4 Hz), Calc. for $C_{20}H_{12}Cl_2N_2O_2$: C, 62.68, H, 3.16, N, 7.31. Found: C, 62.50, H, 3.15, N, 7.29.

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