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A microwave-assisted synthesis of triphenodioxazines [TPDOs]

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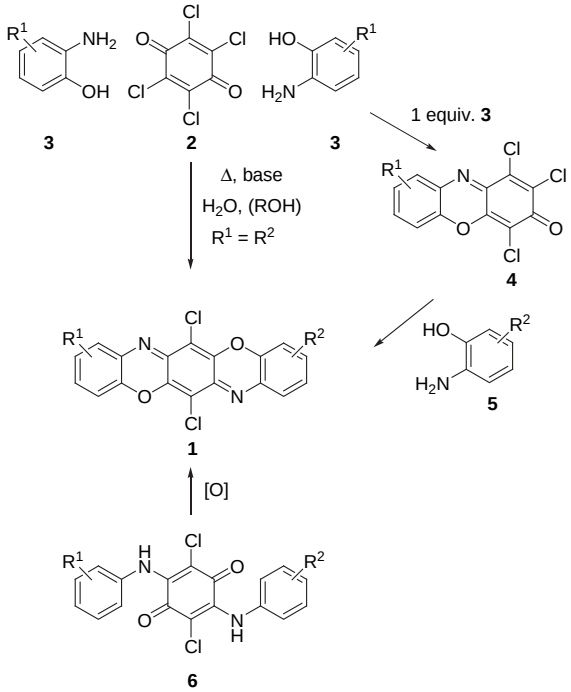
ABSTRACT

A convenient and efficient method for the synthesis of triphenodioxazines [TPDOs] **1** by oxidative cyclisation of 2,5-bis-(arylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-diones **6** using potassium persulfate as the oxidising agent in 95-97% sulfuric acid triggered by microwave irradiation is described.

1. Introduction

Triphenodioxazines [TPDOs] **1** are well known compounds, which have many applications in different fields of life, notably in the dyeing of a diversity of materials[1] including widespread use in a variety of fibres such as textiles,[2] leathers and papers.[3] They are also used in printing and as polymer dyes,[4] as laser[5] and fluorescent dyes[6] and as polymer photo-stabilizers.[7] Such compounds also find applications in the field of inks, especially in their use as components of printing inks, electrophotographic toners and developers, powder coating materials and cosmetics.[8] There are also examples of applications in optical recording systems and in optoelectronic devices, such as optical computing, sensor protection and dynamic holography.[9]

The basic chemistry of their preparation involves either a condensation cyclisation, which may proceed directly or indirectly, or an oxidative cyclisation (Scheme 1). In the direct condensation/cyclisation method, 2 equiv of an *o*-aminophenol **3** is condensed with 1 equiv of *p*-chloranil **2** in the presence of a base to remove the hydrogen chloride produced. Such reactions usually work well in alcoholic or water/alcohol mixtures or simply in aqueous medium. In the indirect method, 1 equiv of



Scheme 1.

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an *o*-aminophenol **3** is condensed with *p*-chloranil **2** to produce a l,2,4-trichloro-3*H*-aryloxazin-3-one intermediate **4**, which on further condensation with another equivalent of an *o*-aminophenol **5** gives unsymmetrical TPDO compounds [**1**; $R^1 \neq R^2$].[10] However, in these methods, both the amino and hydroxyl groups of an aminophenol are reactive towards nucleophilic displacement of the chlorine atoms in chloranil, creating a possibility of anilide formation as side reactions. Furthermore, the method is limited to easily condensable aminophenols on both sides.

On the other hand, oxidative cyclisations feature the ring closure of 2,5-bis-(arylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-dione intermediates **6** to form triphenodioxazines **1**. The advantage of this approach is mainly associated with the fact that the simpler substituted anilines required to form the initial symmetrical or unsymmetrical benzoquinones **6** are much more readily available than the corresponding *o*-aminophenols **3** and **5** required in the condensation cyclisations. Such ring closures of the intermediate *p*-benzoquinones **6** normally require the use of very high boiling solvents, such as nitrobenzene, chloronaphthalens or *o*-dichlorobenzene under reflux and using benzoyl chloride or *p*-toluenesulfonyl chloride as oxidising agents; typical reaction times are 3-9 h.[11] These very high temperatures required by these methods unsurprisingly induce the formation of considerable amounts of side products.

Alternative protocols were therefore developed in which the intermediates **6** were cyclised in oleum using the sulfur trioxide present as the oxidising agent. However, in this method the reactants and/or products can be prone to sulfonation at their various activated positions. In order to tackle this problem, persulfates or other compatible oxidants are used along with oleum, thereby suppressing any sulfonation side reactions.[12]

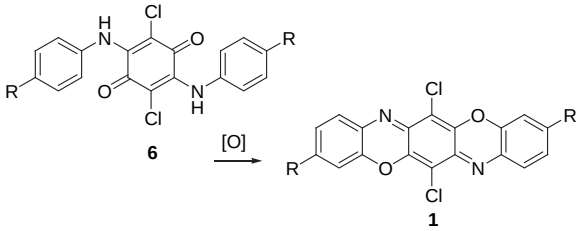
In the patent literature, examples of alternative oxidants include halogens, peroxides, iodine or benzoquinones in combination with sulfuric acid under reflux.[4,13] The reaction times are also relatively lengthy, ranging from 4 to 12 h, giving plenty of opportunity for product decomposition. The overall yields obtained from many of these reactions are therefore often quite low and the desired product(s) are formed along with a number of side products. Some improved and more modern methods include the use of hypervalent iodine reagents as oxidising agents.[14] Although the reported yields are good, the method requires the use of expensive and potentially dangerous reagents.

In view of these limitations and difficulties, we reasoned that, as all of the oxidative cyclisation conditions required heating, such syntheses could possibly be much improved by the application of microwaves, as is the case in so many other synthetic transformations. Examples of the application of microwave irradiation to the improvement of a vast range of synthetic transformation are now legion, and, in general, offer the combined advantages of higher yields achieved in much shorter reaction times.[15] Herein, we report that this indeed seems to be the case in examples of TPDO synthesis.

2. Results

For this study, we chose to examine a combination of potassium persulfate and concentrated sulfuric acid for the synthesis of symmetrical TPDOs **1** from the corresponding bis-(arylamino) derivatives **6**.[4,13] The present microwave method is certainly convenient and economical and routinely delivers 70-75% yields of the desired products **1**. After a number of trials, we settled on the following procedure, which in detail involves heating 0.30-0.32 mmol of an intermediate 2,5-bis-(arylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-dione **6** with 0.80 mmol of potassium persulfate (2.2-2.5 equiv of potassium persulfate for each equivalent of a dianilide intermediate **6**) in 95-97% concentrated sulfuric acid from ambient temperature to 75 °C during around 15 min. The results are presented in Table 1.

Table 1
The oxidative cyclisation of dianilides **6** into symmetrical TPDOs **1** using concd H_2SO_4/persulfate under microwave conditions [50 W]



Entry	R	Reaction time	Temperature	% Yield
1	**a**=*p*-NH_2	15 min	25–75 °C	62
2	**b**=*p*-OMe	15 min	25–60 °C	73
3	**c**=*p*-Me	20 min	25–75 °C	71
4	**d**=*p*-O_2N	40 min	25–95 °C	0

This novel method has thus reduced the preparation time of such triphenodioxazines **1a**–**c** from many hours to just 15 min using this reagent combination. The method has also reduced the temperature required to drive the reactions to completion. By using microwave irradiation, the reaction can be carried out from 25 to 75 °C. Higher temperatures can also be used but this tends to result in extensive decomposition of the potassium persulfate. Of course, as the temperature is increased, potassium persulfate starts to decompose more quickly. Hence, we preferred the compromise of a moderate temperature and use of 2.2–2.5 mol equiv of potassium persulfate in order to compensate for some decomposition of this oxidant. Two mole equivalents of this oxidant are required for cyclising 1 mol equiv of intermediate **6** as there are two reactive sites in the molecule, and 0.2–0.5 mol equiv to compensate the decomposition in the presence of concd H_2SO_4. In addition, the shorter reaction times also compensated for the gradual decomposition of the potassium persulfate. The best temperature range was found to be 70-75 °C at which the reactions were completed within 15 min. At lower temperatures, when persulfate decomposition is less, the reaction times required for completion were longer and hence 15 min at 75 °C was an optimum compromise.

We also studied the electronic effects of substituents and found that these had a great influence on the cyclisation process. In examples of electron donating groups, the cyclisations all worked well under the foregoing conditions while no cyclisation was observed when the powerful electron-withdrawing *para*-nitro substituent was present, even under prolonged irradiation for 35-40 min. This effect has been reported previously.[14] By contrast, in an example having a powerful electron donating group, such as methoxy (entry 2), the reaction proved somewhat faster and was completed within 15 min but at slightly lower temperatures of between 25-60 °C.

The present microwave-assisted method for the preparation of triphenodioxazines **1** is carried out at a maximum temperature of 75 °C and is complete within 15–20 min using very cheap potassium persulfate as oxidising agent in 95-97% H_2SO_4 and certainly has the potential for large scale applications, particularly in a microwave flow system,[16] although, as in the related methods, it too is limited to examples wherein the aryl groups are electron-rich: the *p*-nitro derivative failed to cyclised.

3. Experimental

3.1. General information

All reagents were purchased from Aldrich and were used as received. The microwave instrument used was a CEM DISCOVERY. ^{1}H NMR spectra were recorded using a Bruker DPX spectrometer operating at 400 MHz. All NMR measurements were carried out at 30 °C and chemical shifts are reported as ppm on the delta scale downfield from tetramethylsilane (TMS: δ=0.00). Coupling constants (J) are reported in hertz. 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. Low resolution 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 were obtained using the ionization modes specified. Melting points were determined using a Kofler hot stage apparatus and are uncorrected. Elemental analyses were obtained using a Perkin–Elmer 2400 Elemental Microanalyser.

3.2. Preparation of benzoquinone intermediates 6[17]

*3.2.1. 2,5-Bis-(4-aminophenylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-dione **6a**.* To a stirred solution of *p*-phenylenediamine (4.00 g, 37.0 mmol) in water (10 mL) maintained between 40-45 °C was added an intimate mixture of sodium bicarbonate (3.20 g, 38.1 mmol) and *p*-chloranil (4.55 g, 18.5 mmol) in small portions. Stirring was continued for 1 h and then the temperature of the reaction mixture was increased to 60 °C and maintained at this value for a further 2 h. The course of the reaction was monitored by silica gel TLC [EtOAc/hexanes (30:70)+2% MeOH]. The reaction mixture was then cooled and the resulting precipitate isolated by suction filtration. The solid was washed extensively with cold and hot water and then finally with ethanol and dried under vacuum. The product **6a** was obtained as a brown solid (6.56 g, 77%). An analytical sample was secured by dissolving a little of the product in DMF/acetone followed by separation using silica gel column chromatography (2:3 EtOAc/hexanes). The pure product **6a** showed mp >300 °C; ν_{max} (KBr)/cm^{-1} 3380, 3252, 1651, 1575, 1514, 1490, 1434, 1329, 1291, 1256, 1197, 1170, 1084, 1016, 890, 757; δ_H (DMSO-d_6) 5.98 (4H, br s, 2×NH$_2$), 6.71 (4H, d, J 8.5 Hz, 4×Ar–H), 6.95 (4H, d, J 8.5 Hz, 4×Ar–H), 9.57 (2H, s, 2×NH); calcd 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.

*3.2.2. 2,5-Bis-(4-methoxyphenylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-dione **6b**.* Benzoquinone **6b** was prepared according to the foregoing procedure[17] on a similar scale staring with *p*-methoxyaniline and was isolated in similar yield as a brown solid, mp 282 °C (decomp.), [lit.[17] mp 298 °C]; ν_{max} (KBr)/cm^{-1} 3221, 3013, 1651, 1609, 1568, 1510, 1486, 1417, 1322, 1306, 1244, 1195, 1171, 1112, 1032, 1012, 948, 894, 800; δ_H (DMSO-d_6) 3.76 (6H, s, 2×OMe), 6.90 (4H, d, J 8.3 Hz, 4×Ar–H), 7.11 (4H, d, J 8.3 Hz, 4×Ar–H), 9.62 (2H, s, 2×NH); m/z (EI) 418 (M$^+$, (^{35}Cl); 64%), 386 (57), 350 (41), 250 (7), 174 (22), 146 (8), 108 (45), 84 (15); calcd 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.

*3.2.3. 2,5-Bis (p-tolylamino)-3,6-dichlorocyclohexa-2,5-diene-1,4-dione **6c**.* Benzoquinone **6c** was prepared in similar yield by the foregoing procedure[17] from 4-methylaniline and showed mp >300 °C [lit.[17] mp >310 °C (decomp.)]; ν_{max} (KBr)/cm^{-1} 3232, 1648, 1610, 1561, 1510, 1475, 1404, 1322, 1307, 1248, 1198, 1172, 1109, 1034, 1020, 944, 890, 800; δ_H (DMSO-d_6) 3.34 (6H, s, 2×Me), 7.05 (4H, d, J 8.2 Hz, 4×Ar–H), 7.15 (4H, d, J 8.2 Hz, 4×Ar–H), 9.63 (2H, s, 2×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); calcd 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.

3.3. General procedure for the preparation of triphenodioxazines [TPDOs] 1

A *p*-benzoquinone intermediate **6** (0.32 mmol) was mixed and finely ground with potassium persulfate (0.80 mmol) and the resulting powder transferred to a microwave tube to which 95-97% concentrated sulfuric acid (2.5 mL) was then added. The tube was then capped and subjected to microwave irradiation at 25-75 °C and 50 W power for a period of 15 min with stirring. After the reaction was completed, the tube was cooled and its contents poured into 10 g of crushed ice. The resulting precipitate was removed by suction filtration and washed with water until the filtrate showed no acidity. Analytical samples could be secured by dissolving a small quantity of a crude product in DMF and applying the resulting solution to a silica gel column and eluting with 1:1 EtOAc/petroleum ether. The bulk triphenodioxazines **1** obtained in the present study were recrystallized from DMF. The percentage yield of the isolated and purified triphenodioxazine compounds are given in Table 1.

*3.3.1. 2,9-Diamino-6,13-dichlorotriphenodioxazine **1a**.* By the general procedure, oxidative cyclisation of the benzoquinone **6a** gave the TPDO **1a** as a purple powder, mp >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; δ_H (DMSO-d_6) 6.02 (4H, br s, 2×NH$_2$), 6.62 (2H, d, J 2.3 Hz, 1- and 8-H), 6.68 (2H, dd, J 8.6, 2.3 Hz, 3- and 10-H), 7.41 (2H, d, J 8.6 Hz, 4- and 11-H); calcd 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.

*3.3.2. 6,13-Dichloro-2,9-dimethoxytriphenodioxazine **1b**.* By the general procedure, oxidative cyclisation of the benzoquinone **6b** gave the TPDO **1b** as a purple solid, mp >300 °C [lit.[17] mp >360 °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; δ_H (DMSO-d_6) 3.83 (6H, s, 2×OMe), 7.10 (2H, d, J 2.4 Hz, 1- and 8-H), 7.20 (2H, dd, J 8.7, 2.4 Hz, 3- and 10-H), 7.58 (2H, d, J 8.7 Hz, 4- and 11-H); calcd 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.

*3.3.3. 6,13-Dichloro-2,9-dimethyltriphenodioxazine **1c**.* By the general procedure, oxidative cyclisation of the benzoquinone **6c** gave the TPDO **1c** as a red solid, mp >300 °C [lit.[17] mp >360 °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 (6H, s, 2×Me), 6.99 (2H, d, J=2.2 Hz, 1- and 8-H), 7.08 (2H, dd, J=8.4, 2.2 Hz, 3- ad 10H), 7.46 (2H, d, J=8.4 Hz, 4- and 11-H); calcd 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.

4. Conclusion

We report herein a new microwave method for the preparation of triphenodioxazines [TPDOs] **1**. This new method has reduced the time of reaction from a number of hours to just 15 min and decreased the temperature from 150-200 °C to 25-75 °C.

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