Cent. Eur. J. Chem. • 8(1) • 2010 • 51–57
DOI: 10.2478/s11532-009-0100-5

VERSITA

Central European Journal of **Chemistry**

Synthesis and biological screening of octasubstituted-triphenodioxazines and its sulphur analogues with some novel intermediates

Research Article

Lalchand Heda, Chandresh Pareek*, Dushyant Pareek, Sonraj Mosalpuri

P. G. Research Laboratories, Department of Chemistry, S. D. Govt. College, 305901 Beawar, INDIA

Received 2 February 2009; Accepted 9 July 2009

Abstract: Attempts have been made to prepare for the first time the octasubstituted-triphenodioxazines and triphenodithiazines heterocycles by cyclisation of 3,6-dichloro-2,5-bis(2',4',5'-trichloroanilino)-1,4-benzoquinone and condensation. This wasfollowed by cyclisation of substituted 2-aminobenzenethiol respectively with chloranil and bromanil in ethanolic solution of fused sodium acetate in the presence of benzoyl chloride in nitrobenzene. Their structures were confirmed on the basis of their chemical and spectral analyses.
Moreover, the biological activity of these compounds was evaluated against the test organisms viz - *E.coli, S. aureus, B. subtilis, M.luteus* and *C. albicans*. These compounds synthesized from 2,4,5-trichloroaniline appeared to possess significant antimicrobial activities and an explicit correlation between structure and biological activity was also observed.

Keywords: *Triphenodioxazines • Triphenodithiazine • Benzoquinones • Antimicrobial activity*

1. Introduction

From the literature survey, it appears that the presence of a halogen atom is crucial for significant activity in compounds derived from both 'Nature' and 'Chemical Synthesis'. The influence of a substituent such as chlorine on the biological activity of a potential drug agent still has to be established empirically in biological experiments designed to detect desired activity. However, chlorinated organic chemicals in the molecular weight between 200 and 600 constitute an important and indispensable segment in the arsenal of existing biologically active chemicals used as pharmaceutical agents [1].

A literature study also proposes that almost no octasubstituted-triphenodioxazine (TPDO) and triphenodithiazine (TPDT) derivatives have so far been synthesized and studied. It was thought worthwhile to prepare these new classes of heterocycles to study their antimicrobial activities and determine their MICs (Minimum Inhibitory Concentrations), MBCs (Minimum Bactericidal Concentrations) and MFCs (Minimum Fungicidal Concentrations) against *Escherichia coli* (causative for diarrhea), *Staphylococcus aureus* (causative for wound infection), *Bacillus subtilis*, *Micrococcus luteus* and *Candida albicans* (yeast).

The discovery and development of triphenodioxazine (TPDO), triphenodithiazine (TPDT) and their derivatives not only place them as a useful coloring materials in the textile industry [2] for coloring plastics, varnishes, viscose, rubber, paper [3-5], but also as potential pharmaceutical agents [6,7]. These have been equally useful as antibacterial, muscle-relaxant, and hypnotic agents [8], antifungal [9,10], tranquillizers [11], anti-inflammatory [12], antitumor [13,14], antipsychotics

* *E-mail: pareekcd@yahoo.com*

[15], antihistamines [16], and some recent applications regarding the preparation of nonlinear optical wave guiding polymer films [17-19], bearing a unique photovoltaic property also [20]. Thus, the industrial importance of these compounds lies in the fact that they a find variety of applications in almost every field of life.

A number of TPDO and TPDT compounds have been reported for their multifaceted applications. Therefore, the present communication deals with the synthesis of new class of octasubstituted TPDO and TPDT heterocycles with their utilitarian novel intermediates. The octachlorotriphenodioxazine (1c) and its bromo derivative (1d) were prepared by condensing 2,4,5-trichloroaniline with chloranil / bromanil (tetrahalo-*p*-benzoquinone) respectively in the presence of fused sodium acetate followed by oxidative cyclisation of resulting dianilino-*p*-benzoquinone (1a,1b). Whereas, octachlorotriphenodithiazine (2c) and its bromo derivative (2d) were synthesized in multi-steps through condensation followed by cyclisation of 2-amino-3,5,6-trichlorobenzenethiol (2b) with chloranil and bromanil respectively.

2. Experimental Procedure

2.1. General

All the melting points were determined by open capillary method and are uncorrected. IR spectra were recorded in KBr pellets on FTIR 8201 PC spectrophotometer and ^{1}H NMR spectra in DMSO solvent were run on 300 MHz FTNMR spectrometer using TMS as an internal standard. The FAB MS were recorded on a JEOL SX 102/DA-6000 mass spectrometer whereas UV-vis spectra were recorded in Perkin-Elmer Lambda 15 UV-vis spectrophotometer. Elemental analysis was carried out on Elemental Analyzer Vario EL 111 Carlo Erba 1108 for all the newly synthesized compounds. Spectral and elemental analysis was accomplished at SAIF - CDRI (Lucknow). All the reagents were used as obtained commercially. The purity of the compounds in addition to spectral and elemental analyses was checked regularly in each step using TLC [60 mesh from Merck].

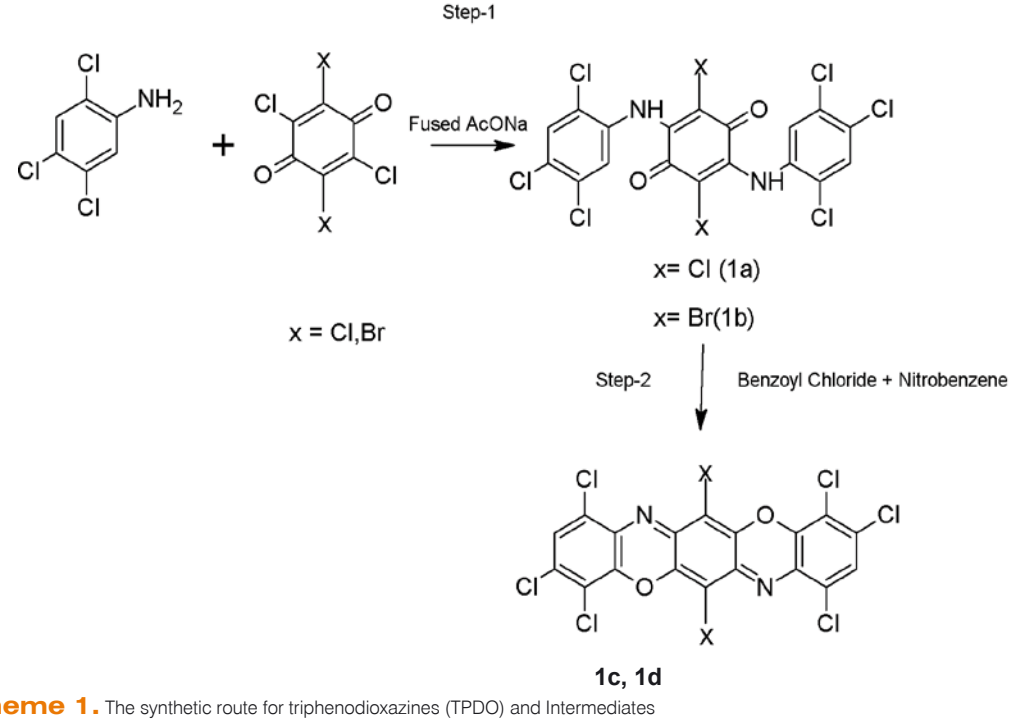
2.2. Experimental procedure for the preparation of octasubstituted triphenodioxazines 1c and 1d

Title compounds 1c and 1d were synthesized in two steps by a method described by Meister, Lucius and Bruning [21]. Some modifications were also employed to get a better yield. The general route for the synthesis is shown in Scheme 1.

2.2.1. Preparation of dianilino-p-benzoquinones 1a and 1b

2.2.1.1. General procedure

To a stirred suspension of chloranil/bromanil (0.01 mol) and anhydrous sodium acetate (0.82 g, 0.01 mol) in ethanol (150 mL), an alcoholic solution



Scheme 1. The synthetic route for triphenodioxazines (TPDO) and Intermediates

of 2,4,5–trichloroaniline (3.93 g, 0.02 mol) was added. The mixture was refluxed at 55^{0}C for 8 hours. The residue obtained was filtered then washed first with hot water and finally with 30% ethanol. Products were re-crystallized from DMF to give the desired intermediates 1a and 1b respectively.

2.2.1.2. 3, 6-dichloro-2, 5-bis (2', 4', 5'-trichloroanilino)-1, 4-benzoquinone '1a'

It was obtained from chloranil (2.46 g 0.01 mol) in 42% yield; mp. did not melt below 360^{0}C; UV (DMF) λ_{max} 370 nm; IR (ν_{max}/cm^{-1}): 3256 (NH str), 1655 (>C=O str), 1576, 1496, 1384, 1353 1281, 1198, 1132, 1083, 1034, 963, 804, 757, 675, 638 cm^{-1}; ^{1}H NMR (DMSO, δ ppm): 8.28 (s, 2NH), 7.55 (s, 2ArH), 7.27 (s, 2ArH); FAB MS (298^{0}C) m/z 565[M$^+$], 566 [M$^+$+1]; Anal.Calcd. for $C_{18}H_6Cl_8N_2O_2$: C, 38.2; H,1.07; N, 4.95; found: C, 38.9; H, 1.02; N, 4.99

2.2.1.3. 3, 6-dibromo-2, 5-bis (2', 4', 5',-trichloroanilino)-1, 4-benzoquinone '1b'

It was obtained from bromanil (4.246 g, 0.01 mol) in 36% yield; mp. did not melt below 360^{0}C; UV (DMF) λ_{max} 375 nm; IR (ν_{max}/cm^{-1}): 3238 (NH str), 1642 (>C=O str), 1560, 1475, 1380, 1375, 1285, 1281, 1190, 1195, 1080, 1030, 970, 810, 750, 680, 665 cm^{-1}; ^{1}H NMR (DMSO,δ ppm): 8.25 (s, 2NH), 7.53 (s, 2ArH), 7.12 (s, 2ArH); FAB MS (298^{0}C) m/z 678[M$^+$], 679 [M$^+$+1]; Anal.Calcd. for $C_{18}H_6Br_2Cl_6N_2O_2$: C, 33.02; H, .31; N, 4.28; found: C, 32.08; H, <1; N, 4.32

2.2.2. Preparation of title compounds 1c and 1d

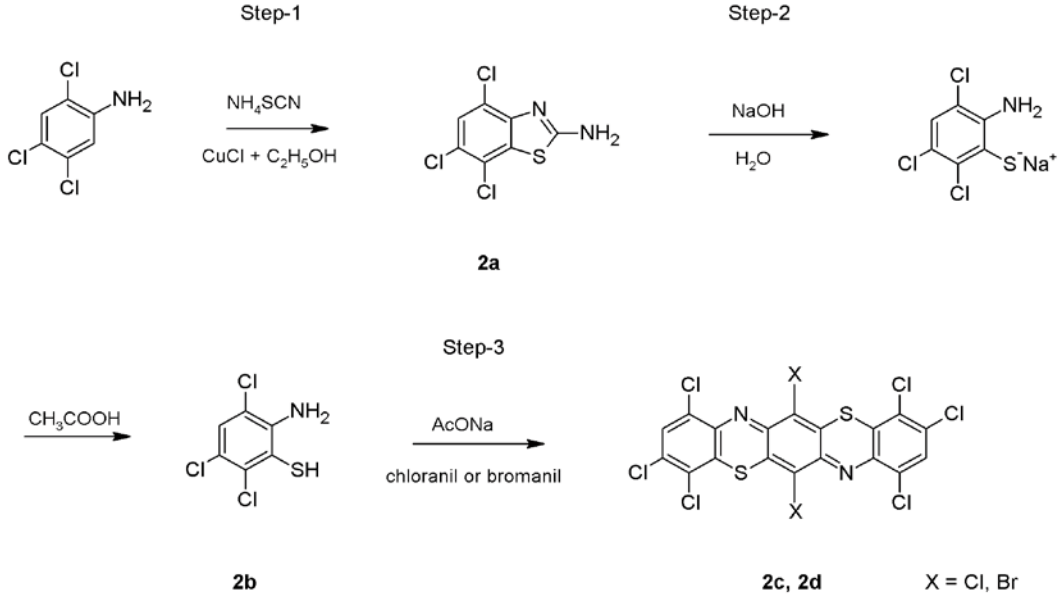
A mixture of dianilino-*p*-benzoquinone 1a, 1b (0.01 mol) respectively with nitrobenzene (40 mL) and benzoyl chloride (20 mL) was stirred under reflux at 80^{0}C for 10-11 hours until the color of the reaction mixture turned dark. The reaction mixture was cooled down overnight to room temperature then filtered. The residue obtained was first washed with 30% ethanol and finally with hot water to give the desired products. After washing several times with petroleum ether, products were re-crystallized from DMF/nitrobenzene to give title compounds 1c and 1d.

2.2.2.1. 1, 3, 4, 6, 8, 10, 11, 13–octachlorotriphenodioxazine '1c'

It was obtained from '1a' (5.6 g, 0.01 mol) as green needles in 36% yield; mp. did not melt below 360^{0}C; UV (DMF) λ_{max} 595 nm; IR (ν_{max}/cm^{-1}): 1655, 1573, 1490, 1424, 1360, 1287, 1195, 933, 872, 827, 666, 639 cm^{-1}; ^{1}H NMR (DMSO, δ ppm) 7.28 (s, 2ArH); FAB MS (298^{0}C) m/z 561 [M$^+$]; 154(100%); Anal.Calcd. for $C_{18}H_2Cl_8N_2O_2$: C, 38.48; H, .36; N, 4.99; found: C, 38.2; H, <1; N, 4.89

2.2.2.2. 6, 13- dibromo - 1, 3, 4, 8, 10, 11 – hexachlorotriphenodioxazine, 1d

It was obtained from 1b (6.55 g, 0.01 mol) as shining green colored crystals in 32% yield; mp. did not melt below 360^{0}C; UV (DMF) λ_{max} 598 nm; IR (ν_{max}/cm^{-1}): 1640, 1565, 1498, 1420, 1360, 1290, 1200, 932, 865, 815, 640, 625 cm^{-1}; ^{1}H NMR (DMSO, δ ppm) : 7.12 (s, 2



Scheme 2. The synthetic route for triphenodithiazine (TPDT) and Intermediates

ArH); FAB MS (298^{0}C) m/z 581 [M$^+$]; 154(100%); Anal. Calcd. for $C_{18}H_2Br_2Cl_6N_2O_2$: C, 33.22; H, <1; N, 4.30; found: C, 33.53; H, .24; N, 4.39

2.3. Experimental procedure for the preparation of octasubstituted triphenodithiazines, 2c and 2d

The general route for the synthesis of 2c and 2d is shown in Scheme 2. Title compounds were synthesized through following multi steps:

2.3.1. Preparation of 2– amino - 4, 6, 7-trichlorobenzothiazole '2a'

Compound 2a was synthesized by a method described by Kaufmann and Kuchler [22], but some modifications were also employed to reach the desired product with a better yield.

To a solution of 2,4,5–trichloroaniline (1.98 g, 0.01 mol) with glacial acetic acid (80 mL) and ammonium thiocyanate (7.6 g, 0.1 mol), a solution of cuprous chloride (9.9 g, 0.10mol) was added with 50 mL of ethanol. The mixture was refluxed for one and half hours with constant stirring at constant temperature 70^{0}C. Approximately 100 mL dilute hydrochloric acid was added in and temperature was raised to 100^{0}C and heated again for the next half an hour, then cooled and neutralized with saturated sodium carbonate. The residue obtained was washed with water and further re-crystallized from ethanol to give the product 2a with 42% yield, mp. 270^{0}C; IR (v_{max}/cm^{-1}): 3250, 1685, 1598, 1640, 1565, 1485, 1450, 1360, 1325, 1309, 1225, 918, 955, 877, 815, 648, 671, 623 cm^{-1}; ^{1}H NMR (DMSO, δ ppm) : 7.56 (s, 1ArH); 3.25 (s, 2NH); FAB MS (298 ^{0}C) m/z 252 [M$^+$]; 253 [M$^+$+1]; Anal.Calcd. for $C_7H_3Cl_3N_2S$: C, 33.16; H, 1.19; N, 11.05; found: C, 33.23; H, 1.04; N, 4.39

2.3.2. Synthesis of 2- amino- 3, 5, 6- trichlorobenzenethiol [23,24] '2b'

Compound 2a was refluxed with NaOH or KOH (each 10 times by weight) in water until the evolution of ammonia ceased. The contents were diluted with ice-cold water, which was further filtered and neutralized with 5N acetic acid under vigorous stirring. The residue was extracted with ether solvent. The ether layer was then evaporated. After evaporation, the solid was re-crystallized from ethanol to give 2b with 58% yields, mp. 325^{0}C (uncorrected); IR (v_{max}/cm^{-1}) : 3229, 3190, 2330, 2230, 1580, 1506, 1054, 1021, 928, 796, 711 cm^{-1}; ^{1}H NMR (DMSO, δ ppm): 7.35 (s, 1ArH), 4.70 (s, 2NH), 1.39 (s, 1SH); FAB MS (298^{0}C) m/z 227 (100%) [M$^+$]; 228 [M$^+$+1]; Anal.Calcd. for $C_6H_4Cl_3NS$: C, 31.53; H, 1.76; N, 6.13; S, 14.03; found: C, 31.45; H, 1.72; N, 6.12; S, 14.11

2.3.3. Preparation of title compounds [25] 2c and 2d

2.3.3.1. General procedure

To a stirred suspension of chloranil/bromanil (0.1 mol) and 2-amino-3,5,6-trichlorobenzenethiol 2c (50.6 g, 0.2 mol) in ethanol (50 mL), anhydrous sodium acetate (8.2 g, 0.1 mol) was added. The mixture was refluxed at 55^{0}C for almost 100 hours, cooled overnight to room temperature and the residue that precipitated was filtered then washed with water followed by 30% ethanol and further crystallized from DMF/acetone to give the desired title products 2c and 2d. Structures were determined from the FAB MS, ^{1}H NMR and FTIR of the respective compounds.

2.3.3.2. 1, 3, 4, 6, 8, 10, 11, 13–octachlorotriphenodithiazine '2c'

It was obtained from chloranil (24.6 g, 0.1 mol) having lavender colored crystals with 34% yield, mp: did not melt below 360^{0}C; UV λ_{max} (DMF) 602 nm; IR (v_{max}/cm^{-1}): 1652, 1564, 1329, 1236, 1113, 893, 742, 795, 679, 588 cm^{-1}; ^{1}H NMR (DMSO, δ ppm): 7.13 (s, 2ArH); FAB MS (298^{0}C) m/z 593 [M$^+$]; Anal.Calcd for $C_{18}H_2Cl_8N_2S_2$: C, 36.40; H, .34; N, 4.72; S, 10.8; found: C, 36.39; H, <1; N, 4.71, S, 11.2

2.3.3.3. 6, 13- dibromo - 1, 3, 4, 8, 10, 11 – hexachlorotriphenodithiazine '2d'

It was obtained from bromanil (42.4 g, 0.1 mol) having dark reddish-lavender colored crystals with 31% yield, mp: did not melt below 360^{0}C; UV λ_{max} (DMF) 610 nm; IR (v_{max}/cm^{-1}): 1640, 1560, 1332, 1225, 1109, 1002, 902, 885, 790, 735, 728, 602, 590 cm^{-1}; ^{1}H NMR (DMSO, δ ppm): 7.02 (s, 2ArH); FAB MS (298^{0}C) m/z 681 [M$^+$]; Anal.Calcd for $C_{18}H_2Br_2Cl_6N_2S_2$: C, 31.66; H, .30; N, 4.10; S, 9.39 found: C, 31.95; H, <1; N, 4.18; S, 9.70

2.4. Biological screening

2.4.1. Preliminary screening for antimicrobial activity

In the study of antimicrobial activity, the test organisms used were: Gram negative bacillus (*E. coli* ATCC25922), Gram positive bacillus (*Bacillus subtilis* ATCC6633) and Gram positive cocci (*Staphylococcus aureus* ATCC25923), *Micrococcus luteus* 'NRRL B-1018' and *Candida albicans* 'ATCC10231' (yeast) collected from the Microbiology lab of the All India Institute of Medical Sciences [AIIMS].

The sample [1a-2d] was dissolved in DMSO (200 µg mL^{-1} concentration for bacterial and 200 µg mL^{-1} for fungal strains). The test was performed by disc diffusion assay as per NCCLS, 1997 [26]. The nutrient agar plates containing an inoculum size of 10^6 cfu mL^{-1} for bacteria and RPMI 1640 supplemented with 1.5% Bacto agar [containing 2×10^5 spores] for fungi were

used. Previously prepared impregnated discs (whatman's filter paper of 6 mm in diameter) of strains were placed aseptically on sensitivity plates with appropriate controls. Streptomycin (10 mcg) and Fluconazole (10 mcg) were used as standard antibacterial and antifungal antibiotics respectively. Plates were incubated at 37^{0}C for 24 hours for bacteria and 30^{0}C for 3 days for fungal spores. Sensitivity was recorded by measuring the clean zone of inhibition in millimeters on agar surface around the disc (Table 1).

2.4.2. Determination of minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC) and minimum fungicidal concentration (MFC)

The MIC was determined by a tube dilution method for each of the test organisms in triplicates. To 0.5 mL of varying concentrations of sample (0 - 200 µg mL^{-1} for bacterial strains and 0-200 µg mL^{-1} for fungal strains), 2 mL of nutrient broth was added. Then, a loopful of test organism (previously diluted to 0.5 McFarland turbidity standards for Bacterial isolates and 10^6 cfu mL^{-1} for fungal strains) was introduced to the tubes. The procedure was repeated on the test organisms using standard antibiotics streptomycin (for bacteria) and fluconazole (for fungi). A tube (containing nutrient broth seeded with test organisms) served as a control. The tubes containing bacterial cultures were then incubated at 37^{0}C for 24 hours for bacteria and 30^{0}C for 3 days for fungal spores. After incubation the tubes were examined for microbial growth.

To determine the MBC [27] and MFC [28] for each set of test tubes in the MIC determination, a loopful of broth was collected from those tubes which did not show any growth and inoculated on sterile nutrient agar (for bacteria) and RPMI 1640 (for fungi) by streaking. Plates inoculated with bacteria and fungi were incubated at 37^{0}C for 24 hours and 30^{0}C for 3 days respectively. After incubation, that concentration was noted as MBC (for bacteria) or MFC (for fungi) at which no visible growth was observed (Table 2).

3. Results and discussion

3.1. Synthesis

In this communication, we have synthesized eight new polychlorinated heterocyclic compounds 1a-1d and 2a-2d. The synthesis of 1a-1b has been achieved by condensation of 2,4,5-trichloroaniline with chloranil and bromanil respectively, which upon further cyclisation yielded the title compounds 1c and 1d respectively. The structure of the product formed has been confirmed by elemental analyses, NMR, IR and Mass spectral studies.

The synthesis of 2c-2d has been achieved by applying a different approach through intermediates 2a and 2b. Compound 2a was synthesized from thiocyanation of aniline with CuCl/NH_4SCN in alcohol, which upon hydrolysis with KOH gave 2b. Cyclisation of 2b with chloranil/bromanil yielded the title products 2c and 2d respectively. The structures of the products have been confirmed again by elemental analyses, NMR, IR and Mass spectral studies.

A UV spectral study has also been accomplished for 1a-1d and 2c-2d. The λ_{max} values suggest that a bathochromic shift is observed after substituting more electronegative Cl by relatively less electronegative Br. The similar impression is noticed after replacing oxygen (1c, 1d) by sulphur (2c, 2d). Although increments in λ_{max} values are reasonably less as the difference in electronegativity is also less and some sort of conformational rigidity must be present in the system.

Table 1. Results of preliminary antimicrobial activity

Compounds	Diameter of zone of inhibition (mm)				
	E.coli ATCC25922	*S.aureus* ATCC25923	*B.subtilis* ATCC6633	*M.luteus* NRRL B-1018	*C.albicans* ATCC10231
1a	18.82 ± 0.32	17.44 ± 0.66	15.13 ± 0.49	08.92 ± 0.03	06.09 ± 0.12
1b	16.05 ± 0.07	09.32 ± 0.42	12.52 ± 0.22	19.35 ± 0.17	05.26 ± 0.42
1c	12.01 ± 0.86	14.56 ± 0.73	12.63 ± 0.46	18.08 ± 0.14	06.52 ± 0.53
1d	06.42 ± 0.11	08.74 ± 0.45	08.72 ± 0.11	07.33 ± 0.76	05.04 ± 0.94
2a	13.78 ± 0.53	06.14 ± 0.20	08.17 ± 0.05	07.22 ± 0.19	12.32 ± 0.08
2b	09.26 ± 0.64	07.72 ± 0.43	06.38 ± 0.03	09.41 ± 0.11	10.55 ± 0.14
2c	17.34 ± 0.14	12.63 ± 0.58	21.23 ± 0.69	08.07 ± 0.53	06.42 ± 0.29
2d	05.82 ± -0.96	09.33 ± 0.67	09.21 ± 0.15	07.61 ± 0.11	06.77 ± 0.33
Ref	18.05[a] ± -0.07	20.83 ± 0.12	16.82 ± 0.20	21.85 ± 0.05	21.05[b] ± 0.08

[a]- *Streptomycin*, [b]- *Fluconazole*

Table 2. Results of Minimum inhibitory concentration, MIC, MBC and MFC ($\mu g\ mL^{-1}$)

Compounds	Diameter of zone of inhibition (mm)									
	E.coli		*S.aureus*		*B.subtilis*		*M.luteus*		*C.albicans*	
	MIC[a]	MBC[b]	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC[c]
1a	30.5**	28.4	12.5	11.8	17.3	15.5	>100	>100	>100	>100
1b	35.2	33.1	15.8	13.2	22.1	20.5	3.6	2.8	>100	>100
1c	45.1	43.6	14.4	12.3	23.3	21.8	9.2	7.6	>100	>100
1d	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100
2a	>100	>100	>100	>100	>100	>100	>100	>100	8.2	7.4
2b	69.5	66.5	>100	>100	>100	>100	>100	>100	12.6	9.8
2c	33.8	32.2	58.4	56.3	12.3*	11.78	>100	>100	>100	>100
2d	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100
Ref	31.2[d]	30.6	0.9	<0.1	15.8	8.5	1.9	0.9	3.9[e]	<0.1

[a] *MIC, minimum inhibitory concentration (the lowest concentration that inhibited the bacterial or fungal growth);*
[b] *MBC, minimum Bactericidal concentration (the lowest concentration at which no bacterial growth was observed);*
[c] *MFC, minimum fungicidal concentration (the lowest concentration at which no fungal growth was observed);*
[d] *- Streptomycin;*
[e] *- Fluconazole;*
[*] *- significant activity.*

3.2. Biological screening

One of the purposes for preparing these new classes of compounds was to evaluate their antimicrobial activity. The preliminary antimicrobial activities for all the products have been shown in Table 1. In the terms of the zone of inhibition, the maximum activity was shown by 1a against *E. coli*; 1b, 1c against *M. luteus* and 2c against *E. coli*, *S. aureus* and *B. subtilis* whereas the minimum zone of inhibition was observed by 1d and 2d against all strains.

Significant activity of 2c was shown against *B. subtilis* in comparison to standard antibiotic Streptomycin, whereas the almost similar zone of inhibition was depicted by 1a against *E. coli* and *B. subtilis*. The results of MICs and MBCs are summarized in Table 2. The results revealed that compound 2c was highly active against *B. subtilis* and almost similar to moderate sensitivity was shown by 1b and 1c against *M. luteus*. Only compounds 2a and 2b expressed moderate sensitivity against *C. albicans* with respect to standard antibiotic Fluconazole.

Based upon the above findings in our study, we can establish a correlation between structure and biological activity, where the activity is significantly decreased by replacing Cl with Br on the title compounds.

4. Conclusion

Four new polychlorinated triphenodioxazine (TPDO) and triphenodithiazine (TPDT) heterocycles were synthesized from 2,4,5-trichloroaniline with two newly reported benzoquinones, aminobenzenethiol and benzothiazole, as intermediates. Biological screening and values of MICs for the newly synthesized compounds suggest that the presence of a Cl atom (like any other substituent) on these compounds serves as a modulator of activity and replacing Cl by Br astoundingly diminishes the biological activity. Hence, it can be stipulated that there is a definite correlation between structure and biological activity. Compounds **1a** and **2c** have significant antimicrobial activity against *E.coli* and *B. subtilis*. Therefore, these active compounds can be exploited as antibacterial agents for the production of new drugs. Moreover, λ_{max} values for TPDO and TPDT heterocycles also make them good chromogenic compounds.

Acknowledgements

The authors express their sincere thanks to Dr. K. G. Ojha, Professor of Applied Chemistry M.D.S. University, Ajmer (Rajasthan) INDIA for his valuable criticism and helpful discussions and authors extend their gratitude to Microbiology Department, J.L.N. Medical College, Ajmer for providing biological screening facility. One of the authors Chandresh Pareek is thankful to SAIF, CDRI Lucknow for the spectral and chemical analyses and to UGC-CSIR for granting TRF to him.

References

[1] K. Numann, Pest Management Science Journal 56, 3 (2000)

[2] K. Venkataraman (Ed.), The Chemistry of Synthetic dyes (Academic Press Inc, New York, 1952) Vol. 2, 761

[3] T. Hirara, Y. Okada, Z. Morita, Dyes and pigments 45(2), 131 (2000)

[4] J. Kraska, Z. Boruszczak, B. Landwiist, Dyes and pigments 43(1), 1 (1999)

[5] H. Walter, R. Vwe, Fiber reactive triphenodioxazine dyes, US patent, 5539109 (July 23, 1996)

[6] (a) R.R. Gupta, K.G. Ojha, Phenothiazines and 1,4–benzophenothiazines: Chemical and Biomedical Aspects (Elsevier, Amsterdam, 1988) Vol. 4, 163; (b) C.O. Okafor, Phosphorus, sulfur, and silicon 4, 79 (1978)

[7] (a) Y.S. Sadanandam, P. Leelavathi, Indian J. Chem. 30B(10), 85 (1991); (b) A.S. Hammam, M.S.K. Youssef, F.M. Atta, T.A. Mohamed, Chemical Papers 61(4), 292 (2007)

[8] K.G. Ojha, S.P. Mathur, A.K. Mathur, A.S. Chittoria, H. Tahiliani, R.K.Sharma, Indian J. Chem. 43B(10), 2254 (2004)

[9] V.H.J. Frade, M.J. Sousa, J.C.V.P. Moura, M. Sameiro, T. Gonçalves, Tetrahedron Letters 48, 8347 (2007)

[10] L.I. Belen'kii, N.D. Kruchkovskaya, Adv. Heterocycl. Chem. 55, 31 (1992)

[11] K.G. Kulkarni, F. Milton, Gen. Pharmacol. 17(6), 671 (1986)

[12] J. Krapcho, C.F. Turk, J. Med. Chem. 16(7), 776 (1973)

[13] M. Batra, P. Kriplani, C. Batra, K.G. Ojha, Bioorg. Med. Chem. 14(24), 8519 (2006)

[14] A.J. Ling, K. Sudhaka, J. Heterocycl. Chem. 18, 759 (1981)

[15] M. Gordan (Ed.), Psychopharmacological Agents, Medicinal Chemistry (Academic Press, New York, 1967) Vol. III, 119

[16] J. Krapcho, A. Szabo, J. Williams, J. Med. Chem. 6, 214 (1963)

[17] T. Okamoto, M. Kozaki, M. Doe, M. Uchida, G. Wang, K. Okada, Chemistry of Materials 17, 5504 (2005)

[18] L.S. Sapochak, F. Strohkendl, M.R. Mclean, L.R. Dalton, C.W. Spangler, E.G. Nickel, Mat. Res. Soc. Symp. Proc., Los Angeles CA (MRS, USA, 1992)

[19] L. Yu et al., Polymer 33, 3239 (1992)

[20] S. Yoshida, K. Kozawa, T. Uchida, Bulletin of Chemical Society of Japan 68(3), 738 (1995)

[21] (a) Meister, Lucius and Bruning, British Patent, 8886, I. G. B. P., 313, 094 (1912); (b) S.K. Jain, K.G. Ojha, R.R. Gupta, Ind. J. Chem. 17B, 278 (1973)

[22] (a) H.P. Kaufmann, K. Kuchler, Chem. Ber. 67B, 944 (1934); (b) John L. Wood, In: R. Adams (Ed.), Organic reactions (Willey, New York, 1967) 3

[23] E.A. Nodiff, M. Hausman, J. Org. Chem. 31, 240 (1966) 625

[24] N.K. Goswami, R.R. Gupta, S.K. Jain, Chemistry and Industry 349 (1979)

[25] L. Horner, K. Sturm, Chem. Ber. 88, 329 (1955)

[26] National committee for clinical laboratory standards performance standards for antimicrobial disk susceptibility tests, 6th edition; approved standards M2-A6. NCCLS; Wayne, PA, 1997

[27] National committee for clinical laboratory standards methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically, 3d edition; approved standard, NCCLS publication M7-A3; Villanova, PA, 1993

[28] National committee for clinical laboratory standards, reference method for broth dilution antifungal susceptibility testing of yeasts, proposed standard, NCCLS Document M27-P; Villanova, PA, 1992