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One Pot Synthesis of Polycyclic Oxygen Aromatics. Part IV[1] Reaction of THP Ether of 2-Bromomethyl Phenols

Tirumalai R. Kasturi*, Asish B. Mandal,
Bangalore G. Sumana and Betagiri Rajasekhar

Department of Organic Chemistry
Indian Institute of Science
Bangalore-560 012, INDIA.

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Abstract: Reaction of 2-bromomethyl-1-(2'-tetrahydropyranyloxy) benzene **3a** with tetrachlorocatechol(**TCC**) in acetone in presence of anhydrous K_2CO_3 resulted in the formation of diastereomeric products to which *cis*- & *trans*- 6-chloro-8-hydroxy-8-(2-oxopropyl)spiro[9*H*-benzo[*a*]xanthen- 9,2'(1'*H*) benzofuran]-7(8*H*)-one (**7a** & **8a**) structures were assigned, along with tetrachlorocatechol ethers (**5a** & **6a**). Similar reaction of **3a** with tetrabromocatechol(**TBC**) gave the expected monobromo compounds **7d** & **8d** along with the ethers **5d** & **6d**. When the reaction was repeated with substrates **3b-c** with **TCC/TBC** in ketonic solvents(acetone/methyl ethyl ketone), the corresponding compounds **5b-c** to **8b-c**, **5e-f** to **6e-f**, **7e-g** & **8e-h** were obtained. A suitable explanation has been given for the formation of acetonyl compound **6** in this reaction.

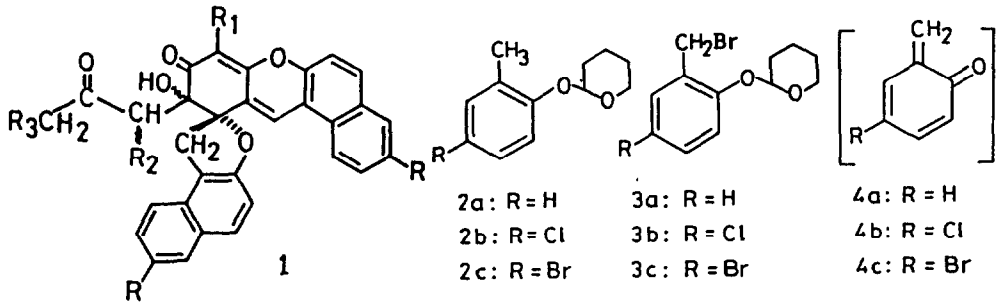
Introduction

We have recently shown[1-3] that the pyranyl ether of 1-bromomethyl-2-naphthol reacts with tetrachlorocatechol(**TCC**) in acetone in the presence of anhydrous K_2CO_3 to give novel diastereomeric polycyclic aromatic compounds **1** in addition to 1,2-naphthoquinone-1-methide dimers resulting from the base catalysed cleavage of the bromo pyranyl ether. A suitable mechanism has also been proposed for the formation of **1**.

A variety of reactions like pyrolysis of *o*-(methoxymethyl)- or, *o*-(hydroxymethyl) phenols,[4a,4b] one-electron oxidation of *o*- substituted phenols,[4c] desilylation of disilylated *o*-hydroxybenzyl alcohols,[4d] dethioalkylation of *o*-[1-(alkylthio)alkyl] phenols in presence of Ag_2O,[4e] etc. generate the *o*-quinone methide **4a**. Generally, these methods, except the one involving oxidation of *o*-substituted phenols, need relatively high temperature. If the pyranyl ether of 2-bromomethyl phenol **3a** could undergo base catalysed cleavage to give *o*-quinone methide **4a** similar to the one reported in the case of 1-bromomethyl-2-naphthol THP ether, this would be a convenient method. With this in view, the preparation and reactions of THP ether of 2-bromomethyl phenol have been studied.

Results and Discussion

The THP ether **2a** was prepared by the reaction of *o*-cresol with dihydropyran in dry CH_2Cl_2 in presence of catalytic amounts of pyridinium-*p*-toluene sulfonate(**PPTS**). The compound obtained by refluxing a CCl_4 solution of **2a** with N-bromosuccinimide (**NBS**) in the presence of benzoyl peroxide



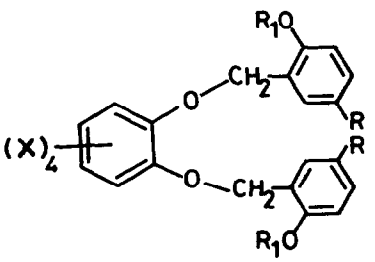
showed the presence of a singlet at δ 4.50 (2H), in addition to the characteristic broad triplet at δ 5.45 (1H) of pyranyl ether, thus confirming the formation of bromo compound **3a**. Attempts to isolate the bromo compound **3a** were unsuccessful, as it started decomposing with removal of solvent. Hence, a concentrated solution[5] of the reaction mixture in CCl_4 was used in subsequent reactions.

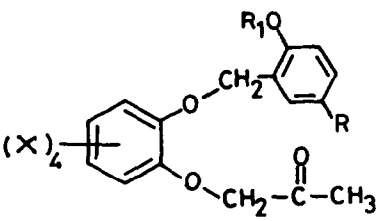
A concentrated solution of bromide **3a** in CCl_4 was diluted with dry acetone (25 ml) and added to a refluxing solution of dry acetone containing **TCC** and K_2CO_3 over a period of 4 hrs in dark and further refluxed for 24 hrs. The neutral material obtained after the work up, was subjected to column chromatography over basic alumina[6] followed by preparative TLC when four pure compounds designated **A, B, C and D** could be isolated.

The less polar compound **A** [$C_{30}H_{30}Cl_4O_6$] showed the following signals in its ^1H NMR (90 MHz) : 1.3-1.9 (6H, m), 3.4-3.9 (2H, m), 5.25 (2H, s), 5.45 (1H, br. s) and 6.8-7.6 (4H, m). The mass spectrum did not show the molecular ion, but the presence of four chlorine atoms was evident from the fragment ions at m/z 246, 248 and 250 in the ratio 3:4:2. On the basis of spectral data and fragment ions formed, the symmetrical structure **5a** was assigned to compound **A**. Compound **B**, analysing for $C_{21}H_{20}Cl_4O_5$ [m/e 492 (M^+,^{35}Cl)] exhibited a saturated carbonyl frequency (1720 cm^{-1}) in the IR spectrum. The presence of an acetonyl side chain was evident by the signals at 2.2 (3H, s) and 4.6 (2H, s) in its ^1H NMR (90 MHz) spectrum. In addition, it showed the presence of the characteristic one proton broad triplet at δ 5.45 of the pyranyl moiety. The appearance of mass spectral fragments at m/z 408 (loss of dihydropyran) and m/z 302 (corresponding to acetonyl tetrachlorocatechol moiety) further corroborated the above findings. Thus, a tentative structure **6a** could be assigned to compound **B**.

The isomeric compounds **C** & **D** [m/e 408 (M^+, ^{35}Cl; $C_{23}H_{17}ClO_5$] showed the presence of a hydroxy ($\sim$3400 cm^{-1}) and two carbonyl ($\sim$ 1700 & 1670 cm^{-1}) groups. In the ^1H NMR spectrum(270 MHz) compound **C** showed the following signals : 2.33 (3H, s), 2.71 (2H, AB_q, J = 14.9 Hz & $\Delta\nu_{AB}$ = 121.9 Hz), 3.31 (2H, AB_q, J = 15.5 Hz & $\Delta\nu_{AB}$ = 74.5 Hz), 6.64 (1H, broad singlet, D_2O exchangeable),

and 6.93-7.48 (9H, m). Compound **D** also showed similar signals at 2.22 (3H, s), 3.00 (2H, AB_q, J = 14.8 Hz & $\Delta\nu_{AB}$ = 144.6 Hz), 3.39 (2H, AB_q, J = 15.8 Hz & $\Delta\nu_{AB}$ = 196.1 Hz), 4.73 (1H, s, D_2O exchangeable) and 6.98-7.49 (9H, m). Based on the above spectral data and in analogy with the earlier reported results[1], structures **7a** & **8a** were assigned to compounds **C** & **D** respectively. Formation of compounds **7a** & **8a** clearly indicated the generation of *o*-quinone methide **4a** from THP ether under mild basic conditions. However, the trimer of *o*-quinone methide could not be isolated. Reaction of **3a** with tetrabromocatechol (**TBC**) in acetone under similar conditions resulted in the formation of compounds **5d- 8d** with spectral characteristics comparable to those of **5a-8a** respectively. When the above reaction was carried out without excluding light the same compounds **5a to 8a** were isolated; however, the yield of **6a** increased to some extent.





5a: R=H, R_1=-THP, X=Cl
5b: R=X=Cl, R_1=-THP
5c: R=Br, R_1=-THP, X=Cl
5d: R=H, R_1=-THP, X=Br
5e: R=Cl, R_1=-THP, X=Br
5f: R=X=Br, R_1=-THP

6a: R=H, R_1=-THP, X=Cl
6b: R=X=Cl, R_1=-THP
6c: R=Br, R_1=-THP, X=Cl
6d: R=H, R_1=-THP, X=Br
6e: R=Cl, R_1=-THP, X=Br
6f: R=X=Br, R_1=-THP

In order to see the generality, the reaction was carried out with substrates **3b** and **3c**. The required THP ethers **2b** & **2c** respectively were prepared from 4-chloro- and 4-bromo- *o*-cresol following the procedure mentioned earlier. Reactions of bromides **3b** and **3c**, prepared from **2b** and **2c** by **NBS** reaction, with **TCC/TBC** in ketonic solvents (acetone/methyl ethyl ketone) in presence of anhydrous K_2CO_3 resulted in the formation of compounds **5b-c** to **8b-c**, **5e-f** to **6e-f**, **7e-g** and **8e-h**.

The mechnism of formation of compounds **7** and **8** should be similar to the one postulated earlier[1] for the formation of **1**. Formation of ethers **5** & **6** could be visualised as in **Scheme-1**. Nucleophilic attack of **TCC/TBC** on the bromide **3a** results in the formation of **9**. This could either give **5a** by replacing bromide in **3a** or form **6a** by displacing bromide of α-bromo acetone which could be generated by the excess **NBS**[5] carried over into the reaction mixture containing acetone. α-Bromination of ketones with **NBS** is in fact well documented in literature[7]. In order to get some evidence, the following experiments

Table - I Characteristic Spectral Data

Compound No.	^{1}H NMR (270 MHz, $CDCl_3$) Proton multiplicity: $ArCH_2$, AB_q ($\Delta\nu_{AB}$; J_{AB})Hz	HO, s	CH_2-CO, AB_q ($\Delta\nu_{AB}$; J_{AB})Hz	CH-CO q(J) Hz	^{13}C NMR (67.89 MHz, $CDCl_3$) assignments of C_1', C_6, C_7, C_{11} and C_{12} carbons respectively	IR (nujol) cm^{-1} ν_{OH} >C = O and α,β-unsaturated >C = O	UV($CHCl_3$) nm λ_{max}
7a	3.31 (74.5; 15.5)	6.64(br)	2.71 (121.9; 14.9)	--	32.00, 104.04, 188.57 38.70, 212.02	3342, 1713, 1674	379(32,650), 309(7,100), 285(6,000), 242(7,300).
8a	3.39 (196.1; 15.8)	4.73	3.00 (144.6; 14.8)	--	38.64, 105.2, 190.48 48.08, 206.75	3406, 1704 1668	383(17,850), 304(5,900), 284(5,400), 241(5,700).
7b	3.27 (70.9; 16.0)	6.66(br)	2.69 (129.5; 16.5)	--	---	3344, 1716, 1674	383(20,100), 313(10,400), 303(10,600), 241(10,300).
8b*	3.35 (145.5; 16.0)	4.76	2.98 (107.8; 14.9)	--	37.89, 105.68, 189.73 47.21, 205.73	3404, 1719, 1668	387(19,400), 305(10,400), 298(9,600), 241(9.400).
7c	3.27 (70.9; 14.7)	6.65(br)	2.68 (129.5; 14.8)	--	---	3332, 1716, 1677	383(13.500), 314(7,100), 276(4,200), 241(6,900).
8c	3.36 (195.9; 16.0)	4.77	2.98 (144.4; 15.0)	--	37.88, 105.69, 189.40 47.29, 205.79	3412, 1713, 1659	386(14,250), 306(8,150), 273(5,400), 242(7,800).
7d*	3.30 (57.8; 16.0)	6.63(br)	2.72 (90.7; 15.5)	--	---	3334, 1716, 1677	382(18,750), 309(5,400), 287(4,600), 242(6,500).
8d	3.38 (194.8; 15.8)	4.71	2.99 (142.0; 14.6)	--	---	3434, 1707, 1653	386(21,100), 305(6,100), 284(5,700), 243(7,400).
7e*	3.26 (55.2; 16.3)	6.65(br)	2.70 (96.5; 15.9)	--	---	3312, 1719, 1683	385(20,700), 304(10,200), 274(6,500), 241(11,500).
8e*	3.35 (144.6; 16.0)	4.74	2.98 (106.3; 14.8)	--	37.48, 95,06, 189.54, 46.91, 205.85	3404, 1716, 1659	388(19,950), 306(10,000), 275(6,750), 241(11,100).
7f*	3.26 (55.5; 16.4)	6.65(br)	2.69 (95.6; 15.6)	--	---	3340, 1719, 1680	386(15,000), 307(8,500), 277(4,800), 244(8,500).
8f*	3.35 (145.6; 16.0)	4.74	2.97 (105.7; 14.8)	--	---	3412, 1713, 1674	386(10,200), 306(5,800), 295(5,200), 243(7,600).
7g	3.30 (77.5; 13.5)	6.80(br)	2.38 - 2.95 (m)	--	---	3382, 1701, 1659	382(18,000), 303(9,700), 272(5,800), 243(10,550).
8g	3.65 (198.0; 16.5)	4.83	2.96 (142.8; 14.9)	--	---	3402, 1716, 1674	385(19,250), 305(10,900), 275(6,900), 242(10,250).
8h	3.61 (196.6; 16.3)	4.73	---	2.88 6.8	---	3400, 1712, 1668	383(19,100), 301(10,200), 271(6,750), 241(10,400).

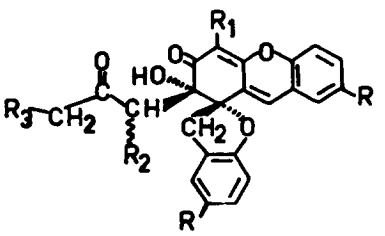
* ^{1}H NMR spectra recorded on 200 MHz.

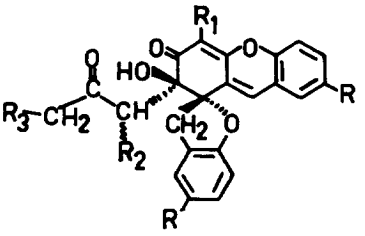
were carried out.

i) After the reaction of **2b** with **NBS** (~3 hrs), the excess **NBS** was quenched with cyclohexene. Subsequent reaction of the bromide **3b** with **TCC/acetone/K_2CO_3** did not give the acetonyl compound **6b**.

ii) The **TCC/acetone/K_2CO_3** reaction of **3b** with additional 0.3 equivalent of **NBS**[8] gave larger yield (~20 % excess) of acetonyl compound **6b**.

iii) Reaction of a concentrated solution of **3b** in CCl_4/acetone along with α-bromo acetone(1 ml) with TCC/acetone/K_2CO_3 gave increased (~45 %) yield of **6b**.

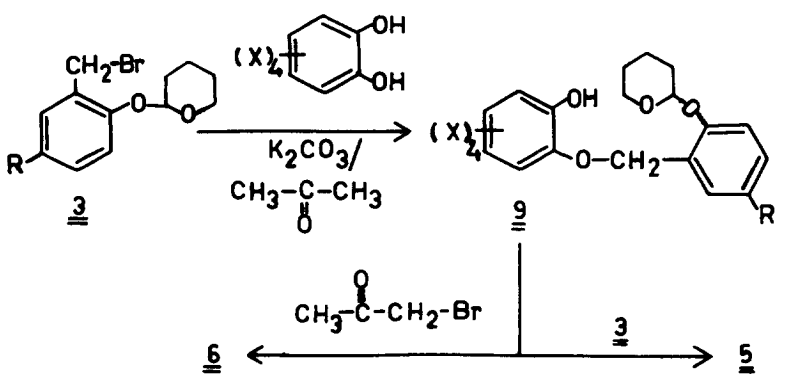




7a: R=R_2=R_3=H, R_1=Cl
7b: R=R_1=Cl, R_2=R_3=H
7c: R=Br, R_1=Cl, R_2=R_3=H
7d R=R_2=R_3=H, R_1=Br
7e R=Cl, R_1=Br, R_2=R_3=H
7f: R=R_1=Br, R_2=R_3=H
7g: R=Br, R_1=Cl, R_2=H, R_3=$-CH_3$

8a: R=R_2=R_3=H, R_1=Cl
8b: R=R_1=Cl, R_2=R_3=H
8c: R=Br, R_1=Cl, R_2=R_3=H
8d: R=R_2=R_3=H, R_1=Br
8e: R=Cl, R_1=Br, R_2=R_3=H
8f: R=R_1=Br, R_2=R_3=H
8g: R=Br, R_1=Cl, R_2=H, R_3=$-CH_3$
8h: R=Br, R_1=Cl, R_2=β-CH_3, R_3=H

These experiments clearly substantiated the postulated mechanism. The increased yield of **6a** in presence of light could be due to the increased formation of α-bromo acetone.



Scheme-1

EXPERIMENTAL SECTION

All melting points and boiling points are uncorrected. UV (nm) and IR (cm^{-1}) spectra were recorded on a HITACHI Model 557 Double wave length/Double beam and HITACHI 270-50 Infrared spectrophotometers respectively. NMR spectra were recorded on a Jeol FX-90 Q,22.49 MHz (^{13}C) or a Bruker ACF-200, 50.32 MHz (^{13}C) or a Bruker WH-270, 67.87 MHz (^{13}C) spectrometers with Me_4Si as internal standard (δ = 0 ppm). MS (70 eV) were recorded on an Atlas CH-4 or a Jeol MS-DX 303 spectrometer fitted with a built-in direct inlet system. Analytical and preparative TLC were carried out using silica gel. Column chromatography was carried out using neutral/basic alumina. All organic extracts were dried over anhydrous Na_2SO_4. Compounds (**7a-g** and **8a-h**) reported herein are racemic mixtures.

2-Methyl-1-(2'-tetrahydropyranyloxy)benzene (2a)

A solution of *o*-cresol (5 gm) and dihydropyran (5.9 ml) in dry methylene chloride (50 ml) containing **PPTS** (1.16 gm) was stirred for 4 hrs at room temperature. The solution was washed with saturated brine to remove the catalyst, followed by ice-cold 10% aq.NaOH (2 x 40 ml), water (2 x 40 ml) and dried. The crude reaction mixture, after the removal of solvent and excess dihydropyran, was purified by column chromatography over basic alumina. Elution with hexane-benzene (1:1) gave the pyranyl ether **2a** (8.25 gm, 93%): b.p. 110°C/6 mm. This method gives the THP ether in much better yield than the one reported.[9]

4-Chloro-2-methyl-1-(2'-tetrahydropyranyloxy)benzene (2b)

A similar reaction of 4-chloro-2-methyl phenol (5 gm) with dihydropyran (4.50 ml) in dry methylene chloride (50 ml) containing **PPTS** (883 mg) yielded the pyranyl ether **2b** (7.08 gm, 89%): b.p.116°C /6 mm; IR (Neat): 1618 and 1600; ^1H NMR(90 MHz, $CDCl_3$): 1.46-1.94 (m, 6H), 2.22 (s, 3H), 3.44-3.96 (m, 2H), 5.32 (br.t, 1H) and 6.88-7.16 (m, 3H); MS: m/e 226 (M^+); Anal. calcd. for $C_{12}H_{15}ClO_2$: C, 63.71; H, 6.63. Found: C, 63.41; H, 6.62%.

4-Bromo-2-methyl-1-(2'-tetrahydropyranyloxy)benzene (2c)

A similar reaction of 4-bromo-2-methyl phenol (5 gm) with dihydropyran (3.4 ml) in dry methylene chloride (50 ml) containing **PPTS**(674 mg) yielded the pyranyl ether **2c** (6.32 gm, 87%): b.p.131.5°C /6 mm; IR (Neat): 1620, 1600; ^1H NMR(90 MHz, $CDCl_3$): 1.4-1.98 (m, 6H), 2.24 (s, 3H), 3.44-3.98 (m, 2H), 5.36 (br. t, 1H) and 6.88-7.26 (m, 3H); (HRMS, m/e calcd. for $C_{12}H_{15}BrO_2$ 270.0255, Found. 270.0233).

2-Bromomethyl-1-(2'-tetrahydropyranyloxy)benzene (3a)

A mixture of pyranyl ether **2a** (3.2 gm, 0.0166 mole), **NBS** (3.2 gm; 0.0182 mole) and dibenzoyl peroxide (40 mg; 0.00016 mole) was refluxed in CCl_4 (40 ml) in dark till the **NBS** reacted completely (3 hrs). It was cooled, the separated succinimide was filtered off and the filtrate washed with water (2 x 30 ml) and dried. The CCl_4 solution, concentrated to 1/4th of its original volume [IR(CCl_4): 1620, 1600; ^1H NMR(90 MHz, CCl_4+$CDCl_3$): 1.44-2.04 (m, 6H), 3.52-4.02 (m, 2H), 4.56 (s, 2H), 5.55 (br.t, 1H) and 6.82-7.40 (m, 4H)] and protected from light was used in subsequent reaction.

4-Chloro-2-bromomethyl-1-(2'-tetrahydropyranyloxy)benzene (3b)

The above reaction was repeated with the pyranyl ether **2b** for 3 hrs to give the bromide **3b**: IR(CCl_4): 1620, 1600; ^1H NMR(90 MHz, CCl_4+$CDCl_3$): 1.46-2.02 (m, 6H), 3.44-3.98 (m, 2H), 4.46 (s, 2H), 5.45 (br.t, 1H) and 6.96-7.16 (m, 3H).

4-Bromo-2-bromomethyl-1-(2'-tetrahydropyranyloxy)benzene (3c)

The above reaction was repeated with the pyranyl ether **2c** for 3 hrs to give the bromide **3c**: IR(CCl_4): 1618, 1600; ^1H NMR (90 MHz, CCl_4+$CDCl_3$): 1.45-2 00 (m, 6H), 3.40-4.04 (m, 2H), 4.45 (s, 2H), 5.48 (br.t, 1H) and 6.92-7.42 (m, 3H).

Reaction of bromide 3 with TCC/TBC in ketonic solvent in presence of K_2CO_3

General Procedure: A solution of bromide **3** in CCl_4 (20 ml), prepared from pyranyl ether **2** after dilution with ketonic solvent (25 ml), was added to a vigorously stirred refluxing solution of **TCC** or **TBC** in ketonic solvent (150 ml) containing anhydrous K_2CO_3 over a period of 4 hrs **in dark**. The reaction mixture was further refluxed for 24 hrs, cooled, K_2CO_3 filtered off and washed with ether. After the removal of solvent, the residue was taken in ether (150 ml) and washed successively with water (4 x 50 ml), 10% aq.NaOH (4 x 50 ml), water (4 x 50 ml) and dried. Ether was removed and the residue chromatographed.

a. Reaction of 3a with TCC in acetone : The product obtained by reaction of **3a**, prepared from **2a** (3.2 gm, 0.0166 mole), with **TCC** (4.08 gm, 0.0166 mole) and K_2CO_3 (3.2 gm, 0.0232 mole) in acetone (150 ml) was chromatographed.

The material obtained by elution with $CHCl_3$-hexane(1:1) was separated into two compounds by **PTLC** ($CHCl_3$-hexane, 3:2). The first compound was characterised as 1,2-di[2-(2'-tetrahydropyranyloxy)-benzyloxy]-3,4,5,6-tetrachlorobenzene **5a** (285 mg; 5.48 %): m.p.95°C (benzene-hexane); ^{13}C NMR (22.49 MHz, $CDCl_3$) : 18.71(t), 25.23(t), 30.32(t), 61.83(t), 71.00(t), 96.21(d), 114.23(d), 121.31(d), 125.29(s), 127.94(s), 129.60(d), 130.04(d), 149.50(s), 154.81(s); Anal. Calcd. for $C_{30}H_{30}Cl_4O_6$: C, 57.50. H, 4.79. Found : C, 57.45; H, 5.20%. The second compound was identified as 1-[2-(2'-tetrahydropyranyloxy)benzyl-oxy]- 2- (2-oxopropyloxy)-3,4,5,6-tetrachlorobenzene **6a** (172 mg, 2.1 %): m.p.105°C (benzene-hexane); Anal. Calcd. for $C_{21}H_{20}Cl_4O_5$: C, 51.21; H, 4.06. Found: C, 50.82; H, 3.95%.

The material obtained by further elution with $CHCl_3$ and $CHCl_3$-EtOAc (1:1) was separated into two compounds by repeated **PTLC** ($CHCl_3$). The less polar compound was shown to be *cis*-6-chloro-8-hydroxy-8-(2- oxopropyl)spiro[9*H*-benzo[*a*]xanthen-9,2'(1'*H*)benzofuran]- 7(8*H*)-one **7a** (352 mg; 10.3%): m.p. 214°C ($CHCl_3$-hexane); MS : m/e 408 (M^+); Anal. calcd. for $C_{23}H_{17}ClO_5$: C, 67.64; H, 4.16. Found: C, 67.54; H, 4.15%. The more polar compound was identified as *trans*-6-chloro-8- hydroxy-8-(2- oxopropyl)spiro[9*H*-benzo[*a*]xanthen-9,2'(1'*H*)benzofuran]- 7(8*H*)-one **8a** (436 mg; 12.8%): m.p.252°C ($CHCl_3$); MS : m/e 408 (M^+); Anal. calcd. for $C_{23}H_{17}ClO_5$: C, 67.64 ; H, 4.16. Found : C, 67.34; H, 4.14%.

b. Reaction of 3b with TCC in acetone : The product obtained by the reaction of **3b**, prepared from **2b** (3.2 gm; 0.0141 mole), with **TCC** (3.46 gm, 0.0141 mole) and K_2CO_3 (2.72 gm; 0.0197 mole) in acetone (150 ml) was chromatographed.

The material obtained by elution with $CHCl_3$-hexane (1:1) was separated into two compounds by **PTLC** ($CHCl_3$:hexane 3:2). These were characterised as 1,2-di[5-chloro-2-(2'-tetrahydropyranyloxy)ben-zyloxy]-3,4,5,6-tetrachlorobenzene **5b** (340 mg; 6.94 %): m.p. 58°C (chloroform-hexane); IR (nujol): 1616 and 1600; ^1H NMR (90 MHz, $CDCl_3$): 1.44-1.84 (6H, m), 3.25- 3.72 (2H, m), 5.09 (2H, s), 5.32 (1H, br. t), 6.96-7.24 (2H, m) and 7.41 (1H, d, J = 1.8 Hz); ^{13}C NMR(22.49 MHz, $CDCl_3$): 18.58(t), 25.08(t), 30.17(t), 61.81(t), 70.26(t), 96.48(d), 115.44(d), 126.28(s), 127.04(s), 127.90(s), 128.34(s), 128.77(d), 128.99(d), 149.14(s) and 152.82(s); Anal. Calcd. for. $C_{30}H_{28}O_6Cl_6$: C, 51.87; H, 4.03. Found: C, 52.03; H, 3.99 %, and 1-[5- chloro-2-(2'-tetrahydropyranyloxy) benzyloxy]-2-(2- oxopropyloxy)-3,4,5,6- tetra-chlorobenzene **6b** (198 mg; 2.66 %): m.p. 72°C (chloroform- hexane); IR (nujol): 1599 and 1716; ^1H NMR (90 MHz, $CDCl_3$): 1.45-1.88(6H, m), 2.24 (3H, s), 3.40-3.76 (2H, m), 4.58 (2H, s), 5.12 (2H, s), 5.35 (1H, br. t), 7.00- 7.31 (2H, m) and 7.46 (1H, d, J = 1.8 Hz); ^{13}C NMR(22.49 MHz, $CDCl_3$): 18.82(t), 25.12(q), 26.45(t), 30.32(t), 62.16(t), 70.78(t), 77.31(t), 96.76(d), 115.89(d), 126.50(s), 126.84(s), 127.28(s), 128.18(s), 128.94(s), 129.38(d), 148.40(s), 148.62(s), 153.26(s) and 203.01(s); MS: m/e 526(M^+); Anal. Calcd. for $C_{21}H_{19}O_5Cl_5$: C, 47.90; H, 3.61. Found: C, 47.45; H, 3.51%.

The material obtained by further elution with $CHCl_3$ and $CHCl_3$-ethyl acetate (1:1) was separated into two compounds by repeated **PTLC** ($CHCl_3$). The first compound was identified as *cis*-2,6,6'-trichloro-8- hydroxy-8-(2- oxopropyl)spiro[9*H*-benzo[*a*]xanthen-9,2'(1'*H*)benzofuran]- 7(8*H*)-one **7b** (308 mg; 9.1%): m.p. 255°C ($CHCl_3$-hexane), MS : m/e 476 (M^+); Anal. calcd. for $C_{23}H_{15}Cl_3O_5$: C, 57.98; H, 3.15. Found: C, 57.83; H, 3.11%. The second compound was characterised as *trans*-2,6,6'-trichloro-8-hydroxy-8- (2-oxopropyl)spiro[9*H*-benzo[*a*]xanthen-9,2'(1'*H*)benzofuran]- 7(8*H*)-one **8b** (398 mg; 11.8%): m.p. 198°C ($CHCl_3$-hexane); MS : m/e 476 (M^+); Anal. calcd. for $C_{23}H_{15}Cl_3O_5$: C, 57.98; H, 3.15. Found: C, 57.66; H, 3.14%.

c. Reaction of 3c with TCC in acetone : The product obtained by the reaction of **3c** prepared from **2c** (3.2 gm; 0.0118 mole), with **TCC** (2.90 gm, 0.0118 mole) and K_2CO_3 (2.28 gm; 0.0165 mole) in acetone (150 ml) was chromatographed.

The material obtained by elution with $CHCl_3$-hexane (1:1) was separated by **PTLC** ($CHCl_3$-hexane 3:2) and characterised as 1,2-di[5-bromo- 2-(2'-tetrahydropyranyloxy)benzyloxy]-3,4,5,6-tetrachlorobenzene **5c** (305 mg; 6.61 %): m.p.88°C (chloroform-hexane); IR (nujol): 1618, 1600; ^1H NMR (90 MHz, $CDCl_3$): 1.45-1.92(6H, m), 3.44-3.72(2H, m), 5.11(2H, s), 5.33(1H, br. t), 6.98(1H, d, J = 8.8 Hz), 7.34(1H, dd, J = 1.8 & 8.7 Hz) and 7.58 (1H, d, J = 2.2 Hz); ^{13}C NMR (22.49 MHz, $CDCl_3$): 18.71(t), 25.23(t), 30.32(t), 62.05(t), 70.34(t), 96.54(d), 113.79(s), 116.11(d), 127.61(s), 128.05(s), 128.49(s), 131.81(d), 132.14(d), 149.28(s), 153.48(s); Anal. Calcd. for $C_{30}H_{28}Cl_4Br_2O_6$: C, 46.03; H, 3.58. Found: C, 45.81; H, 3.67%, and 1-[5-bromo-2-(2'-tetrahydropyranyloxy)benzyloxy]-2-(2-oxopropyloxy)-3,4,5,6-tetrachlorobenzene **6c** (165 mg; 2.45%): m.p. 97°C (chloroform- hexane); IR(nujol): 1600, 1718; ^1H NMR(90 MHz, $CDCl_3$): 1.45- 1.92(6H, m), 2.23(3H, s), 3.42-3.82(2H, m), 4.58(2H, s), 5.12(2H, s), 5.37(1H, br. t), 7.03(1H, d, J = 8.8 Hz), 7.39(1H, dd, J = 2.2 & 8.8 Hz) and 7.62 (1H, d, J=2.2 Hz),; ^{13}C NMR(22.49 MHz, $CDCl_3$): 18.49(t), 24.90(q), 26.23(t), 30.10 (t), 61.94(t), 70.56(t), 77.20(t), 96.54(d), 113.57(s), 116.11(d), 127.06 (s), 127.94(s), 128.38(s), 132.03(d),132.36(d),148.17(s), 148.28(s), 153.48 (s), 202.79(s); (HRMS, m/e Calcd. for $C_{21}H_{19}Cl_4BrO_5$: 569.9170, Found: 569.9168).

The material obtained by further elution with $CHCl_3$ and $CHCl_3$-EtOAc (1:1) was separated into two compounds by repeated **PTLC**($CHCl_3$). These were characterised as *cis*-2,6'-dibromo-6-chloro-8-hydroxy-8-(2-oxopropyl) spiro[9*H*-benzo[*a*]xanthen-9,2'(1'*H*)benzofuran]-7(8*H*)-one **7c** (314 mg; 9.4%): m.p. 263°C ($CHCl_3$-hexane); MS : m/e 564 (M^+); Anal. calcd. for $C_{23}H_{15}ClBr_2O_5$: C, 48.93; H, 2.65. Found: C, 48.63; H, 2.62%, and *trans*- 2,6'-dibromo-6-chloro-8-hydroxy-8-(2-oxopropyl)spiro [9*H*-benzo[*a*]xanthen- 9,2'(1'*H*)benzofuran]-7(8*H*)-one **8c** (388 mg; 11.6%): m.p. 201°C ($CHCl_3$- hexane); MS: m/e 564 (M^+); Anal. calcd. for $C_{23}H_{15}ClBr_2O_5$: C, 48.93; H, 2.65. Found. C, 48.45; H, 2.61%.

d. Reaction of 3a with TBC in acetone : The product obtained by the reaction of bromide **3a** prepared from **2a** (3.2 gm; 0.0166 mole), with **TBC** (7.00 gm; 0.0166 mole) and K_2CO_3 (3.2 gm; 0.0232 mole) in dry acetone (150 ml) was chromatographed.

The material obtained by elution with $CHCl_3$-hexane (1:1) was separated into two compounds by **PTLC** ($CHCl_3$-hexane 3:2). These were characterised as 1,2-di[2-(2'-tetrahydropyranyloxy)-benzyloxy]-3,4,5,6-tetrabromobenzene **5d** (317 mg; 4.76 %): m.p. 121°C (hexane); IR(nujol): 1617 and 1600; ^1H NMR (90 MHz, $CDCl_3$): 1.43-1.84 (6H, m), 3.40-3.82 (2H, m), 5.21 (2H, s), 5.38 (1H, br. t) and 6.84-7.52 (4H, m); Anal. Calcd. for $C_{30}H_{30}O_6Br_4$: C, 44.88; H, 3.74. Found: C, 44.49; H, 3.63 %, and 1-[2-(2'- tetrahydropyranyloxy) benzyloxy]-2-(2-oxopropyloxy)-3,4,5,6-tetrabromobenzene **6d** (158 mg; 1.42%): m.p. 77°C ($CHCl_3$-hexane); IR (nujol): 1600 and 1715; ^1H NMR (90 MHz, $CDCl_3$): 1.56-1.87 (6H, m), 2.21 (3H, s), 3.33-3.87 (2H, m), 4.56 (2H, s), 5.33 (2H, s), 5.39 (1H, br. t) and 6.81-7.56 (4H, m); Anal. Calcd. for $C_{21}H_{20}O_5Br_4$: C, 37.72; H, 2.99. Found: C, 37.31; H, 3.11 %.

The material obtained by further elution with $CHCl_3$ and $CHCl_3$-EtOAc (1:1) was separated into two compounds by repeated **PTLC** ($CHCl_3$). The less polar compound was shown to be *cis*-6-bromo-8-hydroxy-8-(2- oxopropyl)spiro [9*H*-benzo[*a*]xanthen-9,2'(1'*H*)benzofuran]-7(8*H*)-one **7d** (376 mg; 10.0%): m.p. 224°C ($CHCl_3$-hexane); MS: m/e 452 (M^+), Anal. Calcd. for $C_{23}H_{17}BrO_5$: C, 61.05; H, 3.76. Found: C, 60.61; H, 3.74%. The more polar compound was characterised as *trans*-6-bromo-8-hydroxy-8-(2-oxopropyl)spiro[9*H*-benzo[*a*] xanthen-9,2'- (1'*H*)benzofuran]-7(8*H*)-one **8d**(423 mg; 11.2%): m.p. 206°C ($CHCl_3$-hexane); MS: m/e 452 (M^+), Anal. Calcd. for $C_{23}H_{17}BrO_5$: C, 61.05; H, 3.76. Found: C, 60.66; H, 3.73 %.

e. Reaction of 3b with TBC in acetone : The product obtained by the reaction of bromide **3b**, prepared from **2b** (3.2 gm; 0.0141 mole), with **TBC** (5.97 gm; 0.0141 mole) and K_2CO_3 (2.72 gm, 0.0141 mole) in acetone (150 ml) was chromatographed.

The material obtained by elution with $CHCl_3$-hexane (1:1) was separated into two compounds by **PTLC** ($CHCl_3$-hexane 3:2). These were characterised as 1,2-di[5-chloro-2-(2'-tetrahydropyranyloxy)benzyloxy-3,4,5,6-tetrabromobenzene **5e** (325 mg; 5.29 %): m.p. 64°C ($CHCl_3$-hexane); IR (nujol): 1615 and 1600; ^1H NMR (90 MHz, $CDCl_3$): 1.45-1.84 (6H, m), 3.44-3.76 (2H, m), 5.12 (2H, s), 5.34 (1H, br. t), 6.97-7.26 (2H, m) and 7.48 (1H, d, J = 1.7 Hz); Anal. Calcd. for $C_{30}H_{28}O_6Cl_2Br_4$: C, 41.37; H, 3.21. Found: C, 41.02; H, 3.29 %. and 1-[5-chloro-2-(2'-tetrahydropyranyloxy) benzyloxy]- 2- (2-oxopropyloxy)-3,4,5,6-tetrabromobenzene **6e** (174 mg; 1.76 %): m.p. 98°C ($CHCl_3$-hexane); IR (nujol): 1600 and 1715; ^1H NMR (90 MHz, $CDCl_3$): 1.50- 1.85 (6H, m), 2.25 (3H, s), 3.44-3.80 (2H, m), 4.60 (2H, s), 5.12 (2H, s), 5.38 (1H, br. t), 7.03-7.32 (2H, m) and 7.52 (1H, d, J = 1.8 Hz); ^{13}C NMR(22.49 MHz, $CDCl_3$): 18.71(t), 25.01(q), 26.45(t), 30.21(t), 62.05(t), 70.56(t), 76.97(t), 96.65(d), 115.67(d), 121.31(s),

122.19(s), 124.18(s), 124.40(s), 126.39(s), 126.73(s), 129.05(d), 129.27(d), 149.50(s), 150.05(s), 152.93(s) and 202.90(s); MS: m/e 702 (M^+); Anal. Calcd. for $C_{21}H_{19}O_5ClBr_4$: C, 35.89; H, 2.70. Found: C, 35.53; H, 2.79 %.

The material obtained by further elution with $CHCl_3$ and $CHCl_3$-EtOAc (1:1) was separated into two compounds by **PTLC** ($CHCl_3$). These were characterised as *cis*-2,6'-dichloro-6-bromo-8-hydroxy-8(2-oxopropyl)spiro [9*H*-benzo[*a*]xanthen-9,2'(1'*H*)benzofuran]-7(8*H*)-one **7e** (323 mg; 8.8%): m.p. 248°C ($CHCl_3$-hexane); MS: m/e 520 (M^+), Anal. Calcd. for $C_{23}H_{15}Cl_2BrO_5$: C, 53.07; H, 2.88. Found: C, 52.73; H, 2.85%, and *trans*-2,6'-dichloro-6- bromo-8- hydroxy-8- (2-oxopropyl) spiro [9*H*-benzo [*a*] xanthen-9, 2'- (1'*H*) benzofuran]-7(8*H*)-one **8e** (414 mg; 11.2%): m.p.220°C ($CHCl_3$); MS: m/e 520 (M^+), Anal. Calcd. for $C_{23}H_{15}Cl_2BrO_5$: C, 53.07; H, 2.88. Found : C, 52.86; H, 2.86%.

f. Reaction of 3c with TBC in acetone : The product obtained by the reaction of bromide **3c**, prepared from **2c** (3.2 gm; 0.0118 mole), with **TBC** (5.0 gm; 0.0118 mole) and K_2CO_3 (2.28 gm; 0.0165 mole) in acetone (150 ml) was chromatographed.

The material obtained by elution with $CHCl_3$-hexane (1:1) was separated into two compounds by **PTLC** ($CHCl_3$-hexane 3:2). The less polar one was characterised as 1,2-di[5-bromo-2-(2'-tetrahydropyranyloxy) benzyloxy]-3,4,5,6-tetrabromobenzene **5f** (290 mg; 5.13 %): m.p. 67°C ($CHCl_3$-hexane); IR (nujol): 1617 and 1600; ^1H NMR (90 MHz, $CDCl_3$): 1.42-1.88 (6H, m), 3.40- 3.82 (2H, m), 5.11 (2H, s), 5.34 (1H, br. t), 6.94-7.41 (2H, m) and 7.61 (1H, d, J = 1.8 Hz); Anal. Calcd. for $C_{30}H_{28}O_6Br_6$: C, 37.57; H, 2.92. Found: C, 37.19; H, 2.96 %. The more polar one was identified as 1-[5-bromo-2-(2'-tetrahydropyranyloxy)benzyloxy]-2-(2-propyloxy)-3,4,5,6-tetrabromobenzene **6f** (160 mg; 1.81 %): m.p. 96°C ($CHCl_3$-hexane); IR (nujol): 1599 and 1715; ^1H NMR (90 MHz, $CDCl_3$): 1.40-1.96 (6H, m), 2.22 (3H, s), 3.40-3.81 (2H, m), 4.56 (2H, s), 5.10 (2H, s), 5.38 (1H, br. t) and 6.92- 7.68 (3H, m); Anal. Calcd. for $C_{21}H_{19}O_5Br_5$: C, 33.78; H, 2.54. Found: C, 34.01; H, 2.61 %.

The material obtained by further elution with $CHCl_3$ and $CHCl_3$-EtOAc (1:1) was separated into two compounds by **PTLC** ($CHCl_3$). The first compound was characterised as *cis*-2,6,6'-tribromo-8-hydroxy-8-(2-oxopropyl)spiro [9*H*-benzo[*a*]xanthen-9,2'(1'*H*) benzofuran]-7(8*H*)-one **7f** (394 mg; 10.9%): m.p.238°C($CHCl_3$-hexane); MS: m/e 608(M^+), Anal. Calcd. for $C_{23}H_{15}Br_3O_5$: C, 45.39; H, 2.46. Found: C, 44.99; H, 2.47%. The second compound was identified as *trans*-2,6,6'-tribromo-8-hydroxy-8(2-oxopropyl)spiro[9*H*-benzo[*a*]xanthen-9,2'(1'*H*)benzofuran]-7(8*H*)-one **8f** (412 mg; 11.4%): m.p.219°C ($CHCl_3$-hexane); MS: m/e 608 (M^+), Anal. Calcd. for $C_{23}H_{15}Br_3O_5$: C, 45.39; H, 2.46. Found : C, 45.29; H, 2.43%.

g. Reaction of 3c with TCC in methyl ethyl ketone : The product obtained by reaction of **3c**, prepared from **2c**[10] (3.2 gm; 0.0118 mole), with **TCC** (2.90 gm; 0.0118 mole) and K_2CO_3 (2.28 gm; 0.0165 mole) in methyl ethyl ketone (150 ml) was chromatographed.

Elution with chloroform-hexane (1:1) gave **5c** (293 mg, 6.34 %). Further elution with $CHCl_3$-EtOAc (1:1) gave a mixture of three compounds, which were separated into two fractions by repeated **PTLC**($CHCl_3$). Fraction(i) was characterised as *cis*-2,6'-dibromo-6-chloro-8-hydroxy-8-(2-oxobutyl)spiro [9*H*-benzo[*a*]xanthen-9,2'(1'*H*)benzofuran]-7(8*H*)-one **7g** (245 mg; 7.2%): m.p. 258°C ($CHCl_3$-hexane); MS : m/e 578 (M^+); Anal. calcd. for $C_{24}H_{17}ClBr_2O_5$: C, 49.82; H, 2.94. Found: C, 49.49; H, 2.91%.

Fraction(ii) was further separated into two compounds by repeated **PTLC** ($CHCl_3$-hexane, 9:1). One of them was identified as *trans*-2,6'-dibromo-6- chloro-8-hydroxy-8-(1β-methyl-2-oxopropyl)spiro[9*H*-benzo[*a*]xanthen-9,2' (1'*H*)-benzofuran]-7(8*H*)-one **8g** (70 mg; 2.05%): m.p.213°C($CHCl_3$-hexane); MS: m/e 578 (M^+); Anal. calcd. for $C_{24}H_{17}ClBr_2O_5$: C, 49.82; H, 2.94. Found: C, 49.39; H, 2.91%. The other compound was identified as *trans*-2,6'-dibromo-6- chloro-8-hydroxy-8-(2-oxobutyl)spiro[9*H*-benzo[*a*]xanthen-9,2'(1'*H*)-benzofuran]-7(8*H*)-one **8h** (342 mg; 10.02%): m.p. 228°C ($CHCl_3$); MS : m/e 578 (M^+); Anal. calcd. for $C_{24}H_{17}ClBr_2O_5$: C, 49.82; H, 2.94. Found: C, 49.77; H, 2.94%.

Reaction of 3a with TCC/acetone/K_2CO_3

Reaction of **3a**, prepared from **2a** (3.2 gm) as before, with **TCC** (4.08 gm)/K_2CO_3 (3.2 gm) in acetone (150 ml) was carried out in **day light**. The reaction mixture was worked up as before & purified(**PTLC**) to give **5a** (484 mg; 9.3%), **6a** (265 mg, 3.2%), **7a** (55 mg; 1.6%) and **8a** (72 mg; 2.1%).

Reaction of 3b with TCC/acetone/K_2CO_3

i) Reaction of **2b**(3.2 gm) with **NBS**(2.74 gm) was carried out as before for 3 hrs. The excess **NBS** was quenched by addition of cyclohexene(~0.5 ml) and worked up to give a concentrated solution of **3b** in CCl_4. This was added to a mixture of **TCC**(4.08 gm)/K_2CO_3(3.2 gm) in acetone(150 ml) and the reaction was carried out for 24 hrs. Chromatography of the product, as before, gave only **5b**(355 mg; 7.25%), **7b**(296 mg; 8.81%) and **8b**(372 mg; 11.08%).

ii) To a concentrated solution of **3b**, prepared from **2b**(3.2 gm) and **NBS**(2.74 gm) as before, **NBS** (0.3 equivalent) was added and the resulting mixture was treated with **TCC**(4.08 gm)/K_2CO_3(3.2 gm) in acetone(150 ml) and the reaction was continued for 24 hrs. Chromatography of the product gave **5b**(315 mg; 6.42%), **6b**(237 mg; 3.18%), **7b**(275 mg; 8.19%) and **8b**(354 mg; 10.54%).

iii) To a concentrated solution of **3b** in CCl_4 prepared from **2b**(3.2 gm), α-bromo acetone(1 ml) was added and the resulting mixture was treated with **TCC**(4.08 gm)/K_2CO_3(3.2 gm) in acetone(150 ml) as before to give after work up & purification **5b**(296 mg; 6.04%), **6b**(298 mg; 4.01%), **7b**(232 mg; 6.91%) and **8b**(303 mg; 9.02%).

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References and Notes

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8. Excess **NBS** was added just before the addition of concentrated solution of bromide **3b** in CCl_4/acetone to the reaction mixture.

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10. After 3 hrs of usual reaction time, excess **NBS** was quenched by addition of cyclohexene.