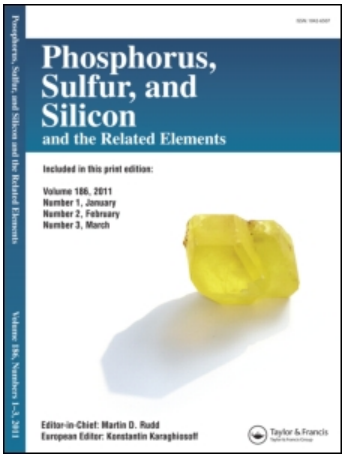

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CHLOROSULFONATION OF 9-ARYL 3,3,6,6-TETRAMETHYLOCTAHYDROXANTHEN-1,8-DIONES

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CHLOROSULFONATION OF 9-ARYL 3,3,6,6-TETRAMETHYLOCTAHYDROXANTHEN-1,8-DIONES

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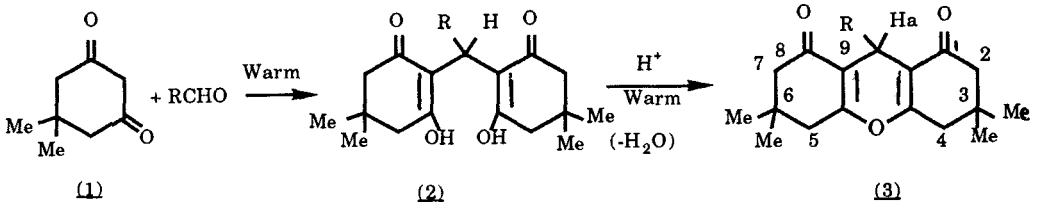
The 9-aryl-3,3,6,6-tetramethyloctahydroxanthendiones (4–20) react with chlorosulfonic acid to give the sulfonyl chlorides (25, 34, 43, 53, 55, 59, 63 and 65). The xanthendione (7) from *m*-anisaldehyde afforded the bis-sulfonyl chloride (30). The products were converted into 35 sulfonamides, 4-hydrazides (48, 56, 57, 69a) and 2 hydrazones (49, 69b) required for screening as potential pesticides. Dimedone (1) (2 moles) and cinnamaldehyde (1 mole) in ethanol-piperidine (catalyst) afforded an abnormal product probably (76), however an equimolar reaction with cinnamaldehyde or the α-methyl derivative in pyridine gave the 2-phenylpyrans (78, 79). Dimedone with salicylaldehyde or *o*-vanillin afforded the pyran derivatives (72, 73); the former reacted with chlorosulfonic acid to give the sulfonyl chloride (74), characterized as the morpholidate (75). The xanthendione (15) with chlorosulfonic acid afforded the chloride (70), characterized as the morpholidate (71). Attempted chlorosulfonation of the substrates (16, 77, 78 and 79) all gave impure products and 13 failed to react. The NMR spectral data of the compounds are briefly discussed.

Key words: 9-Aryl 3,3,6,6-tetramethyloctahydrohydroxanthen-1,8-diones; chlorosulfonation; sulfonamides.

INTRODUCTION

The work descibed in this paper forms part of our general programme concerned with the chemistry and biological activity of aromatic sulfonyl derivatives.[1–3] Dimedone (5,5-dimethylcyclohexan-1,3-dione (1) (2 moles) is well known[4] to react with aliphatic and aromatic aldehydes (1 mole) by a Michael type condensation to yield the 2:1 adducts (2); the latter are readily dehydrated to the corresponding octahydroxanthen-1,8-diones (3) (Scheme I):



(1) (2) (3)

SCHEME I

The derivatives (2 and 3) are generally well-defined crystalline solids which have been used for many years in organic qualitative analysis for the identification of aldehydes.[5–7] In contrast to the ease of formation of the 2:1 condensation product (3), the preparation of the 2-benzylidene derivative of dimedone (1) is much more difficult. It has, however, been reported[8] to be formed by heating (1) with excess benzaldehyde and sodium in absolute methanol.

Reaction of dimedone (1) with aromatic aldehydes will provide a series of the 9-aryl octahydroxanthendiones (3; R=aryl) these should be susceptible to chlorosulfonation by treatment with excess chlorosulfonic acid since they are essentially alkyl substituted benzene derivatives which are known[9] to react under relatively mild conditions. Furthermore, previous studies have clearly demonstrated that keto groups are unaffected by treatment with chlorosulfonic acid: thus hydantoins,[10] coumarins[11] and chalcones[12,13] have been successfully converted into their chlorosulfonyl derivatives.

DISCUSSION

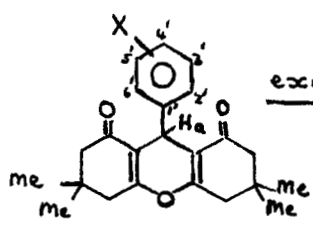
A series of aromatic aldehydes was reacted with dimedone (1) under standard conditions (boiling aqueous ethanol-piperidine catalyst)[4] to give the 2:1 adducts (2, R-aryl) which were subsequently dehydrated by treatment with boiling ethanol-concentrated hydrochloric acid to give the corresponding octahydroxanthendiones (3, R=aryl).[4,5] By this procedure, 9-aryloctahydroxanthen-diones were obtained in excellent yields from benzaldehyde (4) and the following substituted benzaldehydes: 2-methyl (5); 2-, 3- and 4-methoxy (6, 7, 8); 2-, 3- and 4-chloro (9, 10, 11); 4-fluoro (12); 2,6-dichloro (13); 3,4-dimethoxy (14); 3- and 4-hydroxy (15, 16) and 4-phenyl (17) (Chart I). Other derivatives were obtained from thiophene 2- and 3-carboxaldehyde (18, 19) and 1-naphthaldehyde (20) (Chart I). The products (10, 11, 12, 13, 15, 17, 18, 19) were novel.

The NMR spectra of the 9-arylxanthendiones (3) showed that the tertiary allylic proton (Ha) resonated as a relatively low field singlet (δ 5.0 approx.) as this is deshielded by the combined effects of the adjacent double bond and the aromatic ring. The protons of the CH_2CO and CH_2—C=C moieties appeared as two signals (δ 2.5 and 2.2, respectively) while the four methyl protons resonated as two singlets (δ 1.0, 0.95) due their axial-equational conformations.

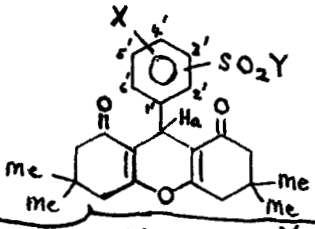
The 9-arylxanthendiones (3) generally reacted smoothly with excess chlorosulfonic acid (10–12 molar equivalents) or 6 molar equivalents in thionyl chloride at room temperature for 2–7 days to give the sulfonyl chlorides (25, 34, 43, 53, 55, 63 and 65) (Charts I and II).

With the *m*-methoxyphenyl derivative (7), the 4,6-bis-sulfonyl chloride (30) was isolated in agreement with previous work[12,13] on the chlorosulfonation of methoxy chalcones. In the case of the other 9-arylxanthendiones shown in Chart I, the pure sulfonyl chlorides could not be isolated and are, therefore, not listed; however the crude products were characterized by formation of the sulfonamide derivatives (21–22, 23–24, 50–52) (Chart I and Table I). Chlorosulfonation was successful with the derivative (12) from *p*-fluorobenzaldehyde but failed with compound (13) from 2,6-dichlorobenzaldehyde presumably due to the stereoelectronic effects of the two chlorine atoms.

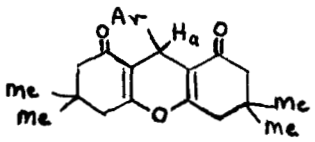
In the 2′-methyl and 2′-methoxysubstrates (5, 6), sulfonation probably occurs in the 5′-position which is *para* to the more powerful electron-donor group. With the 2′- and 3′-chloro compounds (9, 10), sulfonation occurs in the 4′-position (*para* to the electron-donating alkyl moiety). In the 3′, 4′-dimethoxy derivative (14) only monosulfonation occurred probably in the less hindered 5′-position (*ortho* to the



excess $ClSO_3H$



	X
(4)	H
(5)	2'-Me
(6)	2'-OMe
(7)	3'-OMe
(8)	4'-OMe
(9)	2'-Cl
(10)	3'-Cl
(11)	4'-Cl
(12)	4'-F
(13)	2',6'-Cl_2
(14)	3',4'-$(OMe)_2$
(15)	3'-OH
(16)	4'-OH
(17)	4'-Ph



	Ar
(18)	2'-thienyl
(19)	3'-thienyl
(20)	1-naphthyl

	X	Y
(21)	H	4'-NEt_2
(22)	"	$C_5H_{10}N$
(23)	2'-Me	5'-NEt_2
(24)	"	$NHCHMe_2$
(25)	2'-OMe	5'-Cl
(26)	"	NMe_2
(27)	"	$C_5H_{10}N$
(28)	"	NHPh
(29)	"	$C_6H_{12}NO$
(30)	3'-OMe	4',6'-Cl_2
(31)	"	NMe_2
(32)	"	$C_6H_{12}NO$
(33)	"	NHEt
(34)	4'-OMe	3'-Cl
(35)	"	$C_5H_{10}N$
(36)	"	$PhCH_2NH$
(37)	"	2,4-$F_2C_6H_3NH$
(38)	"	$MeO(CH_2)_2NH$
(39)	"	$C_6H_{12}NO$
(40)	"	NEt_2
(41)	"	C_4H_8NO
(42)	"	2-FC_6H_4NH
(43)	2'-Cl	4'-Cl
(44)	"	NMe_2
(45)	"	$C_5H_{10}N$
(46)	"	$C_6H_{12}NO$
(47)	"	2,4-$F_2C_6H_3NH$
(48)	"	$NHNH_2$
(49)	"	$NHN{=}CMe_2$

	X	Y
(50)	3'-Cl	4'-NMe_2
(51)	"	NHEt
(52)	"	C_4H_8NO
(53)	4'-Cl	3'-Cl
(54)	"	$C_5H_{10}N$
(55)	4'-F	3'-Cl
(56)	"	$NHNMe_2$
(57)	"	$NHNH_2$
(58)	3',4'-$(OMe)_2$	5'-$NHCHMe_2$

CHART I. 9-Aryl-3,3,6,6-tetramethyloctahydroxanthen-1.8-diones and their sulfonyl derivatives.

methoxy group). With the thiophene derivatives (18, 19), sulfonation takes place in the 5′-position, adjacent to the electron donating sulfur atom to give the sulfonyl compounds (59–64) (Chart II and Table I). In the 1-naphthyl substrate (20), sulfonation occurs in most electron-rich 4′-position yielding the derivatives (65–69b) (Chart II). Attempted chlorosulfonation of the xanthendiones (16, 17) from *p*-hydroxybenzaldehyde and biphenyl-4-carboxaldehyde afforded impure products

TABLE I

Sulfonyl derivatives of the 9-aryltetramethyloctahydroxanthendiones

Comp. No.	Yield %	m.p., °C	Molecular formula	Microanalysis found (calc.) % C	H	N	S	MS (M^+)
21	73	173–175	$C_{27}H_{35}NO_5S$	66.4 (66.8)	7.2 (7.3)	2.9 (2.9)	6.3 (6.6)	486
22	81	230–232	$C_{28}H_{35}NO_5S$	67.1 (67.6)	7.3 (7.1)	3.1 (2.8)	6.1 (6.4)	497
23	56	210–212	$C_{28}H_{38}NO_5S$	66.6 (66.8)	7.4 (7.5)	2.9 (2.8)	6.2 (6.4)	500
24	65	256–257	$C_{31}H_{46}NO_5S$	68.2 (68.4)	8.6 (8.4)	2.7 (2.6)	—	544
25	83	110–112	$C_{24}H_{27}ClO_6S$	59.4 (60.2)	5.4 (5.7)	Cl 6.8 (Cl 7.4)	7.0 (6.7)	480[a]
26	72	195–196	$C_{26}H_{33}NO_6S$	63.6 (64.0)	6.8 (6.8)	2.9 (2.8)	6.6 (6.3)	487
27	66	175–176	$C_{29}H_{37}NO_6S$	65.3 (66.0)	7.2 (7.1)	2.6 (2.6)	5.7 (6.1)	527
28	44	205	$C_{30}H_{33}NO_6S$	67.1 (67.3)	6.3 (6.2)	2.5 (2.6)	— —	535
29	46	128–130	$C_{33}H_{39}NO_7S$	66.3 (66.8)	6.7 (6.6)	(2.5) (2.4)		593
30	85	160–162	$C_{24}H_{26}Cl_2O_8S_2$	49.0 (50.0)	4.2 (4.5)	(Cl 11.4) (Cl 12.1)	10.5 11.1	580[a]
31	42	175	$C_{28}H_{38}N_2O_8S_2$	55.7 (56.6)	5.9 (6.4)	4.5 (4.7)	10.2 (10.8)	594
32	52	165	$C_{36}H_{50}N_2O_{10}S_2$	58.2 (58.8)	6.5 (6.8)	3.7 (3.8)		734
33	50	195	$C_{28}H_{38}N_2O_8S_2$	56.3 (56.6)	6.6 (6.4)	4.5 (4.7)		594
34	76	141–142	$C_{24}H_{27}ClO_6S$	59.6 (60.2)	5.3 (5.7)	7.2 (Cl 7.4)		480[a]
35	55	250	$C_{29}H_{37}NO_6S$	65.6 (66.0)	6.8 (7.0)	3.0 (2.7)	5.6 (6.1)	527
36	41	205	$C_{31}H_{35}NO_6S$	67.4 (67.8)	6.6 (6.4)	2.7 (2.5)	—	549
37	35	216–218	$C_{30}H_{31}F_2NO_6S$	62.3 (63.0)	6.6 (5.4)	2.7 (2.5)	—	571
38	51	180	$C_{27}H_{35}NO_7S$	62.4 (62.7)	6.8 (6.8)	2.4 (2.7)	—	517
39	58	195–198	$C_{30}H_{39}NO_7S$	64.0 (64.6)	7.1 (7.1)	2.6 (2.5)		557
40	73	195–197	$C_{28}H_{37}NO_6S$	64.7 (65.2)	7.4 (7.2)	2.5 (2.7)		515
41	79	266–270	$C_{28}H_{35}NO_7S$	62.9 (63.5)	6.6 (6.7)	2.6 (2.7)		529
42	58	226–228	$C_{30}H_{32}FNO_6S$	64.7 (65.1)	6.2 (5.8)	2.2 (2.5)		—
43	78	172–175	$C_{23}H_{24}Cl_2O_5S$	56.4 (57.1)	4.8 (5.0)		6.0 (6.6)	484[a]
44	32	255	$C_{25}H_{30}ClNO_5S$	60.8 (61.0)	6.2 (6.1)	2.7 (2.8)	—	492[a]
45	70	255	$C_{28}H_{34}ClNO_5S$	63.3 (63.2)	6.6 (6.4)	2.6 (2.6)	5.8 (6.0)	533[a]
46	50	213–215	$C_{29}H_{36}ClN_2O_6S$	59.8 (60.5)	6.4 (6.2)	5.0 (4.9)	—	577[a]
47	48	243–245	$C_{29}H_{28}ClF_2NO_5S$	59.9 (60.5)	5.0 (4.9)	2.5 (2.4)	—	575[a]

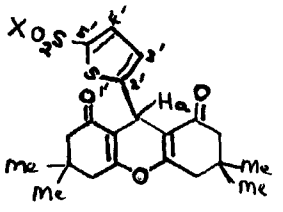
TABLE I (*Continued*)

Comp. No.	Yield %	m.p., °C	Molecular formula	Microanalysis found (calc.) % C	H	N	S	MS (M^+)
48	53	220	$C_{23}H_{27}ClN_2O_5S$	57.5 (57.7)	5.4 (5.6)	6.0 (5.8)	— —	399 (M^+-SO_2NHNH_2)
49	86	215	$C_{26}H_{31}ClN_2O_5S$	59.6 (59.2)	6.1 (6.1)	5.1 (5.2)	6.5 (6.3)	508[a]
50	53	186–187	$C_{25}H_{30}ClNO_5S$	60.4 (61.0)	6.0 (6.1)	2.8 (2.8)	— —	492[a]
51	46	199–200	$C_{25}H_{30}ClNO_5S$	60.8 (61.0)	6.2 (6.1)	3.0 (2.8)		492[a]
52	45	153–155	$C_{27}H_{32}NO_6S$	60.3 (60.7)	6.3 (6.0)	2.8 (2.6)		535
53	84	102–104	$C_{23}H_{24}Cl_2O_5S$	57.8 (57.1)	5.3 (5.0)	—		483[a]
54	74	157–158	$C_{28}H_{34}ClNO_5S$	63.0 (63.2)	6.1 (6.4)	2.4 (2.6)		533[a]
55		110–112	$C_{23}H_{24}ClFO_5S$	58.7 (59.2)	5.4 (5.1)			468[a]
56	33	148–150	$C_{25}H_{31}FNO_5S$	62.7 (63.0)	6.6 (6.5)	3.1 (2.9)		476
57	66	176–178	$C_{23}H_{27}FNO_5S$	61.2 (61.6)	5.8 (6.0)	3.3 (3.1)		448
58	38	208–210	$C_{28}H_{36}NO_7S$	63.0 (63.3)	6.5 (6.8)	2.5 (2.6)	6.2 (6.0)	530
59	64	190	$C_{21}H_{23}ClO_5S_2$	55.0 (55.4)	4.8 (5.1)	— —	13.6 (14.1)	456[a]
60	84	198–200	$C_{23}H_{29}NO_5S_2$	59.0 (59.6)	6.2 (6.3)	3.0 (3.0)		463
61	85	212	$C_{26}H_{33}NO_5S_2$	61.9 (62.0)	6.8 (6.6)	2.8 (2.8)		503
62	73	167	$C_{25}H_{33}NO_5S_2$	60.8 (61.1)	6.5 (6.7)	3.0 (2.8)		491
63	83	145–148	$C_{21}H_{23}ClO_5S_2$	54.8 (55.4)	5.3 (5.1)	— —		457[a]
64	80	193–195	$C_{25}H_{31}NO_6S_2$	59.8 (59.4)	6.2 (6.2)	2.7 (2.8)		505
65	82	150	$C_{27}H_{27}ClO_5S$	64.4 (65.0)	5.5 (5.4)	6.6 (6.4)		500[a]
66	48	190	$C_{29}H_{33}NO_5S$	68.3 (68.6)	6.6 (6.5)	3.0 (2.8)		507
67	52	130–132	$C_{31}H_{37}NO_5S$	69.0 (69.5)	7.0 (6.9)	2.7 (2.6)		535
68	40	190–192	$C_{32}H_{37}NO_5S$	69.7 (70.2)	6.8 (6.8)	2.9 (2.6)		547
69	39	145	$C_{33}H_{39}NO_6S$	68.0 (68.6)	7.0 (6.8)	2.5 (2.4)		577
70	87	202–204	$C_{23}H_{23}ClO_8S_2$	51.9 (52.4)	4.6 (4.4)	— —		528[a]
71	45	176	$C_{27}H_{31}NO_9S$	56.2 (56.1)	5.7 (5.4)	2.3 (2.4)		577
74	66	203–205	$C_{23}H_{25}ClO_6S$	58.9 (59.4)	5.5 (5.4)			465[a]
75	56	146–148	$C_{27}H_{33}NO_7S$	62.7 (62.9)	6.3 (6.4)	2.5 (2.7)		516

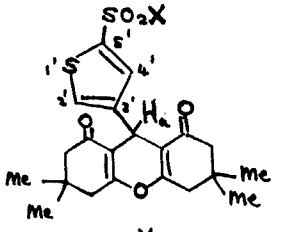
[a] Indicates the highest mass ion fragment of the ion cluster.

(multiple spots on TLC) which could not be characterized as sulfonamide derivatives.

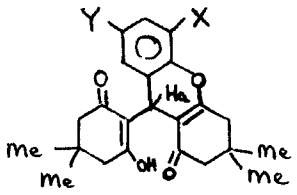
With *m*-hydroxybenzaldehyde, the xanthendione (15) appeared to yield an unstable 4′,6′-bis-sulfonyl chloride which eliminated hydrogen chloride to form the mono-sulfonyl chloride (70), characterized as the morpholidate (71) (Chart II).



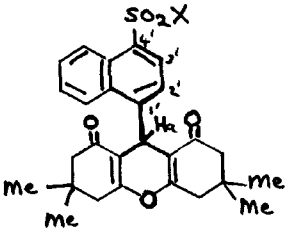
X	
(59)	Cl
(60)	NMe_2
(61)	$C_5H_{10}N$
(62)	NEt_2



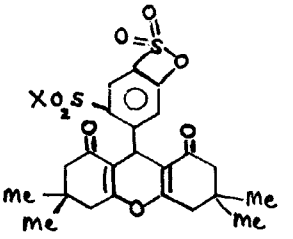
X	
(63)	Cl
(64)	C_4H_8NO



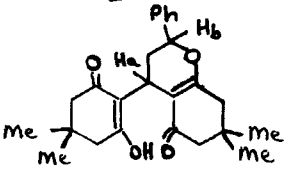
X	Y	
(72)	H	H
(73)	OMe	H
(74)	H	SO_2Cl
(75)	H	$SO_2NC_4H_8O$



X	
(65)	Cl
(66)	NMe_2
(67)	NEt_2
(68)	$C_5H_{10}N$
(69)	$C_6H_{12}NO$
(69a)	$NHNH_2$
(69b)	$NHN{=}CMe_2$



X	
(70)	Cl
(71)	C_4H_8NO



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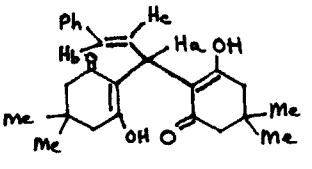


(77)

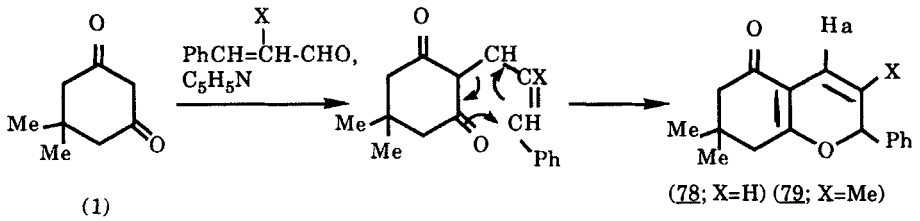
CHART II. 9-Thienyl and naphthyl-3,3,6,6-tetramethyl octahydroxanthen-1.8-dione sulfonyl derivatives and related compounds.

In the reaction of salicylaldehyde with dimedone (2 molar equivalents), the initial product was unchanged after heating with concentrated hydrochloric acid, as was found by previous workers.[4,7] The structure of the product was, therefore, assigned as the pyran (72); the reaction with *o*-vanillin (2-hydroxy-3-methoxybenzaldehyde) appeared to yield an analogous product (73). Chlorosulfonation of 72 afforded the sulfonyl chloride (74), characterized as the morpholidate (75) (Chart II). On the other hand, chlorosulfonation of 73 gave a complex mixture of products which could not be identified as sulfonamides.

The reaction of dimedone (2 moles) with cinnamaldehyde under standard conditions[4] also gave an anomalous product which was unchanged after heating with concentrated hydrochloric acid. The structure was originally assigned as the pyran (76), but later workers[14] proposed the vinylic structure (77) on the basis of the NMR spectrum.

Our spectral data, however, does not support the vinylic structure (77) and is in better agreement with the originally proposed pyran form (76). In particular, the NMR spectrum does not show the *trans* alkenic protons (Hb, Hc) reported[14] as doublets (δ 6.50, 5.75, J 14.0 Hz). We observed two doublets (δ 5.90, 4.50) which we ascribe to the tertiary protons (Hb and Ha respectively) of the pyran structure (76) while the 10 methylene protons appear as a complex multiplet (δ 3.51–2.0).

On the other hand, when equimolar quantities of dimedone (1) and either cinnamaldehyde or α-methylcinnamaldehyde are heated together in pyridine, the corresponding 2-phenylpyrans (78, 79) were formed. The reaction presumably occurs *via* the intermediate 1:1-condensation product which subsequently undergoes intramolecular cyclisation to 78 or 79 (Scheme II)[15]:



(1)

(78; X=H) (79; X=Me)

SCHEME II

Attempted chlorosulfonation of the compounds (76, 78, 79) was unsuccessful and only gave mixtures of unidentified products.

EXPERIMENTAL

Melting points were determined with a Gallenkamp electric apparatus and are uncorrected. IR spectra were measured as Nujol mulls with a Unicam SP100 spectrophotometer. NMR spectra were recorded with a Bruker AC250 spectrometer using tetramethylsilane as internal standard and deuterochloroform as solvent, resonances indicated by an asterisk were reduced by D_2O treatment. Mass spectra were measured with a VG micromass V15 spectrometer operating at 70 eV. TLC was carried out using Camlab silica gel plates sensitized to UV 256 nm and cyclohexane-ethyl acetate 3:1 as eluant.

Preparation of 9-aryl-1,2,3,4,5,6,7,8-octahydro-3,3,6,6-tetramethylxanthen-1,8-diones (3). Dimedone (1) (2.8 g, 0.04 mole) was dissolved in warm 80% ethanol-water (50 ml) then a solution of the appropriate aromatic aldehyde (0.02 mole) in ethanol (15 ml) was added followed by piperidine (6 drops). The mixture was refluxed on the steam bath (30 minutes); the crystalline derivative (2) either separated out on cooling (ice) or after addition of a little water to the solution. The solid was filtered off, washed

with a small amount of aqueous ethanol, and dried. The product was dissolved in ethanol (30 ml) containing concentrated hydrochloric acid (6 drops) and the solution heated on the steam bath for 30 minutes. When the solution was cooled, the xanthendione crystallized out and was collected and dried. By this procedure, the derivatives (4–20) (Chart I) were prepared. The following xanthendiones were novel:

10, m.p. 195°C; 11, m.p. 242–244°C (Found: C, 72.0; H, 6.4. $C_{23}H_{25}ClO_3$ requires C, 71.8; H, 6.5%); 12, m.p. 225°C; 13, m.p. 320°C (Found; C, 65.7; H, 6.0. $C_{23}H_{24}Cl_2O_3$ requires C, 65.9; H, 5.7%). NMR: δ7.42–7.15 (m, 3H, ArH), 4.75 (s, 1H, Ha), 2.42 (s, 4H, CH_2CO), 2.2 (m, 4H, $CH_2C{=}C$), 1.02, 0.98 (2xs, 12H, CH_3); 15, m.p. 231–233°C (Found: C, 75.3; H, 7.2, $C_{23}H_{26}O_4$ requires C, 75.4; H, 7.2%); 17, m.p. 220–223°C (Found: C, 81.3; H, 7.0. $C_{29}H_{30}O_3$ requires C, 81.7; H, 7.1%). IR: ν_{max} 1660 (C=O), 1620 (alk C=C), 1600 (arom C=C), 1150 (C—O—C) cm^{-1}; 18, m.p. 160°C, NMR: δ7.15–6·80 (m, 3H, thienyl H), 5.20 (s, 1H, Ha), 2.42 (s, 4H, CH_2CO), 2.30 (s, 4H, $CH_2C{=}C$), 1.04, 1.02 (2xs), 12H, CH_3); 19, m.p. 198–201°C (Found: C, 70.4; H, 6.7, $C_{21}H_{24}O_3$ requires C, 70.8; H, 6.8%). IR: ν_{max} 1665 (C=O), 1630 (alk C=C), 1605 (arom C=C), 1170 (C—O—C) cm^{-1}; 20, m.p. 236–238°C. NMR: δ7.8–7.0 (m, 6H, ArH), 5.45 (s, 1H, Ha), 2.5 (s, 2H, CH_2CO), 2.2 (d, 4H, CH_2 C=C), 1.05, 0.95 (2xs, 12H, CH_3).

Reaction of Dimedone (1) with Cinnamaldehyde

Method 1. Dimedone (1) (2.8 g, 0.02 mole) was heated with freshly redistilled cinnamaldehyde (1.32 g, 0.01 mole) in ethanol (50 ml) containing piperidine (6 drops) for 30 minutes. The solution, on cooling gave white plates (3 g), m.p. 210–212°C. The product was refluxed with ethanol containing concentrated hydrochloric acid (6 drops) for 1 hour to give 76 (2.85 g), m.p. 215°C (m.m.p. with the first product 212–214°C) (Reference 4, 215–217°C) (Found: C, 75.8; H, 2.8. $C_{25}H_{30}O_4$ requires C, 76.1; H, 7.6%). NMR: (deuteropyridine): δ8.8 (s, 1H, OH), 7.6–7.15 (m, 5H, ArH), 5.9 (d, 1H, H_b), 4.5 (d, 1H, H_a), 3.51–2.0 (m, 10H, CH_2), 1.0, 0.98 (2xs, 12H, CH_3). ^{13}C NMR: δ195.1, 172 (C=O), 146.4, 145 (alkenic C), 128–125 (3 signals, arom C), 112–109 (2 signals, alkenic C), 50–47.5 (CH_2), 33(CMe_2), 28–26.7 (4 signals, CH_3). MS: 394 (M^+), 376 ($M^+ - H_2O$), 254, 241, 170, 128, 83, 78, 55, 41.

Method 2. A solution of dimedone (1) (2.8 g, 0.02 mole) and cinnamaldehyde (3.2 g, 0.024 mole) in pyridine (30 ml) was heated on a steam bath for 3 hours. The solution was cooled and acidified with concentrated hydrochloric acid to give a yellow solid. Recrystallisation (ethanol) afforded the 2-phenylpyran (78; R=H) as yellow plates (1.35 g), m.p. 198–200°C. (Found: C, 79.9; H, 7.4. $C_{17}H_{18}O_2$ requires C, 80.3; H, 7.1%). NMR: δ7.8–7.2 (m, 5H, ArH), 3.8 (d, 2H, alkenic H, *J* 4.0 Hz), 2.57–2.20 (m, 4H, CH_2), 1.10 (s, 6H, CMe_2). MS showed the molecular ion (M^+, 254), other ions at 239 ($M^+ - Me$), 198, 177 ($M^+ - Ph$), 128, 83, 55.

Reaction of Dimedone (1) with α-Methylcinnamaldehyde. The same procedure as in method 2 on the same molar scale afforded the corresponding 2-phenylpyran (79), as an orange-yellow oil (2 g), (Found: C, 81.0; H, 7.7. $C_{18}H_{20}O_2$ requires C, 80.6; H, 7.5%). NMR: δ7.65–7.20 (m, 5H, ArH), 5.6 (s, 1H, Ha), 2.4–2.1 (m, 4H, CH_2), 1.6 (s, 3H, CH_3—C=C), 1.0, 0.96 (2xs, 6H, CM_2).

MS showed the molecular ion (M^+, 268) and other major ions at 253 ($M^+ - Me$), 191 ($M^+ - C_6H_5$), 141, 105, 83, 77, 55, 43.

Chlorosulfonation of the 9-Aryl-3,3,6,6-tetramethyloctahydroxanthen-1,8-diones (4–20). The 9-arylxanthendione (0.01 mole) was gradually added, with swirling, to chlorosulfonic acid (14 ml, 0.12 mole) at 0°C. The solution was allowed to stand at room temperature for 2–7 days, until all effervescence had ceased, and then poured slowly on to crushed ice (100 g) with stirring. When all the ice had melted, the precipitate was filtered off under suction, washed with ice-water and dried in a vacuum desiccator to give the sulfonyl chloride.

An alternative procedure involved the use of a mixture of chlorosulfonic acid (7 ml, 0.06 mole) and thionyl chloride (10 ml, 0.16 mole) under similar conditions.

In some cases, it was not possible to isolate pure sulfonyl chlorides and the crude products were then characterized as the sulfonamide derivatives.

Compound 34. NMR: δ7.0–8.0 (m, 3H, ArH), 4.7 (s, 1H, Ha), 4.0 (s, 3H, OCH_3), 2.5 (s, 4H, CH_2CO), 2.2 (s, 4H, CH_2—C=C), 1.1, 1.0 (2xs, 12H, CH_3). MS: 480, 478 (M^+), 443 ($M^+ - Cl$), 379 ($M^+ - SO_2Cl$), 349, 273.

Compound 53. MS (CI): 483 ($M^+ + H$), 418 ($M^+ - SO_2$), 383 ($M^+ - SO_2Cl$), 273.

Compound 63. NMR: δ7.7 (s, 1H, $Ar4^1 - H$), 7.6 (s, 1H, $Ar\ 2^1 - H$), 4.9 (s, 1H, Ha), 2.5 (s, 4H, CH_2CO), 2.25 (s, 4H, CH_2—C=C), 1.1, 1.0 (2xs, 12H, CH_3).
MS: 457, 455 (M^+), 420 ($M^+ - Cl$), 356 ($M^+ - SO_2Cl$).

Preparation of the sulfonamides. The 9-(chlorosulfonylaryl) xanthendione (0.01 mole) was gradually added to a stirred solution of the appropriate amine (0.03 mole)† in methanol (30 ml) at 0°C. The mixture was left at room temperature 3–5 days and added to ice-water (150 ml) containing dilute hydrochloric acid. The precipitated solid was filtered off, washed with water and dried. Recrystallization from methanol afforded the sulfonamide derivative.

Compound 21. NMR: δ7.75–7.2 (m, 4H, ArH, AA^1BB^1 pattern), 4.8 (s, 1H, Ha), 3.2–2.8 (m, 8H, CH_2CO, $SO_2N\underline{CH_2}CH_3$), 2.55 (s, 6H, $NCH_2\underline{CH_3}$), 2.2 (s, 4H, CH_2 C=C), 1.1, 0.95 (2xs, 12H, CH_3).

Compound 22. TLC showed one spot, R_F 0.48. NMR: δ7.7–7.4 (m, ArH, AA^1BB^1 pattern) 4.82 (s, 1H, Ha), 3.8–3.7 (m, 4H, N—CH_2); 2.5 (s, 4H, CH_2CO), 2.2–2.0 (m, 12H, CH_2—C=C, piperidino H), 1.1, 0.98 (2xs, 12H, CH_3). ^{13}C NMR: δ196.3 (C=O), 148.9–142.3 (4 signals, alkenic C), 135.0–125.5 (6 signals, arom C), 50.7–46.7 (2 signals $\underline{CH_2}CO$), 44.6, 40.8 (2 signals $\underline{C}Me_2$), 32.1–22.1 (7 signals, CH_2), 23.4–22.3 (2 signals, CH_3).

Compound 23. TLC showed one spot, R_F 0.60. NMR: δ7.40–7.18 (m, 3H, ArH), 4.8 (s, 1H, Ha), 3.10 (*q*, 4H, $N\underline{CH_2}CH_3$), 2.6 (s, 4H, CH_2CO), 2.3 (s, 3H, $Ar\underline{CH_3}$), 2.2 (m, 4H, $\underline{CH_2}$ C=C), 2.10 (*t*, 6H, $NCH_2\underline{CH_3}$), 1.0, 0.95 (2xs, 12H, CH_3).

Compound 31. TLC showed one spot, R_F 0.40. NMR: δ8.1 (s, 1H, $Ar5^1$ – H), 7.15 (s, 1H, $Ar2^1$ – H), 4.8 (s, 1H, Ha), 3.0 (d, 4H, CH_2CO), 2.8 (s, 12H, SO_2NMe_2), 2.2 (m, 4H, CH_2—C=C), 1.1, 0.98 (2xs, 12H, CH_3).

Compound 54. TLC showed one spot, R_F 0.54. NMR: δ7.8–7.1 (m, 3H, Ar H), 4.7 (s, 1H, Ha), 3.2 (d, 4H, CH_2CO), 2.3–2.2 (m, 4H, CH_2 C=C), 1.8–1.4 (m, 8H, piperidino H). MS: 533 (M^+), 515 (M^+ – Me), 467 (M^+ – SO_2), 432 (M^+ – SO_2, –Cl), 384 (M^+ – $SO_2NC_5H_{10}$), 382.

Compound 60. ^{13}C NMR: δ196.1 (C=O), 163.4, 155.9 (alkenic C), 135.1–114.4 (4 signals, thienyl C), 50.6, 40.7 ($\underline{CH_2}CO$), 37.9–29.2 (3 signals CH_2), 27.5–27.1 (3 signals, CH_3).

Compound 61. ^{13}C NMR: δ196.1 (C=O), 163.4, 155.6 (alkenic C), 133.9–114.4 (4 signals, thienyl C), 50.6, 46.9 ($\underline{CH_2}CO$), 40.8–25.0 (6 signals CH_2), 23.4, 22.5 (CH_3).

Compound 68. NMR: δ8.5–7.2 (m, 6H, naphthyl H), 5.5 (s, 1H, Ha), 3.2 (m, 4H, NCH_2), 2.5 (s, 4H, $\underline{CH_2}CO$), 2.2–1.4 (m, 10H, CH_2), 1.1, 0.98 (2xs, 12H, CH_3).

Preparation of sulfonohydrazides (48, 57, 69a). The appropriate sulfonyl chloride (43, 55, 65), (0.01 mole) was gradually added to a stirred ice-cold solution of hydrazine hydrate (98%) (0.03 mole) in methanol (20 ml). The suspension was left at room temperature for 2 hours and poured onto crushed ice-water (150 ml) with stirring. The precipitate was filtered off, washed with ice-water and dried (vacuum desiccator) to give the hydrazide.

Compound (69a). A yellow powder (56%), m.p. 268–270°C (decomp.). TLC showed one spot, R_F 0.68. The hydrazide (69a) was treated with acetone at room temperature (1 hour) to give the acetone hydrazone (69b) as orange-yellow plates (75%), m.p. 250°C (Found: C, 67.0; H, 6.6; N, 5.4, $C_{30}H_{34}N_2O_5S$ requires C 67.4; H, 6.4, N 5.2%). IR: ν_{max} 3300 (NH), 1660 (C=O), 1635 (alk C=C), 1595 (arom C=C), 1360, 1170 (SO_2), 1200 (C—O—C) cm^{-1}. NMR: δ9.8* (s, 1H, NH), 8.1–7.0 (m, 6H, naphthyl H), 4.5 (s, 1H, Ha), 2.6–2.0 (m, 8H, CH_2), 1.8 (s, 6H, Me_2C=), 1.2, 1.0 (2xs, 12H, CH_3).

Reaction of dimedone (1) with salicylaldehyde. Dimedone (1) (2.8 g, 0.02 mole) was refluxed with salicylaldehyde (1.2 g, 0.01 mole) in 50% aqueous ethanol (30 ml) containing piperidine (3 drops) as basic catalyst for 30 minutes. The solution on cooling afforded the pyran 72 (80%), m.p. 210–211°C. (Reference 7, 211°C).

Chlorosulfonation of 72. The pyran (72) (2.75 g, 0.0075 mole) was added to portionwise to chlorosulfonic acid (6 ml, 0.09 mole) at 0°C with swirling. The solution was left at room temperature (2 days) and poured onto ice-water mixture. When the ice had melted, the precipitate was collected, washed with ice-water and dried to give the sulfonyl chloride (74) (2.3 g).

NMR: δ7.4–6.85 (m, 3H, ArH), 5.05 (s, 1H, Ha), 2.9–1.9 (m, 8H, CH_2), 1.05, 0.85 (m, 12H, CH_3). MS: 466, 464 (M^+), 447 (M^+ – H_2O), 429 (M^+ – Cl), 365 (M^+ – SO_2Cl).

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†With disulfonyl chlorides, a larger amount (0.06 mole) of the amine was used and with aromatic amines acetonitrile was used as solvent instead of methanol.

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