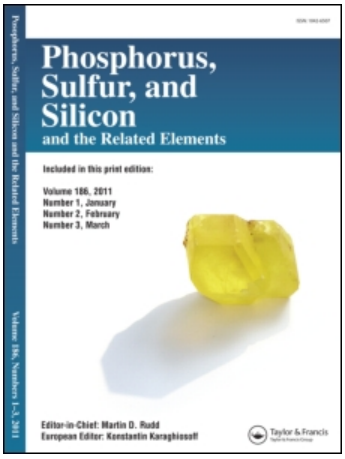

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REACTIONS OF CHLOROSULFONYLBENZYLIDENE HYDANTOINS

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REACTIONS OF CHLOROSULFONYLBENZYLIDENE HYDANTOINS

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5-(Benzylidene- and *o*-chlorobenzylidene-) and cinnamylidene-hydantoins reacted with chlorosulfonic acid to give the corresponding *p*-sulfonyl chlorides (**1**, **35**, **44**). These were converted into 49 derivatives by reaction with amines, hydrazines and azide ion. 5-(*o*-chlorobenzylidene)hydantoin appeared to exist as two geometric isomers. The NMR spectra indicated that alkylation of the benzylidenehydantoins (**3**, **4**, **38**) occurred preferentially at the N(3)-position. The spectral data of the compounds are briefly discussed, together with preliminary biological screening results against insects, weeds and fungi.

INTRODUCTION

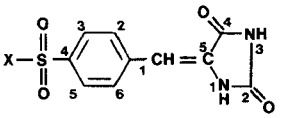
The work forms part of our general programme on the chemistry and biological activity of aryl sulfonyl derivatives.[1–2] We have demonstrated that compounds like cinnamic acid,[3] chalcones[4–5] or dibenzylideneacetone[6] are readily chlorosulfonated due to the activating influence of the olefinic double bond. 5-Benzylidenehydantoins should therefore provide suitable substrates for chlorosulfonation. The sulfonyl derivatives possess potential biological activity since several 5-substituted hydantoins are valuable anti-convulsant drugs[7] and hydantoins also show fungicidal and herbicidal activity.[8–9]

Hydantoins are known[8] to condense with aromatic aldehydes to give the corresponding 5-benzylidene derivatives. Boyd and Robson[10] observed that the condensation occurred in pyridine in the presence of diethylamine or piperidine, but that the former was the more effective condensing agent. The reaction has also been carried out in pyridine alone,[11,12] glacial acetic acid—sodium acetate;[13,14] or ethanolamine–sodium hydroxide.[15]

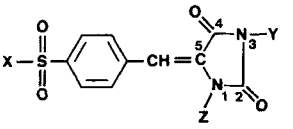
DISCUSSION

5-(Benzylidene) hydantoin was obtained in 55% yield following the procedure of Boyd and Robson;[10] use of either piperidine or ethanolamine gave much lower yields (25%). The chlorosulfonation of 5-(benzylidene)hydantoin has not been previously reported. The optimum conditions involved treatment of the substrate with a large excess of chlorosulfonic acid (16 equivalents) at room temperature for 6 hours to give an excellent yield (87%) of the sulfonyl chloride (1) (Chart 1

CHART 1



(1-30)

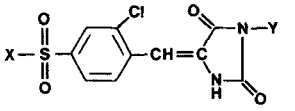


(31; Y=Me, Z=H)

(32; Y=$SCCl_3$, Z=H)

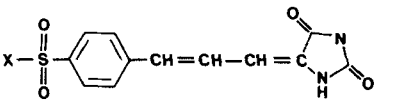
(33; Y=H, Z=Me)

(34; Y=H, Z=Me)

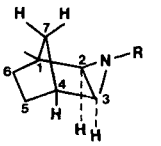


(35-42; Y=H)

(43; Y=$SCCl_3$)



(44-52)



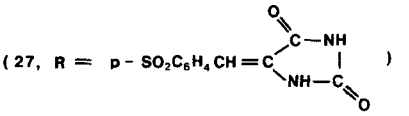


CHART 1

and Table I). (1) was condensed with a range of nucleophilic reagents, such as amines, hydrazines and azide ion under standard conditions (cf. Reference 16) to give the compounds 2–10, 11–14 and 25 (Table I). The hydrazide (11) was converted into the hydrazones (15–24), the 3,5-dimethylpyrazole (30) and the azide (25) was reacted with triethylphosphite and norbornene to give 26, 27 respectively. The anilide (8) reacted with chlorosulfonic acid at low temperature as previously described,[17] to give a low yield (9%) of the sulfanilyl chloride (28) which was characterized as the dimethylamide (29).

Hydantoins are generally alkylated in basic media in the N-3 position,[18] however in arylidenehydantoins the adjacent N(1) proton becomes more acidic facilitating N(1)-alkylation.[19] In the sulfonylbenzylidenehydantoins the

TABLE I

Physical data for the sulfonylbenzylidenehydantoins

Compd no.	Yield (%)	m.p. (°C)	X	Molecular formula	Microanalysis found (calc.) % C	H	N	MS (M^+)	UV (λ_{max} / ε_{max})
1	87	267–270	Cl	$C_{10}H_7ClN_2O_4S \cdot H_2O$	39.7 (39.4)	2.5 (2.3)	9.2 (9.2)	286	320 nm 27, 960
2	80	310–311	NH_2	$C_{10}H_9N_3O_4S \cdot 1\frac{1}{4}H_2O$	41.9 (41.5)	3.6 (4.0)	14.8 (14.5)	267	322 27, 380
3	68	263–264	NMe_2	$C_{12}H_{13}N_3O_4S \cdot \frac{1}{4}H_2O$	48.1 (48.1)	4.4 (4.5)	14.0 (14.0)	295	324 29, 370
4	60	267–268	NEt_2	$C_{14}H_{17}N_3O_4S \cdot \frac{1}{4}H_2O$	51.1 (51.3)	5.3 (5.4)	12.7 (12.8)	323	
5	88	335–338	C_4H_8NO	$C_{14}H_{15}N_3O_5S \cdot \frac{1}{2}H_2O$	48.7 (48.6)	4.5 (4.7)	12.0 (12.1)	337	326 28, 615
6	84	240–242	C_3H_6N	$C_{13}H_{13}N_3O_4S \cdot \frac{1}{4}H_2O$	50.0 (50.1)	4.2 (4.4)	13.2 (13.5)	307	324 28, 710
7	87	292–294	$C_5H_{10}N$	$C_{15}H_{17}N_3O_3S \cdot \frac{1}{4}H_2O$	53.0 (53.0)	5.0 (5.2)	12.4 (12.4)	335	
8	55	234–236	PhNH	$C_{16}H_{13}N_3O_4S \cdot \frac{3}{4}H_2O$	53.9 (53.9)	4.3 (4.1)	11.7 (11.8)	343	326 27, 880
9	33	265–267	*p*-ClC_6H_4NH	$C_{16}H_{12}ClN_3O_4S$	50.7 (50.9)	3.3 (3.2)	11.4 (11.1)	379	326 27, 570
10	21	255–256	*p*-$MeOC_6H_4NH$	$C_{17}H_{15}N_3O_5S$	54.4 (54.7)	3.8 (4.0)	11.0 (11.2)	373	326 28, 045
11	78	218–219	$NHNH_2$	$C_{10}H_{10}N_4O_4S \cdot \frac{1}{4}H_2O$	42.2 (41.9)	3.4 (3.7)	19.3 (19.5)	267*	
12	55	171–172	NHNHMe	$C_{11}H_{12}N_4O_4S \cdot \frac{1}{4}H_2O$	44.1 (43.9)	3.9 (4.2)	18.3 (18.6)	281*	
13	53	148–150	$NHNMe_2$	$C_{12}H_{14}N_4O_4S \cdot \frac{1}{2}H_2O$	43.0 (43.3)	4.8 (5.0)	16.8 (16.8)		
14	45	181–182	NHNHPh	$C_{16}H_{14}N_4O_4S \cdot \frac{1}{2}H_2O$	52.5 (52.3)	4.3 (4.1)	15.0 (15.2)	188*	
15	77	223–224	$NHN{=}CR^1R^2$ $R^1 = R^2 = Me$	$C_{13}H_{14}N_4O_4S$	48.4 (48.4)	4.4 (4.4)	17.1 (17.4)	322	326 29, 575
16	80	231–232	$R^1 = R^2 = (CH_2)_{4-}$	$C_{15}H_{16}N_4O_4S$	51.5 (51.7)	4.4 (4.6)	16.1 (16.1)	286*	

TABLE I (*Continued*)

Compd no.	Yield (%)	m.p. (°C)	X	Molecular formula	Microanalysis found (calc.) % C	H	N	MS (M^+)	UV (λ_{max}) (ε_{max})
17	65	220–221	$R^1 = R^2 = (CH_2)_6$–	$C_{17}H_{20}N_4O_4S$	54.3 (54.2)	5.2 (5.4)	14.8 (14.9)	220*	
18	72	254–255	$R^1 = H$, $R^2 = p$-$NO_2C_6H_4NH$	$C_{17}H_{13}N_5O_6S \cdot H_2O$	47.2 (47.1)	3.2 (3.5)	16.4 (16.2)	355*	325 35, 070
19	66	242–243	$R^1 = H$, $R^2 = p$-$MeOC_6H_4NH$	$C_{18}H_{16}N_4O_5S$	53.7 (54.0)	3.7 (4.0)	14.3 (14.0)	400	325 30, 485
20	85	250–251	$R^1 = H$, $R^2 = p$-ClC_6H_4NH	$C_{17}H_{13}ClN_4O_4S \cdot \frac{1}{2}H_2O$	49.2 (49.3)	3.1 (3.4)	13.8 (13.5)	404	325 31, 540
21	78	237–238	$R^1 = H$, $R^2 = 2$-C_4H_3S	$C_{15}H_{12}N_4O_4S_2 \cdot \frac{1}{4}H_2O$	47.3 (47.3)	3.0 (3.3)	14.8 (14.7)	376	
22	73	235–236	$R^1 = H$, $R^2 = 3$-C_4H_3S	$C_{15}H_{12}N_4O_4S_2 \cdot \frac{1}{4}H_2O$	47.5 (47.3)	3.4 (3.3)	14.9 (14.7)	376	
23	88	191–192	$R^1 = H$, $R^2 = 2$-C_5H_4N	$C_{16}H_{13}N_5O_4S \cdot \frac{1}{4}H_2O$	50.9 (51.1)	3.4 (3.6)	18.4 (18.6)	343*	324 30, 800
24	98	220–222	$R^1 = H$, $R^2 = 3$-C_5H_4N	$C_{16}H_{13}N_5O_4S \cdot \frac{1}{4}H_2O$	50.9 (51.1)	3.5 (3.6)	18.4 (18.6)	343*	
25	75	320–325	N_3	$C_{10}H_7N_5O_4S \cdot \frac{1}{2}H_2O$	40.0 (39.7)	2.4 (2.7)	23.9 (23.2)	293	
26	98	196–197	$N{=}P(OEt)_3$	$C_{16}H_{22}N_3O_7PS$	44.3 (44.5)	5.0 (5.1)	9.9 (9.7)	431	
27	10	237–238	$C_7H_{10}N$	$C_{17}H_{17}N_3O_4S\frac{1}{4}H_2O$	56.3 (56.1)	4.8 (4.8)	11.5 (11.6)	359	
28	9	259–260	p-$ClSO_2C_6H_4NH$	$C_{16}H_{12}ClN_3O_6S_2\frac{1}{4}H_2O$	43.1 (43.0)	2.9 (2.8)	9.4 (9.4)	443	
29	41	274–276	p-$Me_2NSO_2C_6H_4NH$	$C_{18}H_{18}N_4O_6S_2 \cdot \frac{1}{2}H_2O$	47.3 (47.0)	4.1 (4.2)	12.0 (12.2)	450	
30	54	217–218	3,5-dimethyl pyrazolyl	$C_{15}H_{14}N_4O_4S \cdot \frac{1}{2}H_2O$	50.4 (50.7)	3.9 (4.2)	16.0 (15.8)	346	
31	42	237–238	Et_2N	$C_{15}H_{19}N_3O_2S$	53.3 (53.4)	5.7 (5.7)	12.3 (12.5)	337	
32	17	234–236	Me_2N	$C_{13}H_{12}Cl_3N_3O_4S_2$	35.0 (35.1)	2.5 (2.7)	9.5 (9.5)	449†	
33	38	171–173	Cl	$C_{11}H_9ClN_2O_4S$	43.4 (43.6)	2.8 (3.0)	9.5 (9.3)	304	

34	68	195–196	NEt_2	$C_{15}H_{19}N_3O_4S$	53.6 (53.4)	5.7 (5.6)	12.4 (12.5)	337
35	70	234–235	Cl	$C_{10}H_6Cl_2N_2O_4S$	37.1 (37.4)	2.0 (1.9)	8.5 (8.7)	321
36	75	290–292	NH_2	$C_{10}H_8ClN_3O_4S$	39.5 (39.8)	3.0 (2.7)	13.8 (13.9)	301
37	53	160–162	NEt_2	$C_{14}H_{16}ClN_3O_4S$	47.3 (47.0)	4.6 (4.5)	11.5 (11.7)	359
38	60	265–266	C_4H_8NO	$C_{14}H_{14}ClN_3O_5S$	45.4 (45.2)	3.9 (3.8)	11.1 (11.3)	373
39	78	155–157	$NHNH_2$	$C_{10}H_9ClN_4O_4S$	37.6 (37.9)	3.1 (2.8)	17.5 (17.7)	301*
40	89	165–166	$NHN{=}CMe_2$	$C_{13}H_{13}ClN_4O_4S{\cdot}\frac{1}{2}H_2O$	43.0 (42.7)	3.9 (3.8)	15.0 (15.3)	356
41	70	190–192	NHN=CHPh	$C_{17}H_{16}ClN_4O_4S{\cdot}\frac{1}{2}H_2O$	49.2 (49.3)	3.6 (3.4)	13.8 (13.5)	300*
42	36	214–215	N_3	$C_{10}H_6ClN_5O_4S$	36.4 (36.6)	2.0 (1.8)	21.2 (21.4)	327
43	27	188–190	C_4H_8NO	$C_{15}H_{13}Cl_4N_3O_5S$	42.5 (42.7)	3.0 (3.1)	9.8 (10.0)	427†
44	80	212–213	Cl	$C_{12}H_9ClN_2O_4S$	45.5 (45.8)	3.2 (2.9)	9.1 (8.9)	314
45	76	324–326	NH_2	$C_{12}H_{11}N_3O_4S{\cdot}\frac{1}{2}H_2O$	47.3 (47.5)	4.2 (4.0)	13.6 (13.9)	294
46	66	268	NEt_2	$C_{16}H_{19}N_3O_4S$	54.7 (55.0)	5.4 (5.4)	11.8 (12.0)	349
47	74	201–203	C_4H_8NO	$C_{16}H_{17}N_3O_5S{\cdot}1H_2O$	50.1 (50.4)	5.0 (5.0)	10.8 (11.0)	363
48	65	278–279	$PhCH_2NH$	$C_{19}H_{17}N_3O_4S$	59.3 (59.5)	4.6 (4.4)	10.9 (11.0)	383
49	67	250–252	$NHNH_2$	$C_{12}H_{12}N_4O_4S{\cdot}1H_2O$	44.0 (44.2)	4.6 (4.3)	17.0 (17.2)	293*
50	84	264	$NHN{=}CMe_2$	$C_{15}H_{16}N_4O_4S{\cdot}1H_2O$	49.0 (49.2)	4.5 (4.4)	15.0 (15.3)	248
51	34	270–272	$NHN{=}CHC_6H_4NO_2$-*p*	$C_{19}H_{15}N_5O_6S\frac{1}{2}H_2O$	50.3 (50.7)	3.9 (3.6)	15.4 (15.6)	298*
52	51	130	N_3	$C_{12}H_9N_5O_4S{\cdot}1H_2O$	42.4 (42.7)	3.6 (3.3)	21.0 (20.8)	319

* = highest fragment ion.
† = a molecular ion cluster, highest ion quoted.

electron-withdrawing effect of the arylidene moiety is further increased by the sulfonyl group and consequently there is a fine balance between N(1) and N(3)-alkylation in these compounds. When the diethylamide (4) was methylated with methyl iodide-potassium tert-butoxide, the N-methyl derivative (31) was formed (N-1 H, δ 10.65). To determine whether this was the N(1) or N(3)-methyl compound, authentic N(1)-methylhydantoin was converted to the 5-benzylidene derivative which was reacted with chlorosulfonic acid (16 equivalents) for 12 hours to give the sulfonyl chloride (33, 38%). 33 with diethylamine gave 34 (N-3H, δ 11.45) which was not the same as 31 (different m.p.s. and R_F values). 31 must therefore be the N-3 methyl derivative (Chart 1). This assignment is supported by the N-1 and N-3 proton resonances; the literature[20] shows that in the N-1 and N-3 methylbenzylidenehydantoins, the N-1 proton resonates some 2 ppm higher than the N-3 proton. The N-trichloromethylsulfenyl compounds (32, 43) showed the N-H resonance at δ 10.65 and were similarly concluded to be the N-3 derivatives.

o-Chlorobenzaldehyde was condensed with hydantoin in boiling acetic acid–sodium acetate (8 hours) to give 5-(*o*-chloro-benzylidenehydantoin) as lemon needles (70%) m.p. 277–279°C (lit.[21] 275°C) and an isomeric compound as fine colourless needles (8%) m.p. 257–260°C. The condensation was also investigated by Boyd and Robson's method[10] which gave a much lower yield (32%) of the yellow product. Reaction of the benzylidene derivative with a large excess (18 equivalents) of chlorosulfonic acid at 45°C for 6 hours gave the sulfonyl chloride (35, 70%). 35 was condensed with nucleophiles to give the derivatives (36–43) (Table I).

Cinnamaldehyde was condensed with benzaldehyde in the presence of pyridine-diethylamine at 100°C (24 hours) to give 5-(cinnamylidene)hydantoin (40%). However, the condensation in glacial acetic acid–sodium acetate at 130–140°C afforded a higher yield (62%) of the product. Subsequent reaction with chlorosulfonic acid (16 equivalents) at room temperature (72 hours) gave an excellent yield (80%) of the sulfonyl chloride (44), which was characterized as the compounds (45–52) (Table I).

The two forms of 5-(*o*-chlorobenzylidene)hydantoin isolated are probably the Z- and E-geometric isomers (Figure 1). We tentatively assign the major pale yellow product (70%), m.p. 277–279°C as the E-isomer because of the slightly greater stabilization resulting from the weak intramolecular N(1)—H · · · Cl hydrogen bonding. The minor white product (8%), m.p. 257–260°C, on the other hand, is considered to be the Z-isomer; here there is probably some unfavourable steric interaction between the *o*-chlorine and the carbonyl oxygen atoms.

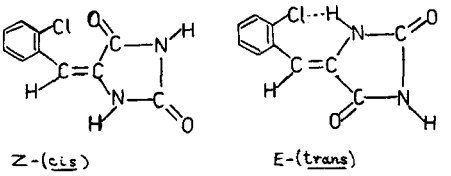


FIGURE 1

Support for the above hypothesis comes from the observation that in the preparation of 5-(*m*- or *p*-chlorobenzylidene)hydantoins, only one isomer was formed possibly because there is no N-H"Cl intramolecular hydrogen bonding. Both compounds appear to have identical TLC, IR and NMR data, although in the NMR spectra, the N-1 and N-3H protons are not resolved and appear as a broad singlet (δ 11.1). The yellow form has the higher molar extinction coefficient (ε 25, 587 as cf. 20, 274).

Johnson and Bates[22] reported the existence of geometrical isomers of 5-(benzylidene)hydantoin. On the other hand, Hahn and Endicott[23] suggested lactim and lactam forms, but these should have different IR spectra.

In the chlorosulfonation of the 5-(benzylidene)hydantoins, the optimum yields were obtained using a very large excess of chlorosulfonic acid (approximately 16 equivalents) at room temperature. Reaction with less reagent (3 equivalents) in excess thionyl chloride afforded a mixture which may arise from initial chlorination of the CONH group. 5-(*m*- and *p*-Chlorobenzylidene)hydantoins were unchanged after treatment with chlorosulfonic acid (16 equivalents) at room temperature (12 hours); at 60°C decomposition occurred. The failure to achieve chlorosulfonation must be associated with the steric size of the chlorine atom.

The UV spectra of the benzylidenehydantoins (Table I) are in good agreement with previous observations;[23,24] there were two absorption bands at 225–230 nm ($\varepsilon \simeq 10{,}000$) and 320–326 nm ($\varepsilon \simeq 30{,}000$). Sulfonation increased the wave length of the absorption maximum by 4–10 nm and the intensity by 3000–5000, presumably as a result of extended conjugation involving the sulfonyl moiety. The aryl hydrazones (18–20, 23) showed a substantial increase in the absorption maximum (Table I), but no change in the wave length.

The IR spectra of the hydantoins exhibited two absorption bands at approximately 1780 and 1720 cm^{-1} in agreement with the literature;[8] the sulfonyl derivatives showed two additional bands at 1370 and 1160 cm^{-1} associated with the SO_2 group.[26]

In the mass spectra, the majority of the compounds showed the molecular ions (M^+); however, as has previously been noted,[26] most of the hydrazides and hydrazones suffered extensive fragmentation and the molecular ions were generally not observed with these derivatives (Table I).

The PMR spectra of the 5-benzylidenehydantoins showed that the N-3 and N-1 protons appeared at approximately δ 11.3 and 10.5 so that the former was the more deshielded; although the difference is less than is generally observed[20] for hyantoins without the 5-benzylidene group.[8,20] The alkylidene proton resonated as a singlet (δ 6.3), however in the 5-cinnamylidene derivatives (**44–52**), these protons appeared as a multiplet (δ 6.8–6.2, J 15 Hz) indicative of *trans* coupling. In the sulfonyl derivatives, the aromatic proton resonances had a well defined A, A′ B B′ pattern confirming the expected *p*-sulfonation. The NMR spectrum of the aziridine (**27**, Chart 1) showed the 2,3- and 1,4-proton resonances as sharp singlets therefore the 2,3-protons are *endo* with respect to the aziridine ring.[26,27] The ^{13}C off-resonance spectra of the dimethylamide (**3**) and the dimethyl hydrazide (**13**) clearly identified the 2-, 4- and 5-carbons atoms of the hydantoin ring and the 1′- and 4′- carbons of the aromatic nucleus which appeared as singlets since they are not attached to protons. The remaining aromatic carbons

each carry one proton and consequently resonated as doublets as did the methine carbon atom, while the methyl carbons appeared as triplets.

The compounds described above have been examined for insecticidal, herbicidal and fungicidal properties. In the preliminary fungicide screen at 100 ppm against vine downy mildew, potato blight, wheat rust, apple and barley mildew and rice blast, 4-chlorobenzylidenehydantoin and compounds **10**, **32**, **39** and **43** were highly active against vine downy mildew and wheat rust. A further 15 compounds showed moderate antifungal activity, but all were inactive against a range of insects and plants.

EXPERIMENTAL

Melting points were determined with a Gallenkamp electric apparatus and are uncorrected. IR spectra were measured as Nujol mulls on a Unicam SP 1000 spectrometer. NMR spectra were recorded on a Bruker WP 80 spectrometer using DMSO-d_6 as solvent and TMS as internal standard, an asterisk indicates resonances that were removed by D_2O treatment. UV spectra were measured on a Perkin Elmer 555 spectrophotometer using solutions in methanol. TLC was carried out on Camlab Polygram silica gel plates sensitized to UV 254 nm.

5-(Benzylidene)hydantoin

Freshly distilled benzaldehyde (5.5 g, 0.052 mol) was mixed with hydantoin (4.5 g, 0.045 mol), pyridine (5 ml) and diethylamine (4 ml). The mixture was heated at 100° for 22 hours under nitrogen, following the procedure of Boyd and Robson.[10] Recrystallisation from ethanol gave the product as a pale yellow powder (4.63 g, 55%), m.p. 219–221°C (lit.[10] 220°C). TLC ($CHCl_3$–MeOH 9:1) showed 1 spot R_F 0.49. IR ν_{max} 3275 (NH), 1780, 1710 (C=O), 1650 (Alk C=C), 1590 (Ar C=C) cm^{-1}. NMR: δ 11.1* (s, 1H, N-3H), 10.4* (s, 1H, N-1H), 7.7–7.2 (m, 5H, ArH), 6.35 (s, 1H, CH=C). (Found: C, 63.5; H, 4.35; N, 14.8. $C_{10}H_8N_2O_2$ requires C, 63.8; H, 4.3; N, 14.9%. MS: 188 (M^+), 117 (C_8H_7N), 90 (C_7H_6), 43 (HNCO). UV: λ_{max} 239 nm (ε 9,500), 316 (ε 24,135).

5-(o-Chlorobenzylidene)hydantoin

Method 1

A solution of *o*-chlorobenzaldehyde (14.05 g, 0.1 mol), hydantoin (10.0 g, 0.1 mol) and sodium acetate (50 g) in glacial acetic acid (50 ml) was refluxed, under nitrogen, for 8 hours (cf. Reference 28). The solution was cooled, the precipitate was filtered off, washed with water and recystallized from aqueous acetone to give the product as pale yellow needles (15.6 g, 70%), m.p. 277–279°C (decomp.) (lit.[21] 275°C). TLC ($CHCl_3$—MeOH 9.5:1) showed one spot R_F 0.43, (Found: C, 54.1; H, 3.0; N, 12.6. $C_{10}H_7ClN_2O_2$ requires C, 53.95; H, 3.2; N, 12.6%). IR ν_{max} 3275 (NH), 1790, 1730 (C=O), 1665 (Alk C=C), 1590 (Ar C=C) cm^{-1}. MS: 224 (M^+), 187 (M—Cl), 115 (C_8H_5N), 89 (C_7H_5), 43 (HNCO). UV: λ_{max} 315 nm (ε 25, 587). NMR δ 11.1* (s, 2H, N − 1, N − 3H), 7.7–7.2 (m, 4H, ArH), 6.56 (s, 1H CH=C). The filtrate, on concentration, gave a second product as fine white needles (1.8 g, 8%), m.p. 257–260°C (decomp.) (Found: C, 53.8; H, 3.2, N, 12.7. $C_{10}H_7ClN_2O_2$ requires C, 53.95; H, 3.2; N, 12.6%). UV: λ_{max} 315 nm (ε 20, 274). Both products gave identical TLC, IR and NMR data.

Method 2

A mixture of *o*-chlorobenzaldehyde (14.05 g, 0.1 mol) and hydantoin (10.0 g, 0.1 mol) was heated with pyridine (11 ml) and diethylamine (15 ml) as previously described.[10] Recrystallization from acetone gave the product as pale yellow crystals (7.12 g, 32%), m.p. 277.5–279°C. (No other product was isolated from the filtrate.) IR: ν_{max} 3275 (NH), 1790, 1730 (C=O), 1665 (Alk C=C), 1595 (Ar C=C). TLC ($CHCl_3$—MeOH 9.5:1), showed one spot R_F 0.43.

5-(m-Chlorobenzylidene)hydantoin

A solution of *m*-chlorobenzaldehyde (7.0 g, 0.05 mol), hydantoin (5.0 g, 0.05 mol) and sodium acetate (40 g) in glacial acetic acid (40 ml) was refluxed, under nitrogen, for 8 hours as previously described.[28] Recrystallization from acetone gave the product as a yellow powder (8.9 g, 80%), m.p. 232–233°C (lit.[29] 233–234°C. TLC ($CHCl_3$—MeOH 9.5:1 showed one spot, R_F 0.44. IR ν_{max} 3280 (NH), 1790, 1735 (C=O), 1660 (Alk C=C), 1590 (Ar C=C).

5-(p-Chlorobenzylidene)hydantoin
p-Chlorobenzaldehyde (16.74 g, 0.12 mol) hydantoin (10.0 g, 0.1 mol), pyridine (11 ml) and diethylamine (9 ml) were heated together as described by Boyd and Robson.[10] Recrystallization from methanol gave the product as pale yellow crystals (13.61 g, 61%), m.p. 299–301°C (lit.[10] 264–266°C. (Found: C, 54.0; H, 3.1; N, 12.4; Cl, 16.0. $C_{10}H_7ClN_2O_2$ requires C 53.95; H, 3.2; N, 12.6; Cl, 15.9%) IR ν_{max} 3260, 3220 (NH), 1760, 1735 (C=O), 1660 (Alk C=C), 1590 (Ar C=C), 815 (C—Cl) cm^{-1}. NMR δ.10.65* (s, 2H, N – 1, N – 3H), 7.46–7.24 (dd, 4H, ArH), 6.3 (s, 1H CH=C). MS: 224 (M^+), 153 (M – CONHCO), 116 (C_8H_6N), 89 (C_7H_5), 43 (HNCO). UV λ_{max} 228 nm (11,000), 320 (27,200).

5-(Benzylidene)-1-methylhydantoin
Benzaldehyde (10.7 g, 0.1 mol) was heated (150°C) with N-1-methylhydantoin (10.0 g, 0.088 mol), pyridine (10 ml) and diethylamine (9 ml) under nitrogen, for 50 hours.

Recrystallization from ethanol gave the hydantoin as a lemon powder (3.75 g, 21%), m.p. 189–191°C. TLC ($CHCl_3$—MeOH 9:1) showed one spot, R_F 0.63. (Found: C, 65.2; H, 4.8; N, 13.8. $C_{11}H_{10}N_2O_2$ requires C, 65.3; H, 5.0; N, 13.85%). IR ν_{max} 3150, 3050 (NH), 1740, 1700 (C=O), 1628 (Alk C=C), 1590 (Ar C=C). NMR: δ 11.20* (s, 1H, N-3H), 8.10–7.10 (m, 5H, ArH), 6.28 (s, 1H, CH=C), 3.0 (s, 3H, Me). MS: 202 (M^+), 131 (M-CONHCO).

5-(Cinnamylidene)hydantoin

Method 1
Freshly distilled cinnamaldehyde (14 g, 0.11 mol), hydantoin (10 g, 0.1 mol), pyridine (10 ml) and diethylamine (2 ml) were mixed together and heated at 100°C for 24 hours.

Recrystallization from ethanol afforded the product as yellow prisms (8.6 g, 40%), m.p. 269–271°C (decomp.) (lit.[14] 272–273°C). TLC (C_5H_{12}—EtOAc 1:1) showed one spot R_F 0.64. (Found: C, 67.1; H, 4.8; N, 13.4. $C_{12}H_{10}N_2O_2$ requires C, 67.3; H, 4.7; N, 13.1%). IR ν_{max} 3200, 3150 (NH), 1740, 1690 (C=O), 1630 (Alk C=C), 1595 (Ar C=C) cm^{-1}. MS 214 (M^+), 171 (M-CONH), 143 (M-NHCONCHO), 115; 43 (HNCO). NMR: δ 10.9* (s, 2H, N-1, N-3H), 7.7–7.2 (m, 5H, ArH), 6.8–6.2 (m, 3H, =CH). UV λ_{max} 235 nm (ε 10,270), 346 (ε 41,370).

Method 2
Cinnamaldehyde (14 g, 0.11 mol), hydantoin (10 g, 0.1 mol), sodium acetate (50 g) and glacial acetic acid (50 ml) were refluxed at 130–140°C for 6 hours as previously described.[13,14] Recrystallization from glacial acetic acid gave the product as pale yellow prisms (13.3 g, 62%), m.p. 273–275°C.

Chlorosulfonation of the hydantoins

5-(p-Chlorosulfonylbenzylidene)hydantoin (**1**)
5-(Benzylidene)hydantoin (15.7 g, 0.084 mol) was added portionwise to chlorosulfonic acid (89 ml, 1.34 mol) at 0°C with swirling. The solution was stirred for 6 hours at room temperature and poured onto ice (500 g). The precipitate was filtered off, washed with water and dried *in vacuo* to give the chloride (20.9 g)). TLC ($CHCl_3$–MeOH 9:1) showed one spot R_F 0.35. IR ν_{max} 3340, 3070 (NH), 1780, 1720 (C=O), 1665 (Alk C=C), 1590 (Ar C=C), 1375, 1170 (SO_2) cm^{-1}. NMR δ 11.1* (s, 1H, N-3H), 10.05* (s, 1H, N-1H), 8.1–7.6 (m, 4H, ArH), 6.45 (s, 1H, CH=C).

5-(2'-Chloro-4'-chlorosulfonylbenzylidene)hydantoin (**35**)
5-(*o*-Chlorobenzylidene)hydantoin (5 g, 0.02 mol) reacted with chlorosulfonic acid (25 ml, 0.36 mol) at room temperature for 6 hours to give 35 (5.1 g). TLC ($CHCl_3$—MeOH 9.5:1) showed one spot R_F 0.75. IR ν_{max} 3410, 3120 (NH), 1800, 1750 (C=O), 1640 (Alk C=C), 1590 (Ar C=C), 1380, 1170 (SO_2) cm^{-1}. NMR: δ 10.85* (s, 1H, N-3H), 9.20* (s, 1H, N-1H), 8.1–7.35 (m, 3H, ArH), 6.45 (s, 1H, CH=C).

5-(p-Chlorosulfonylcinnamylidene)hydantoin (**44**)
5-(Cinnamylidene)hydantoin (3.2 g, 0.015 mol) was reacted with chlorosulfonic acid (12 ml, 0.18 mol) for 72 hours at room temperature to give 44 (3.75 g). TLC ($CHCl_3$—MeOH 9:1) showed one spot R_F 0.40. IR ν_{max} (KBr) 3210, 3120 (NH), 1755, 1700 (C=O), 1640 (Alk C=C), 1590 (Ar C=C), 1370, 1170 (SO_2) cm^{-1}. NMR: δ 11.1* (s, 2H, N-1, N-3H), 7.8–7.2 (m, 5H, ArH), 6.8–6.3 (m, 3H, =CH).

5-(p-Chlorosulfonylbenzylidene)-1-methylhydantoin (**33**)
5-(Benzylidene)-1-methylhydantoin (3.63 g, 0.018 mol) was reacted with chlorosulfonic acid (19 ml, 0.287 mol) at room temperature for 12 hours to give 33 as a lemon powder (2.1 g). TLC ($CHCl_3$—MeOH 9:1) showed one spot R_F 0.44. IR ν_{max} 3150 (NH), 1750, 1720 (C=O), 1650 (Alk

C=C), 1580 (Ar C=C), 1370, 1165 (SO_2) cm^{-1}. NMR: δ 11.32* (s, 1H, N-3H), 8.00–7.3 (dd, 4H, ArH), 6.25 (s, 1H, CH=C), 3.05 (s, 3H, Me).

General procedure for the reaction of the sulfonyl chlorides (**1, 33, 34, 35, 38, 44**) *with amines*
The sulfonyl chloride (0.01 mol) was treated with the amine (0.03 mol) in methanol (30 ml) for 5 hours. The mixture was added to crushed ice (100 g) and the solid product recrystallized from methanol to give the amides (Table I).

Compound (**3**)
IR ν_{max} 3280, 3175 (NH), 1785, 1720 (C=O), 1660 (Alk C=C), 1595 (Ar C=C), 1365, 1160 (SO_2) cm^{-1}. NMR: δ 11.15* (s, 1H, N-3H), 9.75* (s, 1H, N-1H), 7.65 (s, 4H, ArH), 6.35 (s, 1H, CH=), 2.62 (s, 6H, NMe_2). ^{13}C NMR: δ 165.1 (C-4), 155.5 (C-2), 137.5, 133.7 (C-1′, C-4′), 129.8 (C-5), 129.3, 127.5 (C-2′, C-3′, C-5′, C-6′), 105.9 (CH=), 37.3 (NMe_2).

Compound (**34**)
NMR δ: 11.45* (s, 1H, N-3H), 8.1–7.75 (dd, 4H, ArH), 6.45 (s, 1H, CH=C), 3.18 (q, 4H, CH_2CH_3), 3.1 (s, 3H, N-Me), 1.05 (t, 6H, CH_2CH_3).

Compound (**38**)
NMR δ 11.4* (s, 1H, N-3H), 10.85* (s, 1H, N-1H), 8.0–7.55 (m, 3H, ArH), 6.45 (s, 1H, CH=C), 3.80–2.80 (m, 8H, morpholino H).

Hydrazides (**11, 39, 49**)
These were obtained by stirring the sulfonyl chloride (0.01 mol) with a solution of 98% hydrazine hydrate (0.03 mol) in THF (30 ml). The reaction was initially kept at 0°C and then left at room temperature for 4 hours. Addition of ice gave a precipitate which was filtered off, washed with water and dried *in vacuo* to give the products. The hydrazides were characterized *as* the acetone hydrazones (15, 40, 50). Similar condensations with methyl-N,N-dimethyl- or phenyl-hydrazine gave the hydrazides (12, 13, 14).

Compound (**13**)
NMR: δ 11.3* (s, 1H, N-3H), 10.4* (s, 1H, N-1H), 8.5* (s, 1H, SO_2NH), 7.9–7.5 (dd, 4H, ArH), 6.4 (s, 1H, CH=C), 2.3 (s, 6H, NMe_2). ^{13}C NMR δ: 165.3 (C-4), 155.7 (C-2), 138.6, 137.3 (C-1′, C-4′), 130.5 (C-5), 129.5, 127.9 (2′, 3′, 5′, 6′-C), 106.1 (=CH), 47.5 (NMe_2).

Compound (**50**)
IR ν_{max} 3200 (NH), 1750, 1710 (C=O), 1630 (ALk C=C), 1590 (Ar C=C), 1345, 1155 (SO_2) cm^{-1}. NMR: δ 11.15* (s, 1H, N-3H), 10.85* (s, 1H, N-1H), 10.1* (s, 1H, SO_2NH), 8.0–7.65 (dd, 4H, ArH), 7.0–6.25 (m, 3H, =CH), 1.9 (s, 6H, $N{=}CMe_2$).

Azides (**25, 42, 52**)
There were prepared by reaction of the sulfonyl chloride (0.01 mol) with sodium azide (0.02 mol) in aqueous acetone at room temperature for 3 hours. The suspension was added to crushed ice, the solid collected and recrystallized from acetone.

Compound (**25**)
IR ν_{max} 3580, 3325 (NH), 2150 (N_3), 1780, 1720 (C=O), 1660 (Alk C=C), 1590 (Ar C=C), 1365, 1160 (SO_2) cm^{-1}. MS: 293 (M^+), 251 (M-N_3), 203 (M-SON_3), 187 (M-SO_2N_3), 132, 116, 89 (C_7H_5), 64 (SO_2), 28.

The azide (0.003 mol) was heated with triethylphosphite (0.003 mol) in toluene (30 ml) at 80° for 2 hours to give the triethoxyphosphinimine (26). NMR δ 11.25* (s, 1H, N-3H), 10.54* (s, 1H, N-1H), 7.85–7.45 (m, 4H, ArH), 6.35 (s, 1H, CH=C), 4.38–3.80 (m, 6H, CH_2CH_3), 1.4–1.1 (m, 9H, CH_2CH_3).

The azide (0.003 mol) was heated with norbornene (0.003 mol) in DMF (20 ml) at 120° for 6 hours. The solvent was removed under reduced pressure and the crude material chromatographed on silica gel using chloroform as eluent to give the *exo*-aziridine (27). NMR δ: 11.6* (s, 1H, N-3H), 10.5* (s, 1H, N-1H), 7.84–7.78 (dd, 4H, ArH), 6.45 (s, 1H, CH=C), 2.93 (s, 2H, 2,3-H), 2.45 (s, 2H, 1,4-H), 1.57–1.20 (m, 4H, 4,5-H), 1.37 (d, 2H, 7-H).

5-(p-N,N-Diethylsulfamoylbenzylidene)-3-methylhydantoin (**31**)
The diethylsulfonamide (4) (400 mg, 0.0012 mol) was dissolved in DMF (10 ml) containing potassium tert-butoxide (139 mg, 0.0012 mol). The solution was stirred with methyl iodide (0.1 ml, 0.0014 mol)

for 2.5 hours). The mixture was poured onto ice; the precipitate was filtered off, washed with water and dried. The product was chromatographed on silica gel using chloroform-methanol (10:1) as eluant to give 31 (176 mg). IR ν_{max} (KBr) 3230 (NH), 1770, 1715 (C=O), 1658 (Alk C=C), 1595 (Ar C=C), 1330, 1155 (SO_2) cm^{-1}. MS: 337 (M^+), 322 (M-Me), 265 (M-NEt_2), 217 (M-$SONEt_2$), 201 (M-SO_2NEt_2). NMR δ: 10.65* (s, 1H, N-1H), 7.96–7.55 (m, 4H, Ar H), 6.60 (s, 1H, CH=C), 3.25 (q, 4H, CH_2CH_3, *J* 7 Hz), 1.15 (t, 6H, CH_2CH_3, *J* 7 Hz).

5-(p-Morpholinosulfonylbenzylidene-N-3-trichloromethylsulfenylhydantoin (**43**)
The sulfonylmorpholidate (**38**) (0.6 g, 0.002 mol) was stirred with a solution of trichloromethylsulfenyl chloride (0.3 g, 0.002 mol) and triethylamine (0.16 g, 0.002 mol) in acetone (25 ml) for 20 hours. The solvent was removed *in vacuo* and the residue triturated with water and ether to give (**43**) (0.23 g). NMR δ: 10.65* (s, 1H, N-1H), 8.0–7.7 (m, 3H, ArH), 4.79 (s, H, CH=C), 3.75–2.82 (m, 8H, morpholino H). MS: 427 (M^+), 275 (M-$SCCl_3$), 189 (M-$SCCl_3$-C_4H_8NO), 125 (M-$SCCl_3$, -$SO_2NC_4H_8O$), 86 (C_4H_8NO), 43 (HNCO).

Compound (**32**) was similarly prepared: NMR δ: 10.65* (s, 1H, N-1H), 7.92–7.76 (dd, 4H, ArH), 6.82 (s, 1H, CH=C), 2.64 (s, 6H, NMe_2).

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