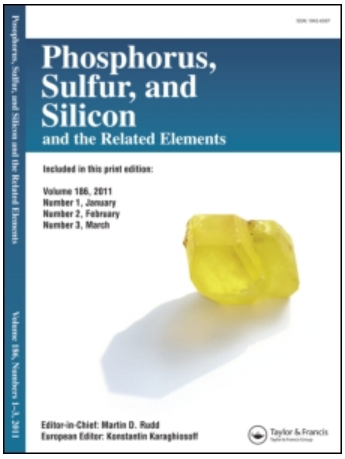

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

CAMPHOR-AND 10-SULFONAMIDOCAMPHOR SULFONOHYDRAZONES AND RELATED COMPOUNDS

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To cite this Article Cremlyn, Richard , Bartlett, Martin and Lloyd, Jane(1988) 'CAMPHOR-AND 10-SULFONAMIDOCAMPHOR SULFONOHYDRAZONES AND RELATED COMPOUNDS', Phosphorus, Sulfur, and Silicon and the Related Elements, 40: 1, 91 — 97
To link to this Article: DOI: 10.1080/03086648808072898
URL: http://dx.doi.org/10.1080/03086648808072898

Phosphorus and Sulfur, 1988, Vol. 40, pp. 91–97
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CAMPHOR-AND 10-SULFONAMIDOCAMPHOR SULFONOHYDRAZONES AND RELATED COMPOUNDS

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(Received February 26, 1988; in final form May 17, 1988)

Camphor-10-sulfonyl chloride (**1**) was converted into the hydrazide (**3**), the *N*-phenyl- and N,N^1-dimethylhydrazides (**14, 15**); the former was characterized as the hydrazones (**5–9**) and the 3,5-dimethylpyrazole (**10**). Camphor-10-sulfonanilide (**17**) and the morpholidate (**19**) were condensed with hydrazine hydrate, to give the hydroazones (**18, 20**) converted into the azines (**21–30**). Camphorhydrazone was similarly prepared, together with the azines (**31–37**). The spectral data are briefly discussed together with the results of preliminary biological screening.

INTRODUCTION

The work forms part of our general programme on the chemistry and biological activity of organic sulfonyl derivatives.[1–3]

Camphor is reported to form the 3-, 8- or 10- sulfonic acids depending on the reaction conditions. The camphor sulfonyl derivatives are of interest, because camphor is produced naturally in the camphor tree (*cinnamonum camphora*). It is therefore likely that these compounds may well be translocated in plants and might be useful as systemic antifungal agents.

DISCUSSION

We previously reported[4] that camphor-10-sulfonyl chlroide (**1**) reacted with excess hydrazine hydrate to give the thiadiazine dioxide (**2**) rather than the hydrazide (**3**). Later work,[5] however indicated that when the condensation was carried at 0°C using an equimolar mixture of hydrazine and triethylamine (**3**) was isolated. We now show when the sulfonyl chloride (**1**) is dissolved in warm hydrazine (6 equivalents) and immediately cooled (0°C) an excellent yield (90%) of **3** was obtained.

When (**3**) was melted cyclization to (**2**) occurred and this dehydration was also observed in the mass spectrometer. The thiadiazine dioxide (**2**) contains an acidic NH proton and condensed with trichloromethylsulfenyl chloride to give (**4**). Camphor-10-sulfonohydrazide (**3**) was converted into the hydrazones (**5–9**) (Table I); **3** by prolonged heating with acetylacetone afforded the 3,5-dimethylpyrazole (**10**). Camphor-10-sulfonyl chloride (**1**) reacted with 0.88 aqueous ammonia to give the thiazine dioxide (**11**, 82%), but gaseous ammonia

TABLE I

Physical data for camphor-10-sulfonohydrazones

Compd no.	Yield (%)	m.p. (°C)	R1	R2	Molecular formula	Microanalysis found (calc.)% C	H	N	MS (M^+)
5	65	122	H	Ph	$C_{17}H_{22}N_2O_3S$	60.9 (61.1)	6.7 (6.6)	8.1 (8.4)	
6	83	128–130	H	p-$MeOC_6H_4$	$C_{18}H_{24}N_2O_4S$	59.3 (59.0)	6.8 (6.6)	7.8 (7.6)	
7	82	119–120	H	p-MeC_6H_4	$C_{18}H_{24}N_2O_3S$	62.1 (62.1)	7.0 (6.9)	8.3 (8.1)	256†
8	66	110–112	H	p-ClC_6H_4	$C_{17}H_{21}ClN_2O_3S$	55.2 (55.3)	5.7 (5.7)	7.5 (7.6)	
9	80	118–120	Me	Ph	$C_{18}H_{24}N_2O_3S$	62.0 (62.1)	7.0 (6.9)	8.2 (8.0)	

† = *Highest mass fragment ion.*

yielded the sulfonamide (**12**, 87%) characterized as the *N*-acetyl compound (**13**). When **12** was kept molten it was converted in **11**; an analogous cyclisation to the conversion of **3**→**2**. (**1**) reacted normally with phenyl- and *N,N*-dimethylhydrazide to give the hydrazides (**14, 15**). In contrast, previous studies[6] showed that with *N*-methylhydrazine, (**1**) gave the *N*-methylthiadiazine dioxide (**16**) and this structure was confirmed by X-ray crystallography. Camphor-10-sulfonanilide (**17**) condensed with hydrazine hydrate, by prolonged boiling (24 hours) in ethanol catalysed by a small quantity of concentrated sulphuric acid, to give the hydrazone (**18**, 89%). The analogous reaction with the sulfonylmorpholidate (**19**) required even more drastic conditions (boiling butanol, sulfuric acid, 24 hours) to give **20** (89%). The hydrazones (**18, 20**) were reacted with aldehydes and ketones to give the corresponding camphorazines (**21–25** and **26–30** respectively) (Table II). DL Camphor condensed with hydrazine hydrate under comparable conditions (boiling butanol, sulfuric acid, 17 hours) to give camphor hydrazone (85%) which was characterized as the azines (**31–37**) (Table III). In condensations with aromatic aldehydes, the reaction must be performed in dry THF; as has been previously observed,[7] the use of hydroxylic solvents leads to formation of the diaryl azines.

The condensation of camphor, camphor-10-sulfonanilide (**17**) and the morpholidate (**19**) with excess hydrazine hydrate (6 equivs.) all required comparatively vigorous conditions. The anilide (**17**) went in boiling ethanol whereas camphor and the morpholidate (**19**) required the use of the higher boiling n-butanol as solvent. The greater reactivity of **17** may be due to N-H · · · O hydrogen bonding which should facilitate attack by hydrazine on the carbonyl group. Such hydrogen bonding would not be possible with camphor or the morpholidate (**19**). The conditions required for these condensations is in sharp contrast to the extremely facile intramolecular cyclisation of the 10-sulfonohydrazide (**3**) to the thiadiazinedioxide (**2**). This is probably due to intramolecular N-H · · · O hydrogen bonding in **3** which holds the hydrazine and carbonyl groups in juxtaposition.

The IR spectra of the various camphor-10-sulfonyl derivatives showed the

TABLE II

Physical data for the 10-sulfonamidocamphor azines

Compd no.	Yield (%)	m.p. (°C)	R1	R2	Molecular formula	Microanalysis found(calc.)% C	H	N	MS (M^+)
21	94	110–112	Me	Me	$C_{19}H_{27}N_3O_2S$	62.9 (63.1)	7.6 (7.5)	11.5 (11.6)	361
22	84	135–136	—$(CH_2)_4$—		$C_{12}H_{29}N_3O_2S$	65.1 (65.0)	7.5 (7.5)	10.8 (10.8)	387
23	85	150	H	Ph	$C_{23}H_{27}N_3O_2S$	67.7 (67.4)	6.9 (6.6)	10.1 (10.3)	409
24	82	156	H	*p*-$MeOC_6H_4$	$C_{24}H_{29}N_3O_3S$	66.0 (65.6)	6.8 (6.6)	9.2 (9.6)	439
25	90	162	H	*p*-$NO_2C_6H_4$	$C_{23}H_{26}N_4O_4S$	60.5 (60.8)	5.9 (5.8)	12.4 (12.3)	454
26	91	oil	Me	Me	$C_{17}H_{29}N_3O_3S.\frac{1}{4}H_2O$	56.4 (56.6)	8.4 (8.3)	11.3 (11.6)	299†
27	80	oil	—$(CH_2)_4$—		$C_{19}H_{31}N_3O_3S.\frac{1}{4}H_2O$	58.8 (59.0)	8.1 (8.2)	10.6 (10.9)	295†
28	48	oil	H	Ph	$C_{21}H_{29}N_3O_3S$	62.8 (62.5)	7.4 (7.2)	10.0 (10.4)	317†
29	56	124	H	*p*-$MeOC_6H_4$	$C_{22}H_{31}N_3O_4S.\frac{1}{2}H_2O$	60.0 (60.3)	7.1 (7.3)	9.4 (9.6)	347†
30	62	149–151	H	*p*–$NO_2C_6H_4$	$C_{21}H_{28}N_4O_5S.\frac{1}{2}H_2O$	55.4 (55.1)	6.1 (6.3)	12.4 (12.2)	362†

† = Highest mass fragment ion

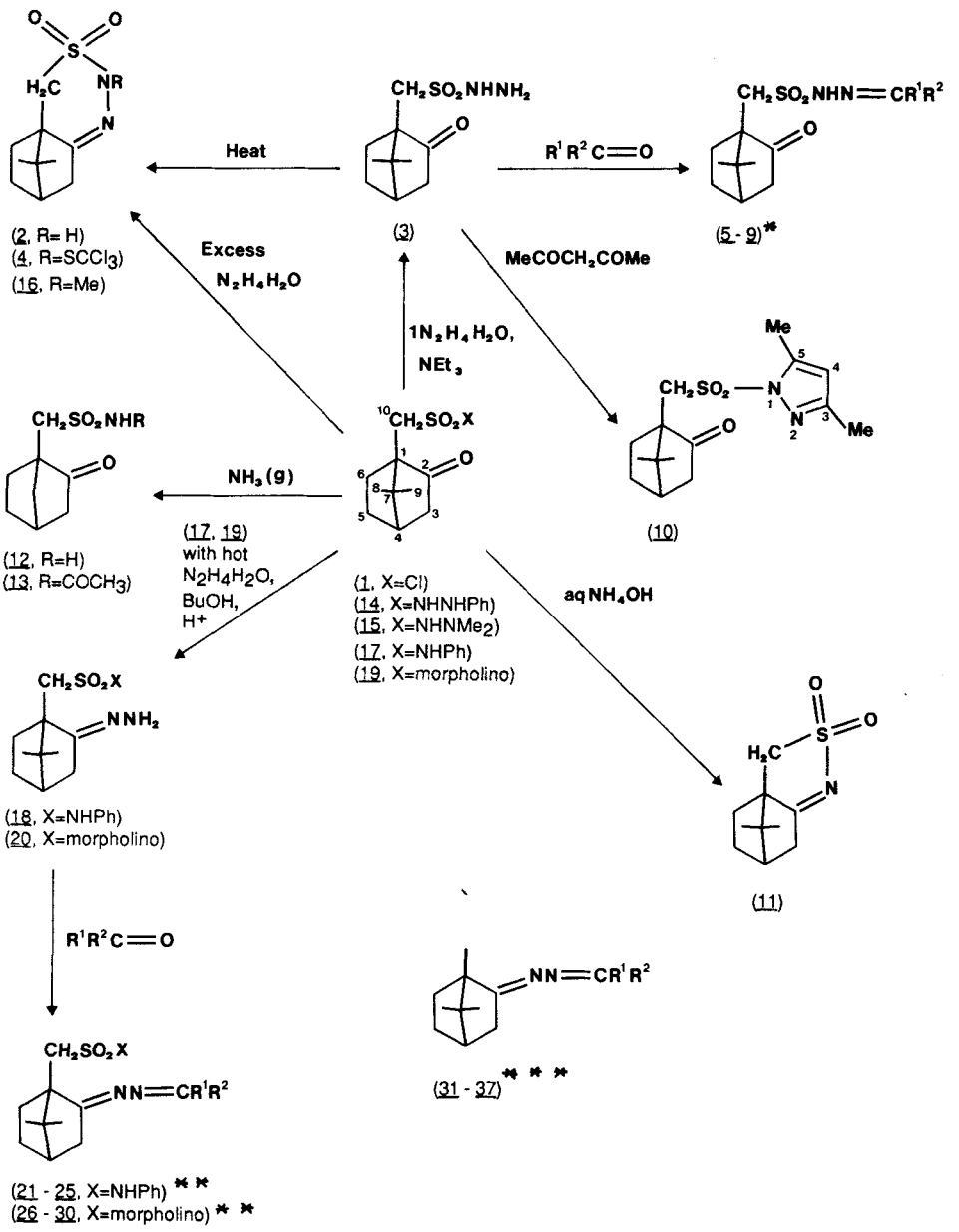
carbonyl stretching absorption at *ca.* 1745 cm^{-1} and the SO_2 bands at ca. 1370, 1150 cm^{-1} (cf Ref. 8). The MS of the majority of the compounds showed the molecular ions (M^+) (Tables I–III) apart from the hydrazides and hydrazones which frequently suffered extensive decomposition in general agreement with our previous observations.[9]

The ^1H NMR spectra showed the attachment of the electron-withdrawing sulfonyl moiety to the 10-methyl group because the methylene resonances

TABLE III

Camphorazines

Compd no	Yield (%)	m.p. (°C)	R1	R2	Molecular formula	C found (calc)%	H	N	MS (M^+)
31	76	103	H	*p*·$NO_2C_6H_4$	$C_{17}H_{21}N_3O_2$	68.0 (68.2)	6.9 (7.0)	14.0 (14.0)	
32	82	66	H	*p*·$MeOC_6H_4$	$C_{18}H_{24}N_2O$	75.7 (76.0)	8.6 (8.4)	10.1 (9.9)	
33	86	75–76	H	*p*·$Me_2NC_6H_4$	$C_{19}H_{27}N_3$	76.6 (76.8)	9.4 (9.1)	14.0 (14.1)	
34	82	75	H	2,4$Cl_2C_6H_3$	$C_{17}H_{20}Cl_2N_2$	62.8 (63.1)	6.3 (6.2)	9.0 (8.7)	
35	84	135–137	H	*m*–HOC_6H_4	$C_{17}H_{22}N_2O$	75.3 (75.6)	8.3 (8.1)	10.5 (10.4)	270
36	80	oil	Me	Me	$C_{13}H_{22}N_2$	75.3 (75.7)	10.5 (10.7)	13.4 (13.6)	
37	82	oil	—$(CH_2)_4$—		$C_{15}H_{24}N_2$	77.4 (77.6)	10.5 (10.3)	12.0 (12.1)	



SCHEME 1

* For the nature of R^1, R^2 see Table 1.
** For R^1, R^2 see Table 2.
*** For R^1, R^2 see Table 3.

(δ 3.0 ppm) had shifted downfield. For the geminal dimethyl group, in agreement with previous arguments,[6] we assign the lower field singlet (δ 0.95) to the 9-methyl protons and the other resonance (δ 0.80) to the 8-methyl group. The ^{13}C NMR spectra showed the carbonyl carbon resonance at much the lowest field (δ 200 ppm), while that for the 10-carbon atom appeared at considerably lower field (δ 48 ppm) as compared with the corresponding signal (δ 19 ppm) in the camphor-8-sulfonyl derivatives.[10]

The preliminary *in vitro* antibacterial screening tests against *streptococcus faecalis, clostridium perfringens* and *staphylococcus aureus* at 100 ppm, showed that compounds **3**, **12**, **15**, **21**, **26** and **36** completely inhibited the bacteria.

The compounds were examined for inhibition of the enzymes α-glucosidase, α-amylase, β-galactosidase and acetylcholesterase: compounds **26** and **32** were active against acetylcholinesterase.

The compounds were also screened for *in vitro* fungicidal activity at 100 ppm against 6 test fungi: *Aspergillus versicolor, Cladosporium cladosporiodes, Penicillium purpurogenum, Phoma violacea, Stachybotrys chartatum* and *Ulecladium atrum.* In this test compounds **3**, **12**, **13** and **15** were active against all the fungi.

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-d6 as solvent, unless otherwise stated. MS spectra were recorded with a VG micromass V15 mass spectrometer. TLC was carried out on Camlab Polygram silica gel plates sensitized to UV 254 nm using ethyl acetate-petroleum ether as eluant unless otherwise stated.

DL Camphor-10-sulfonohydrazide (**3**). A mixture of DL camphor-10-sulfonyl chloride[11] (**1**) (11 g, 0.05 mol) hydrazine hydrate (11 g, 0.22 mol) and methanol (100 ml) was heated until complete solution was formed. The solution was immediately poured onto ice and the product recrystallized from methanol to give the hydrazide (**3**) (10 g, 92%), m.p. 97–98°C (lit.[5] 80–82°C) TLC showed 1 spot R_F 0.62. IR ν max 3430, 3380, 3200 (NH), 1745 (C=O), 1370, 1155 (SO_2) cm^{-1}. MS: no M^+ (246), 228 (M—H_2O), 164 (M—H_2O, —SO_2), 149 (M—H_2O, —SO_2NH), 135; 121, 107, 93, 79, 67, 53.

DL Camphor-1-sulfonohydrazones (**5–9**). The hydrazide (0.01 mol) was heated with the carbonyl compound (0.01 mol) in THF (20 ml) for 10 minutes then left for $\frac{1}{2}$ hour, added to ice, and the solid triturated with acetone and ether to give the hydrazones.

Compound (**6**). IR ν max 3200 (NH), 1735 (C=O), 1610 (ArC=C), 1375, 1150 (SO_2) cm^{-1}.

Compound (**7**). Ir ν max 3210 (NH), 1735 (C=O), 1610 (ArC=C), 1370, 1150 (SO_2) cm^{-1}. MS: no M^+(348), 256 (M—C_7H_7), 151 (camphor), 132, 123, 104, 81, 67, 51.

DL (Camphor-10-sulfonyl)-3,5-dimethylpyrazole (**10**). DL camphor-10-sulfonohydrazide (2.4 g, 0.01 mol) (**3**) was refluxed with pentan-2,3-dione (1 g, 0.01 mol) in ethanol for 8 hours to give **10** (53%), m.p. 119–120°C (Found: C; 57.8; H, 6.8; N, 8.9. $C_{15}H_{22}N_2O_3S$ requires C, 58.1; H, 7.1; N, 9.0%) IR ν max 1740 (C=O), 1360, 1140 (SO_2) cm^{-1}. NMR δ: 8.3 (s, 1H, pyrazole H), 3.9–3.4 (q, 2H, CH_2SO_2), 2.4–1.2 (m, 19H, cyclohexyl and methyl H).

DL Camphor-10-sulfonyl N-phenyl hydrazide (**14**). A solution of DL camphor-10-sulfonyl chloride (**1**) (2 g, 0.008 mol) in acetonitrile (30 ml) was treated dropwise with phenylhydrazine (1.72 g, 0.016 mol) with stirring. After 3 hours, the precipitate was filtered off, and the solvent evaporated. The residue was recrystallized from ethanol to give the phenylhydrazide (1.05 g, 82%), m.p.

154–155°C. (Found: C, 59.6; H, 6.9; N, 9.0. $C_{16}H_{22}N_2O_3S$ requires C, 59.6; H, 6.8: N, 8.7%). NMR($CDCl_3$) δ: 7.4–6.9 (m, 5H, ArH), 6.45* (s, 2H, NH—NH), 3.8–2.7 (q, 2H, CH_2SO_2), 2.5–1.25 (m, 7H, cyclohexyl H), 1.05 (s, 3H, 9—Me), 0.95 (s, 3H, 8—Me). MS (electron impact): No M^+ (322), 273, 198, 151 (camphor), 109, 106, 77, 67. Chemical ionization MS: 323 ($M^+ + 1$).

DL Camphor-10-N,N-dimethylhydrazide (**15**). DL camphor-10-sulfonyl chloride (**1**) (2.5 g, 0.01 mol) was similarly reacted with *N,N*-dimethylhydrazine (1, g, 0.02 mol) to give the *N,N*-dimethylhydrazide (1.7 g, 78%), m.p. 112–114°C after recrystallization from methanol. TLC showed 1 spot R_F 0.47. (Found: C, 52.3; H, 7.8; N, 10.2. $C_{12}H_{22}N_2O_3S$ requires C, 52.5; H, 8.0; N, 10.2%). IR ν max 3250 (NH), 1750 (C=O), 1370, 1150 (SO_2) cm^{-1}. MS: 274 (M^+), 215 (M—$NHNMe_2$), 193, 183, 151, 123, 109, 93, 81, 79, 67, 59. ^{13}C NMR ($CDCl_3$) δ: 216.2 (C—2), 59.4 (C—1), 49.0 (N—$(CH_3)_2$), 48.6 (C—4), 48.0 (C—10), 47.3 (C—7), 43.1 (C—3), 27.2 (C—6), 26.7 (C—5), 20.0 (C—8, 9).

DL Camphor-10-thiadiazine dioxide (3, *R=H*). Camphor-10-sulfonohydrazide (3 g, 0.012 mol) was kept molten (90°C) for 45 minutes. After cooling, the solid formed was recrystallized from ethanol to give the thiadiazine dioxide (2.7 g, 97%), m.p. 186–189°C. (lit. [4]188°C). IR ν max 3200(NH), 1370, 1140(SO_2) cm^{-1}. H NMR δ: 10.2*(s, 1H, NH), 3.5–3.0 (q, 2H, CH_2SO_2), 2.6–1.0 (m, 7H, cyclohexyl H), 0.95 (s, 3H, 9–Me), 0.80 (s, 3H, 8–Me). ^{13}C NMR δ: 165.4 (C–2), 56.2 (C–1), 49.4 (C–7), 48.4 (C–10), 44.7 (C–4), 36.4 (C–3), 31.4 (C–6), 27.2 (C–5), 20.1 (C–8), 18.2 (C–9). MS showed the molecular ion (M^+, 228).

Compound (4). The thiadiazine dioxide (2.3 g, 0.01 mol) was dissolved in acetone (15 ml) containing 5M sodium hydroxide (2 ml, 0.01 mol) and a solution of trichloromethylsulfenyl chloride (1.9 g; 0.01 mol) in ether (15 ml) added. The mixture was vigorously stirred for 2 hours to give the N-trichloromethylsulfenyl derivative (27%) from ethanol., m.p. 142–143°C. (Found: C, 57.4; H, 6.4; N, 12.3. $C_{11}H_{15}Cl_3N_2O_2S_2$ requires C, 57.3; H, 6.5; N, 12.1%). IR ν max 1345, 1130 (SO_2), 725 (C–Cl) cm^{-1}.

DL Camphor-10-thiazine dioxide (**11**). Ammonium hydroxide (10 ml of 33%) was added to a stirred solution of camphor-10-sulfonyl chloride (2 g) in methanol (20 ml). The solution was left for 1 hour to give the thiazine dioxide as needles (1.4 g, 82%), m.p. 212–213°C. IR ν max 1375, 1130 (SO_2) cm^{-1}. (Found: C, 55.9; H, 7.0; N, 6.5. $C_{10}H_{15}NO_2S$ requires C, 56.3; H, 7.0; N, 6.6%). Electron impact MS no M^+(213), but chemical ionization MS showed the ($M^+ + 1$) ion at 214.

DL Camphor-10-sulfonamide (**12**). Gaseous ammonia was passed into a stirred solution of camphor-10-sulfonyl chloride (5 g) in chloroform (50 ml) for 2 hours. The precipitate was filtered off and the solvent evaporated *in vacuo*. The residue was crystallized from aqueous ethanol to give the amide (4 g, 87%), m.p. 128–130°C. (lit[12] m.p. 130°–132°C). (Found: C, 52.0; H, 7.6; N, 6.0. $C_{10}H_{17}NO_3S$ requires C, 51.9; H, 7.4; N, 6.1%). IR ν max 3320, 3220, 3240, 3140 (NH), 1750 (C=O), 1340, 1150 (SO_2) cm^{-1}. MS: no M^+(250), 170 (M—SO_2NH_2), 151 (camphor), 123, 108, 93, 81, 77, 67, 55.

DL Camphor-10-sulfonacetamide (**13**). The sulfonamide (2.3 g, 0.01 mol) was refluxed with acetyl chloride (2.3 g, 0.03 mol) in glacial acetic acid (20 ml) for 2 hours. The excess solvent was distilled off, and the residue recrystallized from ethanol to afford the acetamide (1.2 g, 51%), m.p. 77–78°C. (Found: C, 53.0; H, 7.2; N, 5.1. $C_{12}H_{19}NO_4S$ requires C, 52.7; H, 7.0; N, 5.1%). IR ν max 3300 (NH), 1750 (C=O), 1370, 1150 (SO_2) cm^{-1}. MS: no M^+(273), 258 (M^+–Me), 215 (M—$NHCOCH_3$), 151 (camphor), 123, 109, 93, 81, 67, 55.

DL Camphor-10-sulfonylmorpholidate (**19**). Morpholine (28.1 g, 0.32 mol) was added dropwise to a stirred suspension of camphor-10-sulfonyl chlroide (**1**) (32.4 g, 0.13 mol) in ethanol (125 ml) at 0°C. The mixture was refluxed for 45 minutes and left 1 week at room temperature. The precipitate was filtered off, washed with water and recrystallized from ethanol to give the morpholidate (12.5 g, 32%), m.p. 141–142°C (lit[12] m.p. 140°C). (Found: C, 55.6; H, 7.8; N, 4.3. $C_{14}H_{23}NO_4S$ requires C, 55.8; H, 7.7; N, 4.6%). NMR ($CDCl_3$) δ: 3.8–3.2 (m, 8H, morpholine H), 3.4–2.6 (q, 2H, CH_2SO_2), 2.5–1.4 (m, 7H, cyclohexyl H), 1.1 (s, 3H, 9–Me), 0.9 (s, 3H, 8–Me). IR ν max 1740 (C=O), 1340, 1150 (SO_2) cm^{-1}.

DL 10-(*N-Phenylsulfonamido*) *camphorhydrazone* (**18**). DL camphor-10-sulfonanilide (9.6 g, 0.03 mol) was refluxed with hydrazine hydrate (10.7 g, 0.2 mol) in ethanol (200 ml) containing concentrated sulfuric acid (2 drops) for 24 hours. The ethanol was removed under reduced pressure

and the residue washed with ethanol and ether to give (**18**) (8.9 g, 89%), m.p. 156–159°C. TLC (EtoAc) 1 spot R_F 0.57. (Found: C, 59.9; H, 7.3; N, 13.1. $C_{16}H_{23}N_3O_2S$ requires C, 59.8; H, 7.2; N, 13.1%). IR ν max 3400, 3280 (NH), 1605 (ArC=C), 1370, 1150 (SO_2) cm^{-1}. MS: 321 (M^+), 290(M—N.NH_2), 229, 165, 148, 121, 107, 92, 79, 69, 55.

DL 10-(*N-Morpholinosulfonyl*) *camphorhydrazone* (**20**). A mixture of DL camphor-10-sulfonylmorpholidate (7 g, 0.023 mol), hydrazine hydrate (3.73 g, 0.12 mol), butanol (100 ml) and concentrated sulfuric acid (2 drops) was refluxed for 24 hours. Butanol was evaporated under reduced pressure to give a gum which was triturated with ethanol and ether to give (**20**) (6.0 g, 85%) m.p. 115°C. TLC one spot R_F 0.32. (Found: C, 51.8; H, 8.2; N, 12.9. $C_{14}H_{25}N_3O_3S$. $\frac{1}{2}H_2O$ requires C, 51.8; H, 8.1; N, 13.0%) IR ν max 1740 (C=O), 1340, 1150 (SO_2) cm^{-1}. NMR ($CDCl_3$) δ: 9.50* (s, 2H, NH_2), 3.8–3.2 (m, 8H, morpholine H), 3.1–2.5 (q, 2H, CH_2SO_2), 2.3–1.4 (m, 7H, cyclohexyl H), 1.1 (s, 3H, 9-Me), 0.95 (s, 3H, 8-Me).

DL Camphor hydrazone. DL-camphor (35.6 g, 0.23 mol) was dissolved in *n*-butanol (80 ml), concentrated sulfuric acid (4 drops) was added, followed by hydrazine hydrate (58.6 g, 1.17 mol). The solution was refluxed for 17 hours and was evaporated under reduced pressure to give a solid residue. Recrystallization from ethanol gave the hydrazone (32.5 g, 85%) m.p. 45–46°C. TLC one spot R_F 0.40. (Found: C, 72.0; H, 10.9; N, 16.8. $C_{10}H_{18}N_2$ requires C, 72.3; H, 10.8; N, 16.9%), NMR ($CDCl_3$) δ: 4.6*(s, 2H, NH_2), 2.8–1.6 (m, 7H, cyclohexyl H), 1.1–0.85 (3s, 9H, Me).

General procedure for preparation of the hydrazones and azines. Acetone derivatives (**21**, **16**, **36**) were obtained by stirring the appropriate hydrazide (0.005 mol) in acetone (15 ml) at room temperature for 1 hour.

Cyclopentanone hydrazones (**22**, **27**, **37**) required refluxing cyclopentanone (0.005 mol) and the hydrazide (0.005 mol) in methanol (15 ml) for 1 hour. For the aromatic derivatives (**5–9**, **23–25**, **28–35**), the hydrazide (0.005 mol) and the aromatic aldehyde (0.005 mol) were refluxed in dry THF for 15 minutes.

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