6-Oxocamphene from M-I—M-I (9 mg) was dissolved in acetone (1 ml). Anhydrous chromic acid (1.33 g) was added to the dilute sulfuric acid (1.15 g in 2 ml of water) and well stirred. This oxidant (0.1 ml) was added by drops to the acetone solution at 0°, and the reaction mixture was shaken for 20 min. After 13 hr, R_f 0.41 of M-I changed to 0.58. The reaction mixture was neutralized with 5% NaOH, extracted with methylene chloride (1 ml), and dried over magnesium sulfate. Evaporation of this solvent gave 6-oxocamphene (2.4 mg); mass spectrum: *m/e* (%) 150 (M^+, 54), 135 (24), 107 (base), 106 (78), 93 (40), 91 (60), 79 (34), and 77 (21); NMR: δ ($CDCl_3$) 5.07 and 4.82 (each 1H, s), 3.09 (1H), and 1.21 and 1.11 (each 3H, s).

Camphene-2,10-glycol 10-Acetate from M-V—Acetylation of M-V (100 mg) with acetic anhydride and pyridine gave its monoacetate (84.7 mg); mass spectrum: *m/e* (%) 214 (M^+, 4), 194 (13), 171 (82), 152 (78), 137 (53), 109 (base), and 43 (77); IR: ν ($CHCl_3$) 3550 and 1730 cm^{-1}; NMR: δ ($CDCl_3$) 4.20 (2H, s), 2.08 (3H, s), and 1.03 and 0.93 (each 3H, s); NMR: δ (dimethyl sulfoxide-d_6) 4.03 (2H, s), 2.03 (3H, s), 0.93 and 0.88 (each 3H, s), and 3.27 (1H, s, exchanged with deuterium oxide). The anhydrous ethereal solution (10 ml) of lithium aluminum hydride (38.8 mg) was added to the ethereal solution (20 ml) of the monoacetate (80 mg) under a nitrogen atmosphere and stirred at room temperature for 4 hr. Decomposition of the excess lithium aluminum hydride with ethyl acetate, filtration through a short column packed with magnesium sulfate, and evaporation of the solvent recovered camphene-2,10-glycols.

Camphenylon (VII) from M-V—The ethanol solution (5 ml) of M-V (100 mg) was added to the sodium periodate (130 mg)–1 *N* sulfuric acid solution (6 ml) at 40° and stirred for 13 hr until it became transparent (9). The reaction mixture was neutralized with 5% $NaHCO_3$, extracted with ether, and dried over magnesium sulfate. Evaporation of the solvent gave camphenylon (VII) (23.0 mg); mass spectrum: *m/e* (%) 138 (M^+, 28), 95 (10), 81 (5), 72 (14), 69 (base), 67 (67), and 41 (31); UV: λ_{max} (ethanol) 287 (ε 24) and 240 (21) nm; $[\alpha]_D$ −8.3° (c 2.4, $CHCl_3$).

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New Compounds: Arylsulfonylhydrazones Derived from Various Heterocycles

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Received November 20, 1978, from the **Department of Medicinal Chemistry, School of Pharmacy, and the* ‡*Department of Microbiology, Southwestern Oklahoma State University, Weatherford, OK 73096.* Accepted for publication January 24, 1979.

Abstract □ Ten arylsulfonylhydrazones were prepared from various heterocycles. The antimicrobial activity of these compounds was investigated, as was the cytotoxic activity of one of them.

Keyphrases □ Arylsulfonylhydrazones—derived from various heterocycles, antimicrobial and cytotoxic activity □ Hydrazine—derivatives, various heterocycles, antimicrobial and cytotoxic activity □ Antineoplastic agents, potential—arylsulfonylhydrazones, derived from various heterocycles, antimicrobial and cytotoxic activity

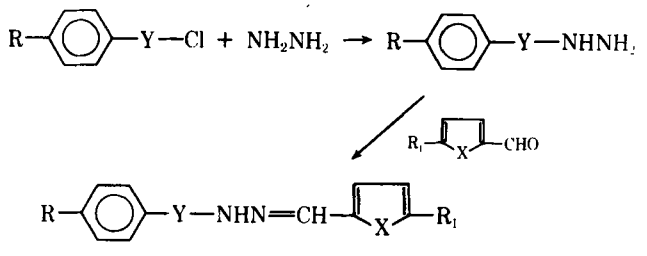
Arylsulfonylhydrazones of 2-formylpyridine and its oxide have been investigated as cytotoxic agents (1). Since studies involving the preparation and biological properties of arylsulfonylhydrazones derived from aromatic heterocycles other than pyridine and quinoline are not numerous, the synthesis and antibacterial screening of the compounds listed in Table I were attempted.

DISCUSSION

Chemistry—The compounds listed in Table I were synthesized by standard procedures, consisting of reaction between hydrazine and *p*-toluenesulfonyl chloride or α-toluenesulfonyl chloride followed by condensation with the appropriate heterocyclic 2-carboxaldehyde (Scheme I). For IV and IX, the requisite 5-nitrofurfural was obtained by the acid hydrolysis of 5-nitrofurfurylidene diacetate according to a literature method (2). Compounds IV, VIII, and IX are not new compounds and were reported previously (3–5).

The hydrazone linkage in the synthesized compounds allows geometric isomers to be formed. Attempts to detect *E*- and *Z*-isomers by TLC in several solvent systems were successful only with III and VII. Compounds III and VII demonstrated the presence of a trace amount of a second compound. However, only in the case of III were the two compounds nonoverlapping and amenable to dry column chromatography.

The IR and NMR spectra of III*a* and III*b* were practically superimposable and offered no aid in configurational assignments. Compound III*a* showed a bathochromic shift in the UV spectrum of only 3 nm (285–288) in going from a polar to a nonpolar solvent (ethanol to benzene), whereas III*b* showed a bathochromic shift of 10 nm (272–282). These data suggest the *Z*-configuration for III*b*, the trace component and more mobile compound on TLC (silica gel, chloroform), and the *E*-configu-

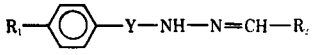


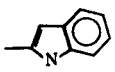
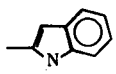
R = H, CH_3; Y = SO_2, CH_2SO_2;
X = O, N, S; R_1 = H, NO_2

Scheme I

0022-3549/79/0700-0930$01.00/0

Table I—Arylsulfonylhydrazones



Compound[a]	R_1	Y	R_2	Formula	Melting Point	Analysis, %		
							Calc.	Found
I	H	$-CH_2SO_2-$		$C_{12}H_{13}N_3O_2S$	169–173°	C	54.74	54.77
						H	4.98	5.04
						N	15.96	16.00
II	H	$-CH_2SO_2-$		$C_{12}H_{12}N_2O_2S_2$	144–146°	C	51.41	51.50
						H	4.31	4.30
						N	9.99	10.03
IIIa and IIIb	H	$-CH_2SO_2-$		$C_{12}H_{12}N_2O_3S$	108–109°	C	54.53	54.46
					110–112°	H	4.58	4.61
						N	10.59	10.43
IV	H	$-CH_2SO_2-$		$C_{12}H_{11}N_3O_5S$	180–182°	C	46.60	46.48
						H	3.59	3.48
						N	13.59	13.58
V	H	$-CH_2SO_2-$		$C_{16}H_{15}N_3O_2S$	188–190°	C	61.33	61.23
						H	4.82	4.96
						N	13.41	13.43
VI	CH_3	$-SO_2-$		$C_{12}H_{13}N_3O_2S$	175–180°	C	54.74	54.80
						H	4.98	5.01
						N	15.96	15.94
VII	CH_3	$-SO_2-$		$C_{12}H_{12}N_2O_3S$	110–112°	C	54.53	54.53
						H	4.58	4.66
						N	10.60	10.52
VIII	CH_3	$-SO_2-$		$C_{12}H_{12}N_2O_2S_2$	140–141°	C	51.41	51.42
						H	4.31	4.30
						N	9.99	9.96
IX	CH_3	$-SO_2-$		$C_{12}H_{11}N_3O_5S$	149–150°	C	46.60	46.71
						H	3.59	3.62
						N	13.59	13.61
X	CH_3	$-SO_2-$		$C_{16}H_{15}N_3O_2S$	174–176°	C	61.33	61.20
						H	4.82	4.92
						N	13.41	13.39

[a] All compounds were recrystallized from alcohol, except IIIa and IIIb which were recrystallized from ether.

ration for IIIa in analogy to previously prepared thiosemicarbazones (6).

Biological—Compounds I–X were screened for antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* and were inactive except for the weak inhibitory activity by IV. Because VII is the pyrrole analog of the active arylsulfonylhydrazone derived from 2-formylpyridine (1), it was chosen for antineoplastic screening, but it was devoid of activity.

EXPERIMENTAL[1]

General Synthetic Procedure—The heterocyclic 2-carboxaldehyde, 0.01 mole, was dissolved in 20 ml of methanol and maintained at ice bath temperatures. To this well-stirred solution was added dropwise the sulfonylhydrazide (0.01 mole) in 20 ml of methanol. After addition, the mixture was stirred for an additional 1 hr and placed in the refrigerator overnight. Then the solvent was removed under vacuum to yield semicrystalline solids. The solids were recrystallized from solvents (Table I) and were easily characterized by their NMR and IR spectra.

Biological Screening—The standard filter paper disk method on an agar culture medium was used to screen for antimicrobial activity against *S. aureus* and *E. coli*[2]. The disk was saturated with a methanol solution of the sulfonylhydrazone, and solutions as concentrated as 100 mg/ml were used before inactivity was pronounced.

Compound VII was screened against P-388 leukemia in CDF-1 mice. The compound was administered intraperitoneally as a suspension in polysorbate 80 and 5% ethanol. Doses as high as 120 mg/kg failed to show increased survival time relative to controls.

[1] Melting points were taken with a Thomas-Hoover Uni-Melt apparatus and are uncorrected. IR spectra were determined with a Beckman AccuLab spectrophotometer. NMR spectra were obtained with a Varian model 360-A spectrometer relative to an internal standard of tetramethylsilane with deuterochloroform or deuterated dimethyl sulfoxide as the solvent. UV spectra were determined with a Beckman model 25 spectrophotometer. TLC was performed on silica gel (Eastman chromagram) and visualized with either iodine vapors or UV light. Dry column chromatography was performed on silica gel Woelm (ICN Pharmaceuticals) with chloroform as the solvent. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

[2] The bacterial cells employed in the screening test were stock cultues originally derived from Midwest Culture Service (Terre Haute, Ind.) and currently designated as *Staphylococcus aureus* (SW43) and *Escherichia coli* (SW17).

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