

SYNTHESIS AND REACTIONS OF SOME DIPHENYL SULFIDES

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Received May 27, 1991

Accepted March 1, 1992

In view of the wide spectrum of activity associated with many pyrazoline derivatives¹⁻³, substituted thiazoles⁴, oxazoles⁵ and diaryl sulfides^{6,7}, we synthesized some new diaryl sulfides carrying the above heterocyclic systems.

EXPERIMENTAL

Melting points are uncorrected. Elemental analyses were performed on Perkin-Elmer 240 elemental analyzer. IR spectra were recorded in KBr pellets. ¹H NMR spectra were recorded on Varian EM-390 spectrometer in suitable deuterated using TMS as an internal standard.

4'-Methyl-2-nitro-4-acetyldiphenyl Sulfide (I)

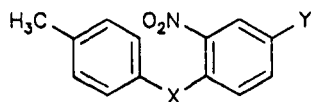
A solution of 8.16 g (0.03 mol) of 3-nitro-4-chloroacetophenone in 40 ml of hot ethanol was added to a mixture of 3.72 g (0.03 mol) of *p*-thiocresol, 3.9 g sodium carbonate and 12 ml H₂O and the resulting mixture was heated on a water bath for 4 h. The precipitated solid was filtered off, washed with water and recrystallized from ethanol, yield 71%, m.p. 110 – 112 °C. For C₁₅H₁₃NO₃S (287.4) calculated: 62.67% C, 4.57% H, 4.87% N, 11.16% S; found: 62.43% C, 4.23% H, 4.63% N, 11.23% S. IR spectrum: 1 680 (C=O); 1 325 (NO₂). ¹H NMR (CDCl₃): 2.5 s, 3 H (CH₃); 2.6 s, 3 H (COCH₃); 6.8 – 8.0 m, 7 H (Ar-H).

3-Nitro-4-(*p*-tolyl)thioacetophenone Phenylhydrazone (II)

A mixture of 0.86 g (0.003 mol) 4'-methyl-2-nitro-4-acetyldiphenyl sulfide (I), (0.003 mol) phenylhydrazine and a drop of acetic in ethanol (20 ml) was heated under reflux for 30 min. On cooling, the solid product obtained was filtered off and recrystallized from benzene. Yield 81%, m.p. 173 – 175 °C. For C₂₁H₁₉N₃O₂S (377.5) calculated: 66.83% C, 5.08% H, 11.14% N, 8.50% S; found: 66.73% C, 4.90% H, 11.02% N, 9.32% S. IR spectrum 3 330 (NH); 1 330 (NO₂).

4'-Methyl-2-nitro-4-(1"-phenyl-5"-formylpyrazole-3"-yl)diphenyl Sulfide (III)

To the Vilsmeier reagent prepared from DMF (10 ml) and POCl₃ (1.1 ml, 0.012 mol), 1.50 g (0.004 mol) of hydrazone II was added and the reaction mixture stirred at 60 – 65 °C for 2 h, then poured into ice-cold water. The product which separated on neutralization with NaHCO₃ was obtained in 76% yield and recrystallized from ethanol-benzene as a bright yellow solid, m.p. 182 – 184 °C. For C₂₃H₁₈N₃O₃S (416.5) calculated: 66.30% C, 4.36% H, 10.09% N, 7.70% S; found: 66.13% C, 4.11% H, 10.23% N, 7.35% S. IR spectrum: 1 685 (CHO); 1 355 (NO₂). ¹H NMR (CDCl₃): 2.4 s, 3 H (CH₃); 6.8 – 8.75 m, 13 H (Ar-H and CH pyrazole ring); 9.9 s, 1 H (CHO).



	X	Y	R		X	Y	R
<i>I</i>	S	COCH ₃		<i>Xa</i>	S		CH ₃
<i>II</i>	S	C=N-NHC ₆ H ₅ CH ₃		<i>Xb</i>			NHC ₆ H ₅
<i>III</i>	S			<i>Xc</i>			NH ₂
<i>IV</i>	S			<i>XI</i>	SO ₂		
<i>V</i>	SO ₂			<i>XII</i>	SO ₂	COCH ₂ Br	
<i>VIa</i>	S	COCH=CH-	H	<i>XIII</i>	S	COCH ₂ -N-	Br ⁽⁻⁾
<i>VIIb</i>			OCH ₃	<i>XIV</i>	S	COCH ₂ NH ₂ ·HCl	
<i>VIIc</i>			NO ₂	<i>XV</i>	S	COCH ₂ NH-CO-	
<i>VIIa</i>	S		H	<i>XVI</i>	S		
<i>VIIIb</i>			OCH ₃				
<i>VIIIc</i>			NO ₂				
<i>VIIIa</i>	SO ₂	COCH=CH-	H				
<i>VIIIb</i>			OCH ₃				
<i>IX</i>	S	COCH ₂ Br					

4'-Methyl-2-nitro-4-(indol-3"-yl)diphenyl Sulfide (IV)

A mixture of 0.69 (0.0013 mol) of hydrazone *II* and polyphosphoric acid (3 ml) was heated on a water bath for 15 min. On cooling and dilution with water, the precipitate formed was filtered off and recrystallized from benzene as brownish crystals in 54% yield, m.p. 243 – 245 °C. For $C_{21}H_{16}N_2O_2S$ (360.4) calculated: 69.95% C, 4.48% H, 7.77% N, 8.89% S; found: 69.83% C, 4.53% H, 7.53% N, 8.80% S. IR spectrum: 3 380 (NH indole ring); 1 340 (NO_2).

4'-Methyl-2-nitro-4-cinnamoyldiphenyl Sulfide Derivatives (VIa – VIc)

To a mixture of *I* (0.003 mol) and the aromatic aldehyde (0.004 mol) in ethanol (20 ml) was added with stirring 10% NaOH (1 ml). The mixture was further stirred for 3 h at room temperature. The solid product obtained was filtered off, washed with ethanol and recrystallized from the proper solvent. Physical and spectral data are summarized in Table I.

4'-Methyl-2-nitro-4-(1"-phenyl-5"-arylpirazoline-3"-yl)diphenyl Sulfide Derivatives (VIIa – VIIc)

A mixture of *VIa – VIc* (0.003 mol), phenylhydrazine (0.004 mol) in absolute ethanol (20 ml) and a few drops of piperidine were heated under reflux for 4 h. The products separated on cooling were filtered off and recrystallized from the suitable solvent. Details are summarized in Table I.

4'-Methyl-2-nitro-4-bromoacetyldiphenyl Sulfide (IX)

To a solution of *I* (0.025 mol) in glacial acetic acid (50 ml) was added dropwise with stirring at room temperature 1.25 ml (0.025 mol) of bromine in glacial acetic acid (10 ml) during 2 h. The precipitate formed was filtered off, washed with water and recrystallized from ethanol in 76% yield, m.p. 84 – 86 °C. For $C_{15}H_{12}BrNO_3S$ (366.5) calculated: 49.15% C, 3.30% H, 21.84% Br, 3.82% N, 8.75% S; found: 49.03% C, 3.03% H, 21.76% Br, 3.77% N, 8.53% S. IR spectrum: 1 685 (C=O); 1 340 (NO_2).

4'-Methyl-2-nitro-4-(2"-substituted thiazol-4"-yl)diphenyl Sulfide Derivatives (Xa – Xc)

A mixture of *IX* (0.003 mol), thioureas or thioacetamide (0.003 mol) in ethanol (20 ml) was heated under reflux for 7 h. The products obtained on cooling were filtered off, washed with sodium bicarbonate and recrystallized from the proper solvent. Physical and spectral data listed in Table I.

Reaction of IX with Hexamethylenetetramine

A mixture of *IX* (0.003 mol) in chlorobenzene (15 ml) and hexamethylenetetramine (0.003 mol) was stirred at room temperature for 12 h, the product *XIII* was filtered off and recrystallized from chlorobenzene in 83% yield, m.p. 212 °C. For $C_{21}H_{24}BrN_5O_3S$ (506.4) calculated: 49.74% C, 4.78% H, 15.79% Br, 13.82% N, 6.32% S; found: 49.56% C, 4.53% H, 15.84% Br, 13.63% N, 6.11% S. IR spectrum: 1 675 (C=O); 1 330 (NO_2).

Hydrolysis of Compound XIII

Compound *XIII* (2 g) in a mixture of hydrochloric acid–ethanol (3 : 15 ml) was stirred at room temperature for 14 h. The product formed was filtered off and recrystallized from water to give *XIV* as pale yellow crystals in 35% yield, m.p. 240 °C (decomposed). For $C_{15}H_{15}ClN_2O_3S$ (338.8) calculated: 53.14% C, 4.47% H, 10.48% Cl, 8.27% N, 9.46% S; found: 52.97% C, 4.31% H, 10.68% Cl, 8.12% N, 9.13% S. IR spectrum: 3 200 – 3 300 (NH_2); 1 685 (C=O); 1 330 (NO_2).

TABLE I
Physical and spectral data of sulfides *Via* – *Vtc*, *VIIa* – *VIIc* and *Xa* – *Xc*

Com- pound	M. p., °C Yield, %	Formula (M. w.)	Calculated/Found			Spectral data	
			% C	% H	% N		% S
<i>Via</i>	193 – 195 ^{a,b} 60	C ₂₂ H ₁₇ N ₃ O ₅ S (375.4)	70.35 69.99	4.57 4.43	3.73 3.69	8.54 8.48	IR: 1 660 (C=O); 1 340 (NO ₂)
<i>Vib</i>	183 – 185 ^{a,b} 62	C ₂₃ H ₁₉ N ₃ O ₄ S (405.8)	68.10 68.30	4.73 4.68	3.45 3.39	7.91 7.83	IR: 1 655 (C=O); 1 340 (NO ₂) ¹ H NMR (CDCl ₃): 2.45 s, 3 H (CH ₃); 3.8 s, 3 H (OCH ₃); 6.85 – 8.70 m, 13 H (Ar-H and $\overset{\text{O}}{\text{C}}\text{-CH-CH}$)
<i>Vtc</i>	212 – 214 ^{a,b} 68	C ₂₂ H ₁₆ N ₂ O ₅ S (421.3)	62.69 62.53	3.83 3.78	6.65 6.61	7.61 7.58	IR: 1 665 (C=O); 1 340 (NO ₂)
<i>VIIa</i>	160 – 162 ^b 70	C ₂₈ H ₂₃ N ₃ O ₂ S (465.3)	72.21 72.43	4.99 4.87	9.03 9.21	6.88 6.77	IR: 1 600 (C=N); 1 340 (NO ₂)
<i>VIIb</i>	110 – 112 ^a 69	C ₂₉ H ₂₅ N ₃ O ₂ S (495.3)	70.26 70.41	5.09 5.21	8.18 8.43	6.39 6.43	IR: 1 610 (C=N); 1 340 (NO ₂)
<i>VIIc</i>	136 – 138 ^a 72	C ₂₈ H ₂₂ N ₄ O ₄ S (510.3)	68.84 68.73	4.35 4.21	10.97 10.88	6.28 6.21	IR: 1 615 (C=N); 1 340 (NO ₂)
<i>Xa</i>	166 – 168 ^{a,b} 67	C ₁₇ H ₁₃ N ₃ O ₂ S ₂ (355.3)	57.42 57.54	3.69 3.57	11.82 11.67	18.04 18.21	IR: 3 340 (NHCH ₃); 1 615 (C=N) ¹ H NMR (CDCl ₃): 2.4 s, 3 H (CH ₃); 2.7 s, 3 H (CH ₃ thiazole ring); 6.8 – 8.7 m, 8 H (Ar-H and CH thiazole ring)
<i>Xb</i>	208 – 210 ^b 63	C ₂₂ H ₁₇ N ₃ O ₂ S ₂ (419.3)	62.29 62.43	4.09 4.21	10.02 10.23	15.29 15.31	IR: 3 350 (NHPh); 1 630 (C=N); 1 320 (NO ₂)
<i>Xc</i>	248 – 250 ^c 69	C ₁₆ H ₁₃ N ₃ O ₂ S ₂ (393.3)	55.93 55.87	3.82 3.71	12.24 12.43	18.67 18.83	IR: 3 350, 3 110 (NH ₂); 1 630 (C=N) ¹ H NMR (CF ₃ COOH): 2.45 s, 3 H (CH ₃); 6.9 – 8.7 m, 8 H (Ar-H and CH thiazole ring)

Crystallized from: ^a benzene; ^b ethanol; ^c dioxane.

TABLE II
Physical and spectral data of sulfones V, VIIIa, VIIIb, XI and XII

Com- pound	M. p., °C Yield, %	Formula (M. w.)	Calculated/Found				Spectral data
			% C	% H	% N	% S	
V	260 – 262 ^a 36	C ₂₁ H ₁₆ N ₂ O ₄ S (392.2)	64.30 63.98	4.11 4.22	7.17 7.21	8.17 8.24	IR: 3 385 (NH indole ring); 1 320, 1 150 (SO ₂); 1 330 (NO ₂)
VIIIa	213 – 215 ^b 50	C ₂₂ H ₁₇ NO ₃ S (407.2)	64.83 64.77	4.21 4.33	3.43 3.39	7.87 7.81	IR: 1 660 (C=O); 1 330, 1 140 (SO ₂) ¹ H NMR ((CD ₃) ₂ SO): 2.4 s, 3 H (CH ₃); 7.3 – 8.7 m, 14 H (Ar-H and CH=CH)
VIIIb	210 – 212 ^c 52	C ₂₂ H ₁₆ N ₂ O ₇ S (452.2)	58.38 58.21	3.57 3.48	6.19 6.21	7.08 7.21	IR: 1 665 (C=O); 1 340, 1 345 (SO ₂)
XI	180 – 182 ^d 56	C ₁₇ H ₁₅ N ₂ O ₄ S (443.3)	59.94 59.88	4.41 4.33	8.19 8.23	9.33 9.11	IR: 3 345 (NHCH ₃); 1 620 (C=N); 1 360, 1 155 (SO ₂) ¹ H NMR ((CD ₃) ₂ SO): 2.4 s, 3 H (CH ₃); 2.6 s, 3 H (CH ₃ thiazole ring); 7.4 – 8.6 m, 8 H (Ar-H and thiazole ring)
XII	160 – 162 ^d 62	C ₁₃ H ₁₂ BrO ₅ S (430.2)	41.84 41.73	2.81 2.80	3.25 3.19	7.45 7.39	IR: 1 690 (C=O); 1 355, 1 360 (SO ₂) ¹ H NMR (CDCl ₃): 2.4 s, 3 H (CH ₃); 4.3 s, 2 H (COCH ₂ Br); 7.3 – 8.4 m, 7 H (Ar-H)

Crystallized from: ^a ethyl acetate; ^b acetic acid; ^c dioxane; ^d ethanol.

Reaction of Derivative *XIV* with Benzoyl Chloride

A mixture of 1.01 g (0.003 mol) of phenacylammonium chloride *XIV* and 0.003 mol of benzoyl chloride in pyridine (10 ml) was heated on a water bath for 1 h. The mixture was poured in water, the product formed was filtered off, washed with water and recrystallized from ethanol to give *XV* in 38% yield m.p. 182 – 184 °C. For $C_{22}H_{18}N_2O_4S$ (406.5) calculated: 64.98% C, 4.47% H, 6.89% N, 7.89% S; found: 64.73% C, 4.18% H, 6.75% N, 7.98% S. IR spectrum 3 290 (NH); 1 690 – 1 630 (2 C=O); 1 335 (NO₂).

4'-Methyl-2-nitro-4-(2"-phenyloxazol-5"-yl)diphenyl Sulfide (*XVI*)

Compound *XV* (1.21 g, 0.003 mol) in 10 ml of POCl₃ was heated under reflux for 10 h. The mixture after cooling was poured in cold water, the product formed was filtered off, washed with water and recrystallized from benzene to give 4'-methyl-2-nitro-4-(2"-phenyloxazol-5"-yl)diphenyl sulfide *XVI* in 43% yield, m.p. 204 °C. For $C_{22}H_{16}N_2O_3S$ (388.4) calculated: 68.00% C, 4.16% H, 7.21% N, 8.25% S; found: 68.21% C, 4.23% H, 7.40% N, 8.50% S. IR spectrum: 1 620 (C=N oxazole ring); 1 335 (NO₂).

Oxidation of Sulfides *IV*, *Via*, *Vib*, *IX* and *Xa* to their Corresponding Sulfones (*V*, *VIIIa*, *VIIIb*, *XII* and *XI*)

To the above sulfides (0.005 mol) in glacial acetic acid (20 ml) was added dropwise hydrogen peroxide (30%, 10 ml). The reaction mixture was kept at room temperature for 7 – 10 days. Crystalline products were recrystallized from the proper solvent. Results are summarized in Table II.

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