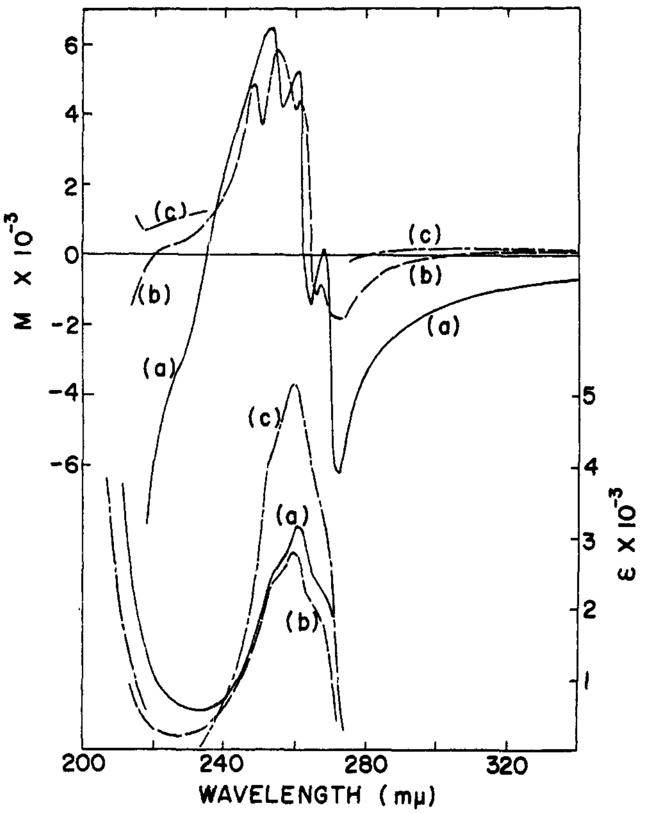

Figure 2.—Rotatory dispersion and absorption curves for nicotine–hydrogen chloride in water. Mole ratios of HCl/nicotine are (a) 0.0, (b) 1.0, (c) 5.0.

tributable to two conformers.[9] The magnitude of this Cotton effect decreased only when hydrogen chloride was added in excess. The steep descent of the dispersion curve of nicotine below 230 mμ may be partly attributed to a rotation associated with the excitation of the nonbonding electrons of pyrrolidine nitrogen to the unoccupied, antibonding σ^* orbital. This transition, in fact, is known to occur at about 195 mμ, and shows a hypochromic effect in acidic solution.[7] The above assignment may be supported by the fact that the magnitudes of both absorption and rotation in this location are decreased by the addition of hydrogen chloride.

Figure 2 shows the rotatory dispersion and the absorption curves of nicotine and its protonated species in water. In the presence of excess hydrogen chloride, the intensity of the band at 260 mμ is too large to measure the rotatory dispersion. By comparing Figure 1 with Figure 2, it would be concluded that the effects of protonation upon the rotatory dispersion of nicotine are similar both in 95% alcohol and in water.

Table I lists the $[M]_D$ values of nicotine in the presence of various amounts of hydrogen chloride. The $[M]_D$ value increases with the hydrogen chloride concentration until the mole ratio (HCl/nicotine) reaches 1.0, and decreases slightly upon a further addition of hydrogen chloride. This behavior is very similar to that of nicotine-Lewis acid system.[4] The initial increase is due to the decrease of the magnitudes of the negative circular dichroism bands at 268 and around 200 mμ. The little change of the $[M]_D$ values in the following stage can be interpreted as the result of the cancellation of two contrary effects, one of which is that mentioned just above and the other, the decrease of the magnitude of the positive circular dichroism band at 245 mμ. Accordingly, it may be concluded that the protonation on the pyridine nitrogen has a considerable effect on the optical rotation of nicotine, in spite of the nearly equal $[M]_D$ values of 1 and 2. The result obtained by the measurement at 589 mμ alone (Table I) could not lead to this conclusion.

TABLE I

$[M]_D$ VALUES OF NICOTINE IN THE PRESENCE OF HYDROGEN CHLORIDE

HCl–nicotine	$[M]_D$ in 95% alcohol	$[M]_D$ in water
0.0	−211	−113
0.5	−75	−44
1.0	+21	+36
2.0	+20	+28
5.0	+20	+27

Experimental Section

(*S*)-Nicotine was dried over potassium hydroxide pellets, and then distilled under nitrogen atmosphere, bp 127.2° (18 mm). The rotatory dispersion and circular dichroism curves were determined using a Japan Spectroscopic Co., ORD/UV-5 spectropolarimeter. The instrument employed for the optical rotation measurement at 589 mμ was an Applied Electric Laboratory automatic polarimeter. Absorption spectra were recorded on a Hitachi EPS-2 spectrophotometer. All measurements were made at about 15°.

(*S*)-**Nicotine.**—Rotary dispersion as shown in degrees in Figure 1 (c 2.53 × 10^{-3} mole/l., 95% alcohol) gives $[M]_{300}$ −1340, $[M]_{276}$ −5560 (trough), $[M]_{256}$ 6330 (peak), $[M]_{220}$ −8290. Rotary dispersion as shown in degrees in Figure 2 (c 2.51 × 10^{-3} mole/l., water) gives $[M]_{300}$ −1475, $[M]_{272}$ −6380 (trough), $[M]_{263}$ 6580 (peak), $[M]_{220}$ −5780.

(*S*)-**Nicotine Monohydrochloride** (1).—Rotary dispersion as shown in degrees in Figure 1 (c 2.53 × 10^{-3} mole/l., 95% alcohol) gives $[M]_{305}$ 0, $[M]_{277}$ −1980 (trough), $[M]_{256}$ 4850 (peak), $[M]_{220}$ −2760. Rotary dispersion as shown in degrees in Figure 2 (c 2.50 × 10^{-3} mole/l., water) gives $[M]_{310}$ 0, $[M]_{272}$ −1880 (trough), $[M]_{256}$ 5800 (peak), $[M]_{219}$ 0.

(*S*)-**Nicotine Dihydrochloride** (2).—Rotary dispersion as shown in degrees in Figure 1 (c 2.47 × 10^{-3} mole/l., 95% alcohol, purity 65%, see text) gives $[M]_{300}$ 0, $[M]_{276}$ −1580 (trough), $[M]_{256}$ 4450 (peak), $[M]_{222}$ 0. Rotary dispersion as shown in degrees in Figure 2 (c 2.50 × 10^{-3} mole/l., water) gives $[M]_{300}$ 150, $[M]_{281}$ 0, $[M]_{220}$ 800.

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[9] K. M. Wellman, P. H. A. Laur, W. S. Briggs, A. Moscowitz, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 66 (1965).

Hydrazinolysis of Some Chlorosulfonated Pentavalent Phosphorus Esters

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The preparation and characterization of tris(*p*-chlorosulfonylphenyl) phosphate (1) and bis(*p*-chlorosulfonylphenyl) methylphosphonate (2) has been described recently.[1] This account summarizes the results obtained when these novel phosphorus compounds bearing sulfonyl chloride functions (1 and 2) are treated with hydrazine. In addition, the chlorosulfonation of several dialkyl benzylphosphonates and the subsequent

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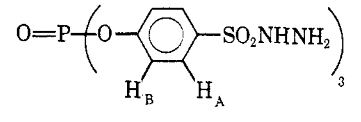
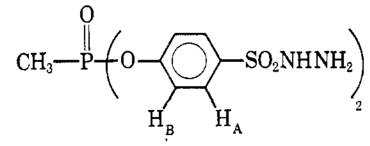
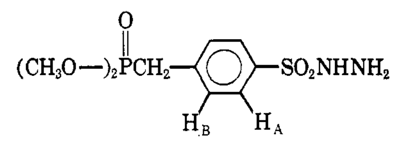
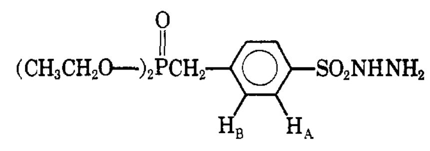
[1] J. E. Herweh, *J. Org. Chem.*, **31**, 2422 (1966).

TABLE I

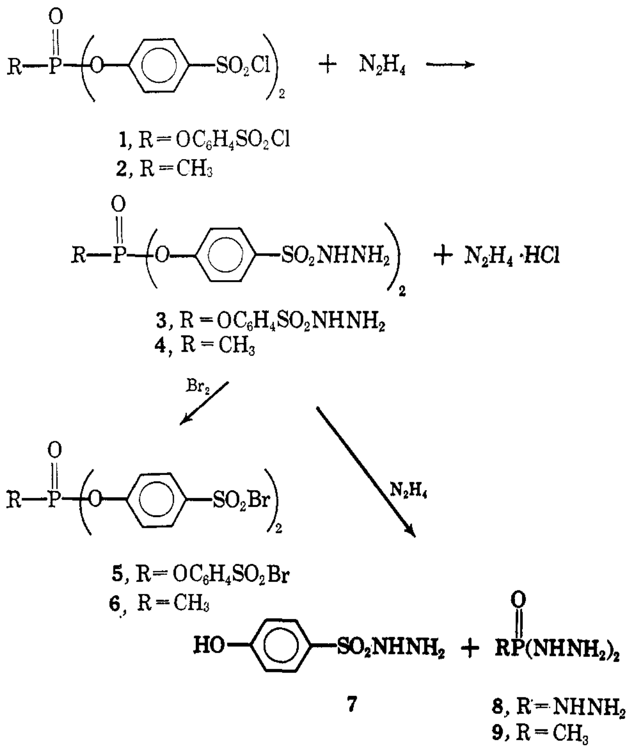
PMR SPECTRA OF THE HYDRAZINOLYSIS PRODUCTS

Compound[a]	Multiplicity	Chemical shift (τ), ppm[b]	J_{PH}, cps	Assignment
 **3**	Singlet (broad)	6.40		NH_2
	Double doublet	2.40	0.8[c]	H_B of Ar
	Doublet	2.03	c	H_A of Ar
	Broad band	1.50		NH α to SO_2
 **4**	Doublet	8.00	ca. 18	CH_3P
	Singlet (broad)	6.20		NH_2
	Double doublet	2.52	1.1[c]	H_B of Ar
	Doublet	2.10	c	H_A of Ar
	Broad band	1.58		NH α to SO_2
 **14a**	Doublet	6.58	22	$ArCH_2P$
	Doublet	6.35	10.5	OCH_3
	Singlet	6.32		NH_2
	Double doublet	2.47	2.2[d]	H_B of Ar
	Doublet	2.17	d	H_A of Ar
	Broad band	1.64		NH α to SO_2
 **14b**	Triplet	8.81	e	CH_3
	Doublet	6.63	21.3	$ArCH_2P$
	Singlet	6.30		NH_2
	Double quartet	5.98	8.0[f]	OCH_2
	Double doublet	2.47	2.2[d]	H_B of Ar
	Doublet	2.15	d	H_A of Ar
	Broad band	1.62		NH α to SO_2

[a] All spectra were determined in DMSO-d_6. [b] For each compound, chemical shifts are given as the centers of the observed multiplets. [c] J_{AB} = 8.7 cps. [d] J_{AB} = 8.2 cps. [e] J_{HH} = 7.5 cps. [f] J_{HH} = 7.0 cps.

aminolysis and hydrazinolysis of the chlorosulfonated reaction products are discussed.

Treatment of tris(*p*-chlorosulfonylphenyl) phosphate (**1**) with aqueous 85 or 95% hydrazine at 0–5° in tetrahydrofuran gave the expected tris(*p*-hydrazidosulfonylphenyl) phosphate (**3**) in *ca.* 60% yield. Relatively nonpolar solvents, such as benzene, were not suitable reaction media. The major reaction product was identified as **3** by elemental analysis and by infrared and pmr spectra (Table I). In addition, bromimetric analysis[2] was found to be effective in assessing the purity of **3**. By way of further characterization, **3** was converted to tris(*p*-bromosulfonylphenyl) phosphate (**5**), using a procedure reported for conventional sulfonylhydrazides.[3]



1, R = $OC_6H_4SO_2Cl$
2, R = CH_3

3, R = $OC_6H_4SO_2NHNH_2$
4, R = CH_3

5, R = $OC_6H_4SO_2Br$
6, R = CH_3

7

8, R = $NHNH_2$
9, R = CH_3

A secondary hydrazinolysis reaction also occurred, thereby reducing the yield of **3**. This reaction cleaves the aryloxy–phosphorus bonds and yields *p*-hydroxyphenylsulfonylhydrazide (**7**) and presumably phosphorotrihydrazidate (**8**). Efforts to eliminate this side reaction by the slow addition of hydrazine to **1** at low temperatures were unsuccessful. *p*-Hydroxyphenyl sulfonylhydrazide (**7**) was isolated in variable amounts along with the major product **3** and accounted for up to 16% of the starting sulfonyl chloride **1**. No attempts were made to isolate the water-soluble phosphorotrihydrazidate (**8**).[4]

Hydrazinolysis of the aryloxy–phosphorus ester linkage probably occurs after hydrazine has attacked the sulfonyl chloride group. The susceptibility of **3** to cleavage by hydrazine was demonstrated by allowing it to react with hydrazine at room temperature in tetrahydrofuran. After *ca.* 1 hr at room temperature and overnight refrigeration, **7** (46%) was isolated. The presence of the electron-withdrawing sulfonyl group on the phenyl ring enhances the lability of the aryloxy–

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(2) A. C. Poshkus, J. E. Herweh, and F. A. Magnotta, *J. Org. Chem.*, **28**, 2766 (1963).

(3) L. M. Litvinenko, V. A. Dadali, V. A. Savelova, and T. I. Krichevtsova, *Zh. Obshch. Khim.*, **34**, 3730 (1964).

(4) R. Klement and K. Knollmüller, *Chem. Ber.*, **93**, 834 (1960).

phosphorus bond toward hydrazinolysis. When triphenyl phosphate is treated with aqueous 85% hydrazine, under conditions similar to those used for the hydrazinolysis of **1**, no apparent reaction occurred; the phosphate and hydrazine (as its sulfate) were recovered in 91 and 93% yield, respectively. Similar results were obtained when the reaction was repeated in the presence of hydrazine hydrochloride.

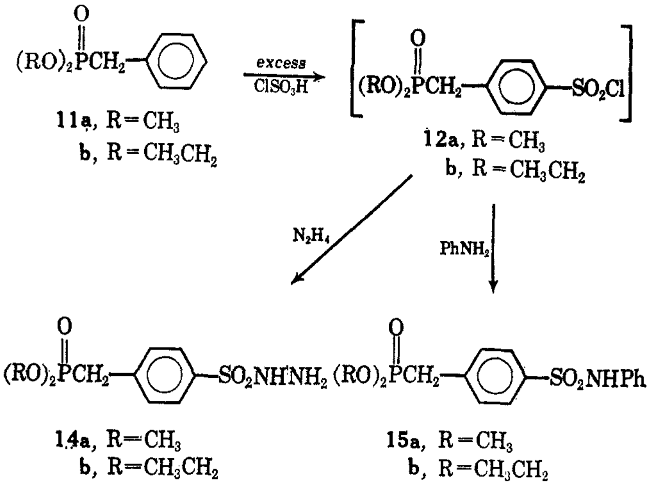
It was further found that p-chlorosulfonylphenyl phosphorodichloridate [**10**, p-$Cl_2P(O)OC_6H_4SO_2Cl$] undergoes essentially complete hydrazinolysis under mild conditions of time and temperature to give **7** as the primary isolable reaction product. Phenyl phosphorodichloridate is reported to yield the corresponding dihydrazidate on treatment with excess 95% hydrazine under mild conditions. Cleavage of the aryloxy–phosphorus bond was not observed.[5]

Hydrazinolysis of bis(p-chlorosulfonylphenyl) methylphosphonate (**2**) in acetonitrile using 95% hydrazine afforded the desired product **4** in 73% crude yield. Concomitant cleavage of the aryloxy–phosphorus bond by hydrazine also occurred and some p-hydroxyphenyl sulfonylhydrazide (**7**) was obtained. The use of aqueous 85% hydrazine in tetrahydrofuran gave unsatisfactory results, possibly owing to extensive hydrazinolysis of the aryloxy–phosphorus ester linkage. Other solvents (benzene, dimethylformamide, absolute ethyl alcohol) were also briefly examined with little success. The structure **4** assigned to the reaction product was confirmed by elemental and bromimetric analyses and infrared and pmr spectra (Table I). The bis(p-hydrazidosulfonylphenyl) methylphosphonate (**4**) was also converted to the corresponding sulfonyl bromide **6**.

As is true of **3**, bis(p-hydrazidosulfonylphenyl) methylphosphonate (**4**) undergoes hydrazinolysis on treatment with 95% hydrazine in tetrahydrofuran at room temperature. After 4 hr a 39% yield of p-hydroxyphenyl sulfonylhydrazide (**7**) was obtained. When the reaction was repeated, with aqueous 85% hydrazine the yield of **7** was 50%. Methyl phosphonodihydrazidate (**9**) was not isolated.

A notable feature of the pmr spectra of both **3** and **4** (Table I) is that a long-range coupling of phosphorus to H_B of the phenyl rings ($^4J_{PH}$ = 0.8 for **3** and 1.1 cps for **4**) is exhibited. This long-range interaction has also been observed in the corresponding sulfonyl chlorides **1** and **2**[1] and similar $^4J_{PH}$ have been observed in a number of other organophosphorus compounds.[6]

In addition to chlorosulfonation and subsequent hydrazinolysis of organophosphorus compounds possessing aryloxy groups, several dialkyl benzylphosphonates (**11**) were examined. The chlorosulfonation proceeded smoothly under mild conditions to give crude dialkyl p-chlorosulfonylbenzylphosphonates (**12**) as oils in high yield. Both chlorosulfonates underwent rapid thermolysis at 150 to 170°. The dimethyl analog **12a** gave methyl chloride (accounting for up to 80% of the available chlorine) and an acidic glassy residue, believed to be a mixture of anhydrides. Similarly, thermolysis of the diethyl derivative **12b** produced ethyl chloride and a nonvolatile acidic residual glass also thought to be a mixture of anhydrides. Ethylene was also formed. If the weight loss (on heating) is attributed solely to the formation of ethyl chloride and ethylene, 63% of the available ethyl groups can be accounted for.



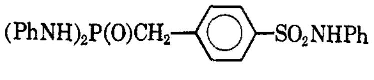
11a, R=CH_3
b, R=CH_3CH_2

12a, R=CH_3
b, R=CH_3CH_2

14a, R=CH_3
b, R=CH_3CH_2

15a, R=CH_3
b, R=CH_3CH_2

The residues from thermolysis of **12a** and **12b** were treated consecutively with thionyl chloride and aniline to yield N,N′-diphenyl-p-phenylsulfamylbenzylphosphonodiamidate (**13**) in 80 and 50% yield, respectively.



13

The facile decomposition of the dialkyl p-chlorosulfonylbenzylphosphonates (**12**) at 150–170° may be contrasted to the behavior of simple dialkyl alkylphosphonates.[7,8]

The structure of the crude chlorosulfonated dialkyl benzylphosphonates (**12**) was confirmed by their conversion to the corresponding dialkyl p-phenylsulfamylbenzylphosphonates (**15**) and dialkyl p-hydrazidosulfonylbenzylphosphonates (**14**). These products were identified by elemental analysis and by their infrared and pmr spectra (Table I and the Experimental Section). The identity of **14a** and **14b** was further substantiated by bromimetric analysis.

Of interest is the fact that the hydrazinolysis of chlorosulfonated dialkylbenzylphosphonates (**12**) produced **14** as the only isolable product, in contrast to results obtained with tris(p-chlorosulfonylphenyl) phosphate (**1**) and bis(p-chlorosulfonylphenyl) methylphosphonate (**2**) which underwent a secondary cleavage reaction to yield **7**.

As is true of **3** and **4** the pmr spectra of products **14** and **15** obtained from the hydrazinolysis and aminolysis of the chlorosulfonated dialkyl benzylphosphonates (**12**) exhibited long-range coupling of phosphorus with the H_B proton of the phenyl ring ($^4J_{PH}$ = 2.2 cps for **14** and 2.1 for **15**; Table I and Experimental Section).

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[5] L. F. Audrieth, R. Gher, and W. C. Smith, *J. Org. Chem.*, **20**, 1288 (1955).

[6] (a) M. Gordon, Ph.D. Thesis, University of Pittsburgh, 1965; (b) C. E. Griffin, R. B. Davison, and M. Gordon, *Tetrahedron*, **22**, 561 (1966).

[7] C. E. Higgins and W. H. Baldwin, *J. Org. Chem.*, **26**, 846 (1961).

[8] On heating diethyl benzylphosphonate (**11b**) at 230 ± 3° for 3.5 hr, ethylene was evolved and accounted for 1.4% of the available ethyl groups. Thermolysis at 250 ± 5° for 5 hr produced 36.1% of the calculated quantity of ethylene.

Experimental Section[9]

General.—The sulfonyl chlorides **1** and **2** were prepared as previously described.[1] Dimethyl benzylphosphonate (**11a**, Hooker Chemical Co.) was freshly distilled prior to use, while diethyl benzylphosphonate (**11b**) was synthesized according to a known procedure.[10] The 95% hydrazine (Eastman Organic Chemicals) was used as received; aqueous 85% hydrazine was obtained by dilution of 95% hydrazine with an appropriate amount of water.

Tris(*p*-hydrazidosulfonylphenyl) Phosphate (3).—Aqueous 85% hydrazine (41.3 g, 1.10 moles) was added dropwise in 2 hr to a stirred solution of the sulfonyl chloride **1** (113.6 g, 0.18 mole) in 830 ml of tetrahydrofuran maintained at 0 ± 3°. After the addition, the stirred turbid reaction mixture containing a white solid was allowed to warm to room temperature (45 min) and then filtered. The slightly gummy filter cake was washed with two 50-ml portions of tetrahydrofuran and the solid was dissolved in water (140 ml) to give a weakly basic solution. A white solid byproduct **7** precipitated on neutralization of the aqueous solution. The filtered and dried precipitate (1.9 g, 0.01 mole, mp 164–168° dec) was recrystallized two times from absolute alcohol to afford analytically pure *p*-hydroxyphenyl sulfonylhydrazide (**7**) melting at 178–179° dec (lit.[11] mp 165–166° dec); infrared absorption spectrum (Nujol) 3.0 (m), 3.36 (s), 3.44 (m, shoulder), 6.25 (m), 6.32 (m), 6.93 (m), 7.62 (m), 7.77 (m), 8.52 (s), 8.67 (s), 9.17 (m), 12.07 (m), 13.85 (m), and 14.1 (m) μ.

Anal. Calcd for $C_6H_8N_2O_3S$ (**7**): C, 38.29; H, 4.28; N, 14.89; S, 17.04; mequiv of Br/g, 42.6. Found: C, 38.15; H, 4.36; N, 14.96; S, 16.99; mequiv of Br/g, 41.9.

The combined main tetrahydrofuran filtrate and washings were washed with saturated sodium chloride and dried over magnesium sulfate. The dried tetrahydrofuran solution was filtered and diluted with pentane; 36.7 g of crude tris(*p*-hydrazidosulfonylphenyl) phosphate (**3**) precipitated (mp 110–115° dec). Additional **7** (7.4 g, 39 mmoles) was obtained on distilling (*in vacuo*) the tetrahydrofuran–pentane solution to dryness. A second crop of **3** (42.3 g, mp 100–105° dec) was obtained upon extracting the magnesium sulfate filter cake with dimethylformamide (two 75-ml portions) and subsequently diluting the combined extracts with water (total volume 950 ml). The combined crops of crude **3** (79 g) were triturated with hot absolute alcohol and filtered, and the cooled filter cake was washed with ether to afford 67.2 g (61.3%) of **3** melting at 154–156° dec.

Analytically pure **3** (mp 155–157° dec) was obtained by diluting its solution in dimethylformamide with water. Infrared absorptions (KBr) occurred at 3.0 (m), 6.74 (m), 7.54 (m), 7.67 (m), 7.75 (m), 8.37 (s), 8.6 (s), 8.67 (s), 9.19 (m), 10.3 (s, broad), 11.92 (m), and 14.7 (m, broad) μ.

Anal. Calcd for $C_{18}H_{21}N_6O_{10}PS_3$ (**3**): C, 35.52; H, 3.48; N, 13.81; P, 5.09; S, 15.81; mequiv Br/g, 19.7. Found: C, 35.68; H, 3.60; N, 13.86; P, 5.11; S, 16.21; mequiv of Br/g, 19.2.

Tris(*p*-bromosulfonylphenyl) Phosphate (5).—The sulfonylhydrazide **3** (6.09 g, 0.01 mole) was treated with bromine (10 g, 63 mmoles) according to a reported procedure[3] to yield 6.5 g of white solid **5** melting at 107–113°. Two recrystallizations from a benzene–hexane mixture provided analytically pure **5** melting at 120.5–123°; infrared absorption spectrum (KBr) 6.35 (m), 6.77 (s), 7.29 (s), 7.68 (m), 8.34 (s, broad), 8.5 (s), 8.62 (vs), 9.28 (m), 10.3 (s), 10.38 (s), 10.74 (m), and 11.95 (m) μ.

Anal. Calcd for $C_{18}H_{12}Br_3O_{10}PS_3$ (**5**): C, 28.63; H, 1.60; Br, 31.75; P, 4.10; S, 12.74. Found: C, 28.61; H, 1.57; Br, 31.63; P, 4.20; S, 12.90.

Bis(*p*-hydrazidosulfonylphenyl) Methylphosphonate (4).—Hydrazine (95%, 82.2 g, 2.44 moles) was added dropwise in 4 hr to a stirred solution of the sulfonyl chloride **2** (246.5 g, 0.55 mole) in acetonitrile (1000 ml) maintained at −5 ± 2°. Upon completing the addition, the reaction mixture, consisting of a granular white solid and a clear yellow solvent layer, was stirred at room temperature for 2 hr. The reaction mixture was filtered at 0° and the filter cake was washed with fresh acetonitrile. The dried filter cake (219.5 g) was treated consecutively with portions of cold water[12] (total volume 350 ml), ethyl alcohol, and ether to yield 91.8 g of crude **4**, mp 120–124° dec. Neutralization and cooling of the combined weakly basic water washings precipitated *p*-hydroxyphenylsulfonylhydrazide (**7**, 2.1 g, 11 mmoles), identified by melting point and mixture melting point. Additional **7** (9.7 g, 52 mmoles) was obtained on concentrating (*in vacuo*) the combined alcohol–ether washings.

The combined main acetonitrile filtrate and washings were extracted with 50-ml portions of saturated aqueous sodium chloride and dried over magnesium sulfate and the filtered solution was concentrated to dryness. The slightly gummy, white, solid residue was washed consecutively with cold water, absolute alcohol, and finally ether. The dried crude sulfonylhydrazide **4** (80.5 g), mp 127–133° dec, together with crude **4** (91.8 g) isolated earlier, was dissolved in warm (40°) dimethylformamide (180 ml). Addition of the filtered dimethylformamide solution to cold water precipitated a white solid. The filtered solid was washed with cold alcohol and then with ether to give 138.3 g (57.6%) of pure **4**, mp 133.5–135° dec. Infrared absorption (KBr) occurred at 3.0 (m), 3.03 (m), 3.08 (s), 6.32 (m), 6.75 (m), 7.1 (m), 7.42 (s), 7.72 (s), 7.87 (m), 8.13 (m), 8.28 (s), 8.59 (s), 8.67 (s), 8.83 (m), 9.15 (m), 10.57 (s), 10.85 (s), 11.75 (m), 11.89 (s), 13.4 (m), and 14.6 (m, broad) μ.

Anal. Calcd for $C_{13}H_{17}N_4O_7PS_2$ (**4**): C, 35.78; H, 3.93; N, 12.84; P 7.10; S, 14.70; mequiv of Br/g, 18.4. Found: C, 35.84; H, 4.27; N, 12.91; P, 7.12; S, 14.84; mequiv of Br/g, 19.0.

Bis(*p*-bromosulfonylphenyl) Methylphosphonate (6).—The sulfonylhydrazide **4** (4.37 g, 0.01 mole) was treated with bromine (6.7 g, 42 mmoles) to yield 5.0 g of a pale yellow solid, mp 104–110°. Three recrystallizations from a benzene–hexane mixture sharpened the melting point (107–110.5°). The infrared spectrum (KBr) exhibited absorption at 3.24 (w), 6.63 (s), 6.75 (s), 7.14 (m), 7.33 (s), 7.61 (s), 7.73 (s), 7.84 (s), 8.12 (s, broad), 8.29 (s), 8.51 (s), 8.62 (s), 9.27 (s), 10.5 (m), 10.85 (s, broad), 11.87 (s), 11.97 (s), and 13.5 (m) μ.

Anal. Calcd for $C_{13}H_{11}Br_2O_7PS_2$ (**6**): C, 29.23; H, 2.08; Br, 29.92; P, 5.80; S, 12.01. Found: C, 29.28; H, 1.99; Br, 29.84; P, 5.60; S, 12.09.

Hydrazinolysis of *p*-Chlorosulfonylphenyl Phosphorodichloridate (10).—A solution of **10**[13] (3.09 g, 0.01 mole) in benzene (30 ml) was added dropwise in 30 min to a stirred suspension of 95% hydrazine (2.1 g, 62 mmoles) in 30 ml of dry benzene at 5 ± 2°. After 2.5 hr at room temperature, the reaction mixture was filtered and the gummy white filter cake was washed with fresh solvent and dried.

The benzene-insoluble solid dissolved in water to give a weakly basic solution. The cooled, neutralized, aqueous solution precipitated 1.5 g (8 mmoles) of *p*-hydroxyphenyl sulfonylhydrazide (**7**), mp 168–172° dec. An admixture with an authentic sample failed to depress the melting point.

Chlorosulfonation of Dialkyl Benzylphosphonates (11).—Dimethyl benzylphosphonate (**11a**, 60 g, 0.3 mole) was added dropwise in 70 min to stirred chlorosulfonic acid (349.5 g, 3.0 moles) maintained at 15 ± 5°. After 19 hr at room temperature, the clear, pale yellow reaction mixture was carefully added to crushed ice. The resulting hydrolysis mixture was extracted with chloroform and the combined (125 ml) chloroform extracts were washed consecutively with 25-ml portions of aqueous 10% sodium bicarbonate (twice), saturated sodium chloride (three times), and finally dried over magnesium sulfate. Removal of the chloroform by distillation at about 20 mm (pot temperature <45°) left a clear, slightly amber oil that upon further evacuation at *ca.* 1 mm and 25° weighed 72.3 g.

A portion of the crude chlorosulfonated phosphonate was submitted to distillation *in vacuo* (*ca.* 0.1 mm and still temperatures up to 230°) but failed to yield any readily condensable distillate. A clear, amber, glassy still residue remained and gave a strongly acidic solution with water.

Another portion of the reaction product was precipitated from benzene solution by addition to hexane. The solvent layer was decanted and the precipitated oil **12a** dried *in vacuo*. Infra-

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[9] Melting and boiling points are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Infrared absorption spectra were obtained with a Perkin-Elmer Model 137B Infracord spectrophotometer. Pmr spectra were determined with a Varian Associates A-60 spectrometer using tetramethylsilane (TMS) as an internal standard. Chemical shifts are given on the τ scale in ppm relative to TMS (τ = 10.00 ppm).

[10] B. C. Saunders, G. J. Stacey, F. Wild, and I. G. E. Wilding, *J. Chem. Soc.*, 699 (1948).

[11] N. V. Savitskaya and M. N. Shchukina, *Zh. Obshch. Khim.*, **24**, 2052 (1954); *Chem. Abstr.*, **49**, 14665*b* (1955).

[12] Bis(*p*-hydrazidosulfonylphenyl) methylphosphonate (**4**) is soluble in water at 90° to the extent of 0.2g/ml and 0.1 g/8 ml in boiling ethyl alcohol.

[13] The phosphorodichloridate **10**, bp 171.5–183° (0.07 mm), was prepared according to the procedure of R. Anschütz, *Ann.*, **358**, 92 (1908), bp 203° (13.5 mm).

red absorption (neat) appeared at 3.39 (m), 3.44 (m), 3.52 (m), 6.29 (m), 6.9 (m, broad), 7.10 (s), 7.28 (s), 8.0 (s, broad), 8.51 (s, broad), 9.25 (s, shoulder), 9.53 (s, broad), 11.52 (m), 12.0 (m), and 12.35 (m) μ.

Anal. Calcd for $C_9H_{12}ClO_5PS$ (**12a**): Cl, 11.87; P, 10.37; S, 10.74. Found: Cl, 7.78; P, 10.20; S, 10.48.

Diethyl benzylphosphonate (**11b**, 68.5 g, 0.3 mole) was allowed to react with chlorosulfonic acid (349.5 g, 3.0 mole) in a manner similar to that described for the dimethyl analog **11a** and afforded 80.7 g of crude chlorosulfonated phosphonate **12b**.

Reactions of Chlorosulfonated Dialkyl Benzylphosphonates (12). A. Pyrolysis.—A portion (21.6 g, 72 mmoles)[14] of the crude chlorosulfonated dimethyl benzylphosphonate (**12a**) was heated to 150° over a period of 2 hr. Gas evolution commenced at *ca.* 145° and heating of the clear, pale yellow reaction mixture at 150 ± 5° was continued until gas evolution ceased (6 hr). The volatile decomposition product, condensed in a Dry Ice–isopropyl alcohol cooled trap, was identified as methyl chloride by its infrared absorption spectrum.

The amber decomposition residue (18.7 g) solidified to a clear glass on cooling. An aqueous, strongly acidic solution of the residue was neutralized with dilute alkali; distillation to dryness left a cream-colored solid. The solid was allowed to react with excess thionyl chloride (83.5 g, 0.7 mole) at 80° and after distillation of the excess thionyl chloride, the reaction product, an oil, was treated with aniline (49.3 g, 0.53 mole) in refluxing benzene. The cooled reaction mixture was filtered and the filter cake, after washing with water and drying, yielded 27.7 g of a pale tan product **13** melting at 190–210°. Repeated recrystallization of the crude anilide **13** from glacial acetic acid raised the melting point to 242–247°. Infrared absorptions (KBr) occurred at 2.98 (s), 3.0 (s), 6.25 (s), 6.67 (s), 6.76 (s), 7.08 (s), 7.62 (s), 7.7 (s), 7.78 (s), 8.13 (s), 8.23 (s), 8.67 (s), 9.12 (s), 10.61 (s), 10.84 (s), 12.0 (s), 13.3 (s), 13.47 (s), and 14.47 (s) μ.

Anal. Calcd for $C_{25}H_{24}N_3O_3PS$ (**13**): N, 8.80; P, 6.49; S, 6.72. Found: N, 8.76; P, 6.58; S, 6.70.

The crude product **12b** obtained from chlorosulfonation of diethyl benzylphosphonate (**11b**, 25.15 g, 77 mmoles) was also pyrolyzed. Gas evolution started at 159°; after 1 hr at 170 ± 2°, 4.2 ml of a low-boiling liquid condensed in a Dry Ice–isopropyl alcohol cooled trap. An infrared absorption spectrum of the condensate indicated the presence of ethylene and ethyl chloride. The cooled pyrolysis residue (20.7 g), an amber glass, was allowed to react with excess thionyl chloride (95.2 g, 0.8 mole) and then with aniline (55.8 g, 0.6 mole) as previously described to yield 19 g (0.04 mole) of N,N′-diphenyl-*p*-phenylsulfamylbenzylphosphonodiamidate (**13**), identified by melting point and mixture melting point.

B. **Reaction with Aniline.**—Aniline (37.2 g, 0.4 mole) in 50 ml of chloroform was added to a stirred solution of the crude chlorosulfonated dimethyl benzylphosphonate (**12a**, 25.5 g, 85 mmoles) in chloroform (150 ml) at room temperature. After 16 hr at room temperature, the amber-colored reaction mixture containing a white solid was gently refluxed for 5 hr. The cooled reaction mixture was filtered; the filter cake, after washing with fresh chloroform and air drying, was identified as aniline hydrochloride (8 g, 62 mmoles).

Aniline (0.22 mole) was recovered from the combined chloroform filtrate and washings by conventional means. Removal of the chloroform by distillation at about 20 mm (pot temperature <40°) left an oil (21.8 g) that solidified on standing. The solid was recrystallized once from benzene to give 19.2 g (54 mmoles) of **15a** (mp 133–136°). Several recrystallizations from 95% ethyl alcohol raised the melting point to 137.5–139.5°; infrared spectrum (KBr) 3.22 (m), 3.26 (m), 3.29 (m), 3.40 (m), 6.29 (m), 6.70 (m), 7.03 (m), 7.14 (m), 7.5 (s), 7.65 (m), 7.97 (m), 8.12 (s), 8.38 (m), 8.52 (m), 8.58 (s), 9.16 (m), 9.55 (s), 9.83 (s), 10.78 (m), 11.53 (s), 11.84 (m), 12.1 (m), 13.33 (m), 13.7 (m), and 14.5 (m) μ; pmr spectrum (acetone-d_6 solution)[15] τ 6.70 (CH_2P, 2, J_{PCH} = 21.6 cps), 6.38 (CH_3OP, 2, J_{POCH} = 10.5 cps), 2.78 (C_6H_5, c), 2.51 (H_B of C_6H_4 *ortho* to CH_2P, double doublet, J_{AB} = 8.5 cps, $^4J_{PH}$ = 2.1 cps) and 2.2 ppm (H_A of C_6H_4 *ortho* to SO_2, 2, J_{AB} = 8.5 cps).

Anal. Calcd for $C_{15}H_{18}NO_5PS$ (**15a**): C, 50.70; H, 5.10; N, 3.94; P, 8.72; S, 9.02. Found: C, 50.88; H, 4.99; N, 3.86; P, 8.90; S, 9.22.

The crude chlorosulfonated diethyl analog **12b** (26.9 g, 82 mmoles) was treated with aniline (37.2 g, 0.4 mole) in a manner similar to that described above and yielded 22.3 g (58 mmoles) of **15b**, mp 117–118°. Three recrystallizations of **15b** from benzene gave an analytical sample, mp 118–119.5°. Infrared absorptions (KBr) occurred at 3.22 (m), 3.25 (m), 3.28 (m), 3.31 (m), 3.38 (m), 3.46 (m), 6.32 (m), 6.72 (s), 6.79 (m), 7.02 (m), 7.49 (s), 7.63 (m), 8.11 (s), 8.19 (s), 8.63 (s), 9.16 (s), 9.53 (s), 9.81 (s), 10.27 (m), 10.68 (s), 10.8 (m), 11.6 (m), 13.3 (s), 13.61 (m), and 14.53 (m) μ; pmr spectrum (DMSO-d_6 solution) τ 8.90 (CH_3C, ethyl, 3, J_{HH} = 7.0 cps), 6.69 (CH_2P, 2, J_{PCH} = 22 cps), 6.07 (CH_2OP, double quartet, J_{POCH} = 8.1 cps, J_{HH} = 7.0 cps), 2.81 (C_6H_5, c), 2.55 (H_B of C_6H_4 *ortho* to CH_2P double doublet, J_{AB} = 8.2 cps, $^4J_{PH}$ = 2.1 cps), and 2.22 ppm (H_A of C_6H_4 *ortho* to SO_2, 2, J_{AB} = 8.2 cps).

Anal. Calcd for $C_{17}H_{22}NO_5PS$ (**15b**): C, 53.25; H, 5.79; N, 3.65; P, 8.08; S, 8.36. Found: C, 53.36; H, 5.73; N, 3.74; P, 8.10; S, 8.18.

C. **Hydrazinolysis.**—Aqueous 85% hydrazine (7 g, 0.19 mole) was added dropwise in 20 min to a stirred solution of the crude chlorosulfonated dimethyl benzylphosphonate (**12a**, 24.1 g, 81 mmoles) in tetrahydrofuran (100 ml) maintained at 2 ± 4°. After the addition was complete, the reaction mixture was stirred at 0° for 2 hr and filtered to give a white solid (23.8 g after drying). The filtrate, after washing with aqueous saturated sodium chloride and drying over magnesium sulfate, was diluted with petroleum ether (bp 30–60°, 300 ml) and a gummy solid (2.0 g, after drying) precipitated. The combined solid fractions (25.8 g) were washed with portions of cold water until free of chlorine. The dried, aqueous, insoluble reaction product **14a** (17.6 g, 0.06 mole) melted at 128–132° dec. Recrystallization of crude **14a** consecutively from hot water and absolute alcohol raised the melting point to 142–144° dec. Infrared absorptions (KBr) occurred at 2.99 (m), 3.06 (w), 3.18 (m), 3.39 (w), 3.52 (w), 6.32 (w), 7.15 (w), 7.55 (s), 7.58 (m), 7.98 (m), 8.15 (s), 8.35 (m), 8.43 (m), 8.62 (vs), 8.8 (m), 9.15 (m), 9.43 (vs), 9.50 (vs), 11.50 (s), 11.70 (m), and 12.53 (m) μ.

Anal. Calcd for $C_9H_{15}N_2O_5PS$ (**14a**): C, 36.73; H, 5.14; N, 9.52; P, 10.53; S, 10.90; mequiv of Br/g, 13.6. Found: C, 36.85; H, 5.16; N, 9.40; P, 10.49; S, 10.90; mequiv of Br/g, 13.5.

The reaction was repeated with crude chlorosulfonated diethyl benzylphosphonate (**12b**, 29.5 g, 0.09 mole) and aqueous 85% hydrazine (7.2 g, 0.19 mole) and yielded **14b** (18.4 g, 57 mmoles) melting at 126–128° dec. Two recrystallizations from absolute ethyl alcohol provided analytically pure hydrazide **14b** mp (130.5–132° dec); infrared absorption spectrum (KBr) 2.90 (s), 3.03 (m), 3.06 (m), 3.2 (s), 3.37 (m), 3.47 (m), 6.32 (m), 7.15 (m), 7.55 (s), 7.6 (s), 7.97 (s), 8.06 (s), 8.33 (m), 8.58 (vs), 8.82 (m), 9.14 (m), 9.48 (vs), 9.7 (vs), 10.2 (s), 10.3 (s), 11.75 (m), 12.08 (m), 12.68 (m), 14.03 (m), and 14.6 (m, broad) μ.

Anal. Calcd for $C_{11}H_{19}N_2O_5PS$ (**14b**): C, 40.99; H, 5.94; N, 8.69; P, 9.61; S, 9.95; mequiv Br/g, 12.4. Found: C, 40.86; H, 6.10; N, 8.90; P, 9.85; S, 10.04; mequiv Br/g, 12.6.

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[14] Based on the assumption that the product is the desired dimethyl *p*-chlorosulfonylbenzylphosphonate (**12a**).

(15) The numbers within the parentheses and preceding the coupling constant refer to the multiplicity of the observed signal (c = complex multiplet).

Gynocardin

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Although gynocardin was first isolated in 1904 by Power and Gornall[1] from the seeds of *Gynocardia odorata,*

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(1) F. B. Power and F. H. Gornall, *Proc. Chem. Soc.*, **20**, 137 (1904).