# Thiocarbonyls. X. The Isomeric 2,4,6-Tris(halophenyl)-1,3,5-thianes (1)

E. Campaigne and M. P. Georgiadis

The Chemistry Laboratories, Indiana University

Nine pairs of isomeric 2,4,6-tris(halophenyl)-1,3,5-trithianes have been assayed in the crude state by n.m.r. techniques, and separated and purified by chromatography. Contrary to previous reports, the α-(cis, trans)-isomers are the major products in most cases. These compounds are shown to exist as puckered chair trithiane structures, even in the more hindered α-(cis, trans)-o-halophenyl cases, by the clear resolution of axial and equatorial trithiane ring protons in a ratio of 2:1. An o-halogen on an axial phenyl group in the α-isomers causes the aromatic group to exert an anisotropic deshielding effect on adjacent axial protons, so as to cause the axial and equatorial proton peaks to appear as a singlet in some solvents. Melting point differences, in several cases quite large, from those previously reported have been observed for six of the eighteen triaryltrithianes reported.

Treatment of aromatic aldehydes with hydrogen sulfide under acid catalysis leads to the formation of mixtures of α- and β-2,4,6-triaryl-1,3,5-trithianes (I) (2). The isomeric symmetrically-substituted trithianes, usually separated by their different solubilities, have been shown by X-ray diffraction (3), dipole moment (4,5), electron diffraction (6) and n.m.r. (7) to have the puckered chair cis, trans-configuration (Iα) and the all-equatorially substituted cis, cis- configuration (Iβ).

I
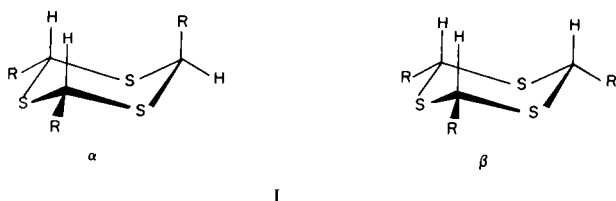
Traditional methods of extraction of the more soluble isomer, and crystallization to purity, have led to errors in estimation of relative yields and in a few cases to incorrect structural assignments (2). Recent success in the separation of α- and β-isomers of the fluorophenyl trithianes by thin layer chromatography, the easy assignment of correct structures by n.m.r., and the availability of n.m.r. to establish the ratio of α- and β-isomers in crude mixtures (8), suggests the desirability of reinvestigating earlier reports of similar systems. Some forty or more different aromatic aldehydes have been converted to mixtures of

triaryltrithianes (2,9,10), and it will be necessary to resynthesize the crude mixture of isomers, analyze the ratio of isomers by n.m.r., separate the isomers by chromatography, and characterize each of the pure isomers (cf., Reference 8).

We have now reexamined the nine pairs of isomers formed from the respective ortho, meta and para-substituted chloro, bromo, and iodobenzaldehydes. A few of these were reported long ago (11), but the complete set was carefully examined by Stanfield and Reynolds (10) who were able to isolate and characterize all nine pairs of isomers. While these authors did not attempt a quantitative estimate of isomer ratios, they indicated that the β-isomers predominated in their crude mixtures. The results of our experiments are summarized in Tables I and II. The crude yields of isomer mixtures are in good agreement with those earlier reported (10). However, in every case the amount of α-isomer was equal to or greater than the amount of β-isomer. The ratio of α:β is 2:1 for all of the meta- and para-halophenyl cases (except for the para-iodo case, where a relatively low yield of crude product complicates the reaction). The ratio of α:β isomers in all the ortho-halophenyl cases is approximately 1:1. These findings are almost identical to those earlier observed for the fluorophenyl system (8) where a reasonable mechanism was proposed to account for the preferred cis, trans (α)-configuration and for alteration of the isomeric ratio by steric hindrance in the formation of the trithiane ring for the ortho-cases.

The ratio of isomers in each crude mixture was

TABLE I

Properties of 2,4,6-Tris(halophenyl)-1,3,5-trithianes

	o-Chloro- α	o-Chloro- β	m-Chloro- α	m-Chloro- β	p-Chloro- α	p-Chloro- β	o-Bromo- α	o-Bromo- β	m-Bromo- α	m-Bromo- β	p-Bromo- α	p-Bromo- β
Crude Yield %	91.5		91		97		92		90		90	
Ratio of isomers												
by n.m.r. (a)	50	50 (b)	66	33	60	35	50	50	60	36	66	33
by column chromatography			65	32.5	62	38			60	36	65	34
by prep. T.L.C.	50	50	[62 (c)]	31 (c)]	[54 (c)]	27 (c)]	50	50			[59.6 (c)]	30 (c)]
Melting Points in °C												
Found:	163- 163.5	224- 224.5	119- 119.5	163- 163.5	161-(d) 162	195- 196	187- 187.5	220- 221	137.0- 137.5	183- 183.5	183- 184	205- 206
Reported: (e)	162.7- 163.5	223.9- 224.6	115.8- 116.4	163.0- 163.2	137.4- 138.2	189.6- 190.4	186.0- 186.7	220.6- 221.0	141.6- 142.3	177.3- 177.9	182.2- 183.0	205.3- 205.9

(a) The products show two spots and polymers in T.L.C.; (b) In repeated runs the ratio α:β was 51:42, and 46:54; (c) Each pure isomer shows one spot on T.L.C.; (d) *Anal.* Calcd. for $C_{21}H_{15}Cl_3S_3$: C, 53.63; H, 3.22; S, 20.48; Cl, 22.67. Mol. Wt. 469.82. Found: C, 53.87; H, 3.32; S, 20.32; Cl, 22.80 Mol. Wt. ("Mechrolab" vapor pressure osmometer) 473. (e) G. A. Stanfield and L. B. Reynolds, Jr., *J. Am. Chem. Soc.*, 74, 2878 (1952).

TABLE II

Properties of 2,4,6-Tris(iodophenyl)trithianes

	o-Iodo-		m-Iodo-		p-Iodo-	
	α	β	α	β	α	β
Crude Yield %	88		85		84	
Ratio of Isomers by n.m.r. (a)	55	45	66	33 (b,c)	48	33
Anal. Calcd. for: $C_{21}H_{15}I_3S_3$	Found		Found		Found	
I 51.17	51.19	51.38	51.41	51.36	51.15	50.95
S 12.92	12.72	12.64	12.63	12.72	12.99	12.98
Mol. Wt. (d) 744.08	747	743	748	740	754	760
Melting Points/°C Found:	194.5-195	211.5-212	172-172.5	212.2-212.7	212.2-212.8	218-(e) 219
Reported: (f)	188.7-189.6	202.0-202.6	196.2-197.4	212.6-213.1	113.6-114.8	211.3-212.1

(a) Crude material shows on T.L.C. two spots + faint spots due to byproducts. (b) In repeated run the ratio of α:β was 64:36. (c) The ratio of α:β by nmr for crude mixture free of by-product, which showed only two spots on T.L.C., was 60:40. When the same crude mixture was separated on preparative T.L.C. plates, 27 mg. of α and 18 mg. of β-isomer were obtained. (d) "Mechrolab" vapor pressure osmometer model 301A, in $CHCl_3$. (e) Shrinkage at 215° and melts at 218-219° with decomposition. (f) C. A. Stanfield and L. B. Reynolds, Jr., *J. Am. Chem. Soc.*, 74, 2878 (1952).

established by relative heights of the n.m.r. peaks for the trithiane protons in the crude mixtures (*cf.*, Figures I, II and IV). As was noted previously (8) it was necessary to dissolve the total sample for each n.m.r. spectrum, rather than use the more conventional saturated solution, to avoid false analyses by concentration of a more soluble isomer. In addition, the isomeric pairs were separated by column or preparative thin layer chromatography, in some cases with a complete material balance, and actual yields of pure isomers were found to be in close agreement with estimates by the n.m.r. assay. The R_f values depend on the surface offered by the molecules, and their dipole moments. The all-equatorial substituted β-isomers, with more surface and higher dipole moment (5) should therefore have the lower migration rate, and this was observed in all cases (see Table III). The increase in R_f values as each halogen substitution changes from *para* to *meta* to

ortho in the β-isomers varies directly with the expected decrease in dipole moment. There is relatively little difference between R_f values for all the α-isomers, and they are always greater than the corresponding β-isomers.

With only one exception, the melting points of the isomeric chloro- and bromophenyltrithianes (Table I) are in close agreement with those previously reported (10). α-2,4,6-Tris(p-chlorophenyl)-1,3,5-trithiane melted at 161-162°, twenty-four degrees higher than the earlier report (10), but analysis, molecular weight and n.m.r. are characteristic. Since different melting points were found for all but two of the six iodophenyl isomers, these were all characterized by analyses and molecular weights, and are therefore reported in a separate table (Table II). The difference of 100° in the observed and reported (10) melting point of α-2,4,6-tris(p-iodophenyl)-1,3,5-trithiane is surprising.

TABLE III

R_f Values of 2,4,6-Tris(halophenyl)-1,3,5-trithianes (a)

Compound	Isomer α	β
p-Fluoro- (b)	0.51	0.06
m-Fluoro- (b)	0.44	0.14
o-Fluoro- (b)	0.46	0.39
p-Chloro-	0.53	0.06
m-Chloro-	0.47	0.10
o-Chloro-	0.48	0.37
p-Bromo-	0.59	0.06
m-Bromo-	0.48	0.14
o-Bromo-	0.49	0.36
p-Iodo-	0.60	0.08
m-Iodo-	0.50	0.12
o-Iodo-	0.51	0.39

(a) Thin film layer was made with the adjustable Desaga-Brinkmann applicator (250 μ) and Merck Silica Gel G was used. Solvent: Cyclohexane:ether (9:1); distance traveled by the solvent 15.2 cm. (b) E. Campaigne and M. Georgiadis, *J. Org. Chem.*, 28, 1044 (1963).

TABLE IV

N.M.R. Spectra of 2,4,6-Triaryl-1,3,5-trithianes (a)

Compound I	Isomer	Type H	c.p.s (TMS)	δ ppm (TMS)
R = phenyl (b)	α	e	330	5.50
		a	315	5.25
	β	a	309	5.15
R = o-halophenyl				
o-Fluoro (c)	α	e	363.9	6.066
		a	358.9	5.981
	β	a	340.9	5.682
o-Chloro-	α	a+e?	372	6.200
	β	a	351	5.850
o-Chloro- (d)	α	e	377	6.291
		a	379	6.317
	β	a	360	6.000
o-Bromo-	α	a+e	367.3	6.121
	β	a	345	5.750
o-Bromo- (d)	α	e	374.5	6.241
		a	377.5	6.291
	β	a	356	5.933
o-Iodo-	α	e	357.5	5.958
		a	359.5	5.991
	β	a	336	5.600
o-Iodo- (d)	α	e	364	6.133
		a	368	6.067
	β	a	345	5.750
R = m-halophenyl				
m-Fluoro- (c)	α	e	332	5.533
		a	319	5.317
	β	a	313	5.217
m-Chloro	α	e	333	5.550
		a	318	5.300
	β	a	312	5.200
m-Bromo-	α	e	334.5	5.575
		a	318	5.300
	β	a	311	5.183
m-Iodo-	α	e	332.5	5.541
		a	316.5	5.275
	β	a	308	5.133
R = p-halophenyl				
p-Fluoro- (c)	α	e	334	5.567
		a	319	5.317
	β	a	309	5.150
p-Chloro	α	e	333.5	5.558
		a	318.5	5.308
	β	a	312.5	5.208
p-Bromo-	α	e	333.5	5.558
		a	318	5.300
	β	a	312	5.200

TABLE IV (Continued)

N.M.R. Spectra of 2,4,6-Triaryl-1,3,5-trithianes (a)

Compound I	Isomer	Type H	c.p.s. (TMS)	δ ppm (TMS)
p-Iodo-	α	e	332	5.533
		a	316	5.267
	β	a	309	5.150

(a) a = axial; e = equatorial; TMS = Internal Standard, CS_2 solvent unless specified. (b) E. Campaigne, N. F. Chamberlain and B. E. Edwards, *J. Org. Chem.*, 27, 4718 (1962). (c) E. Campaigne and M. Georgiadis, *J. Org. Chem.*, 28, 1044, (1963). (d) $CDCl_3$ solvent.

TABLE V

Relative Chemical Shift of Axial and Equatorial Protons in α (cis, trans)-2,4,6-Triaryl-1,3,5-trithianes (a)

Compound Iα	Δ, e-a c.p.s.
R = C_6H_5(b)	15
R = C_6H_4F (c)	
o-Fluoro-	5
m-Fluoro-	13
p-Fluoro-	15
R = C_6H_4Cl	
o-Chloro- (d)	-2
o-Chloro-	0
m-Chloro-	15
p-Chloro-	15
R = C_6H_4Br	
o-Bromo- (d)	-3
o-Bromo-	0
m-Bromo-	16.5
p-Bromo-	15.5

R = C_6H_4I

o-Iodo- (d)	-4
o-Iodo-	-2
m-Iodo-	16
p-Iodo-	16

(a) Solvent, carbon disulfide, unless otherwise specified. (b) E. Campaigne, N. F. Chamberlain and B. E. Edwards, *J. Org. Chem.*, 27, 4718 (1962). (c) E. Campaigne and M. Georgiadis, *ibid.*, 28, 1044 (1963). (d) Solvent, deuteriochloroform.

TABLE VI

Deshielding Effects of Halogen Substituted Equatorial Phenyl Groups on Axial Protons in β-2,4,6-Tris(halophenyl)-1,3,5-trithianes

	Para Δ cps (a)	Meta Δ cps (a)	Ortho Δ cps (a)
F	0	4	32
Cl	3.5	3	42
Br	3.0	2	36
I	0	-1	27

(a) Difference between phenyl substitution (309 cps) and halogen-substituted phenyl.

TABLE VII

Deshielding Effects of ortho-Halogen Substituted Phenyl Groups on Axial and Equatorial Protons in α-2,4,6-Tris(o-halophenyl)-1,3,5-trithianes.

	Δ cps (a) aH	Δ cps (a) eH	ΔΔ a-e
F	44	34	10
Cl	57	42	15
Br	52	37	15
I	45	30	15

(a) Difference between phenyl substitution (a = 315 cps, e = 330 cps) and o-halosubstituted phenyl substituents.

TABLE VIII

Material Balance of Isomeric Triaryltrithiane Preparations

Tris(p-chlorophenyl)trithianes (b)

α, Crude	0.62 g.		
Recrystallized (pure)		54%	0.54 g.
β, Crude	0.38 g.		
Recrystallized (pure)		27%	0.27 g.
Red Oil from Crude α		6%	0.06 g.
Red Oil from Crude β		6%	0.06 g.
			0.93 g.

Tris(m-chlorophenyl)trithianes (b)

α, Crude	0.65 g.		
Recrystallized (pure)		62%	0.62 g.
β, Crude	0.33 g.		
Recrystallized (pure)		31%	0.31 g.
Red Oil from Crude α		2%	0.02 g.
Red Oil from Crude β		2%	0.02 g.
			0.97 g.

Tris(p-bromophenyl)trithianes (b)

α, Crude	0.65 g.		
Recrystallized (pure)		59.6%	0.596 g.
β, Crude	0.36 g.		
Recrystallized (pure)		30%	0.30 g.
Red Oil from Crude α		6%	0.06 g.
Red Oil from Crude β		3%	0.03 g.
			0.986 g.

(a) Crude preparations separated on a silical gel column. (b) 1.00 g. of crude reaction product chromatogrammed in each case.

The 60 MHz n.m.r. peaks for axial and equatorial trithiane ring protons in the isomeric tris(halophenyl)-trithianes are summarized in Table IV. Peaks for the triphenyl and trifluorophenyl analogs, previously reported (7b, 8) are included for convenient comparison. The trithiane ring protons in all these examples resonate at δ 5.1-6.3, characteristic for this type (7,8). Equatorial trithiane ring protons are more deshielded than axial protons in the phenyl or meta- or para-halophenyl substituted trithianes, and effects of halogens in these cases are negligible (See Tables V and VI), since the n.m.r. spectra of the triphenyl, tris-p-halophenyl, and tris-m-halophenyltrithianes are almost superimposable (cf., Figure I).

The spectra of α-2,4,6-tris(halophenyl)-1,3,5-trithianes, like that of α-2,4,6-triphenyl-1,3,5-trithiane, exhibit two peaks for the ring protons in a ratio of 2:1 (cf., Figure I). The axial proton resonance of the β-isomers is always

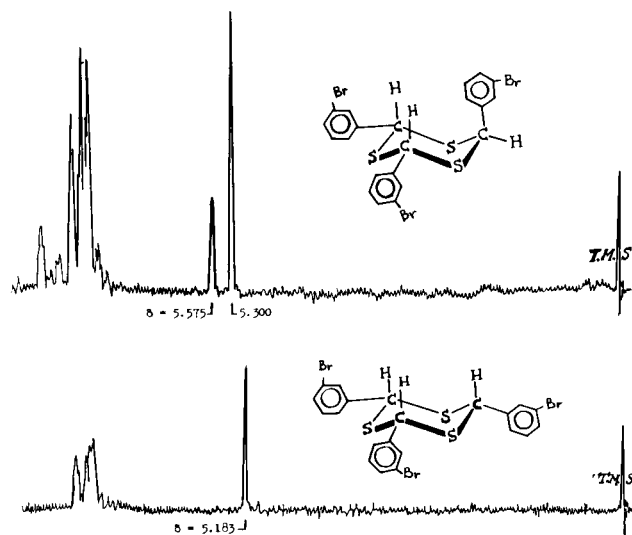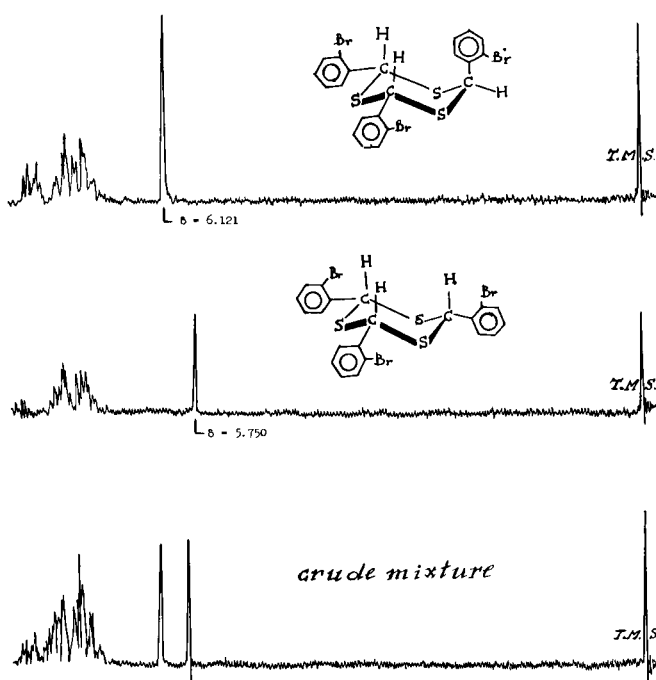Figure I. N.M.R. Spectra of Tris(m-Bromophenyl)tri-thianes (carbon disulfide).

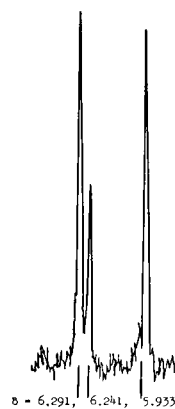Figure II. N.M.R. Spectra of Tris(o-Bromophenyl)tri-thianes (carbon disulfide).

Figure III. N.M.R. Spectrum of the Ring Protons of Crude Mixture of Tris(o-bromophenyl)trithianes (deuteriochloroform).
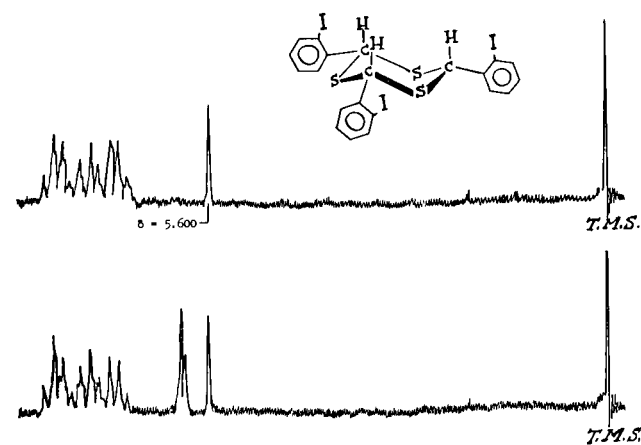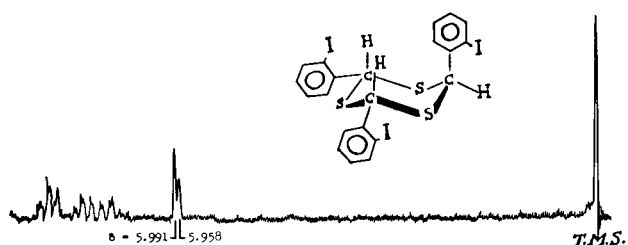

Figure IV. N.M.R. Spectra of Tris(o-Iodophenyl)trithianes (carbon disulfide).

further upfield than the axial proton resonance of the α-isomers (carbon disulfide solvent, See Table IV). Since the structures of the isomeric 2,4,6-tris(p-chlorophenyl)-1,3,5-trithianes and 2,4,6-tris(p-bromophenyl)-1,3,5-tri-thianes have been determined by other means (5), the consistency, magnitude and order of chemical shift indicate

that all 2,4,6-tris(*meta*- or *para*-halophenyl)-1,3,5-trithianes have a chair conformation of the trithiane ring.

An *ortho*-halogen exerts a strong deshielding effect on the axial trithiane ring protons, as shown in Table VI, which shows a downfield chemical shift of the axial protons of some 30 to 40 cps. units in the β-2,4,6-tris(*o*-halophenyl)-1,3,5-trithianes, compared to β-triphenyl-trithiane. This deshielding effect of *ortho*-halophenyl substituents on axial protons is magnified in the α-2,4,6-tris(*o*-halophenyl)-1,3,5-trithianes (Table VII). Each axial proton now comes under the secondary influence of an *ortho*-halophenyl group in an axial position, causing a further deshielding. The reason for the anamolous order of halogens (Cl > Br > F $\gtrless$ I) observed in Table VI is not clear. Jackman (12) states that a direct correlation between the diamagnetic shift with the size of the halogen is not possible because the carbon-halogen bonds will also contribute to the shielding of protons on adjacent rings and as yet there is no adequate way of allowing for this effect.

The result of this unequal downfield shift is that the peaks of the axial and equatorial protons in the n.m.r. spectra of the α-2,4,6-tris(*o*-halophenyl)-1,3,5-trithianes in carbon disulfide are very close, or even identical (*cf.*, Table IV, *o*-chloro and *o*-bromo cases, and Figure II). Such an observation might cast some doubt on a chair structure for the trithiane ring in these cases, since a twist-conformation would be expected to exhibit only one peak for tri-thiane ring protons. However, the relative acidity of axial and equatorial protons on trithianes is different in dif-ferent solvents (7b) and in the more polar deuteriochloro-form, the axial and equatorial protons of the α-2,4,6-tris(*o*-halophenyl)-1,3,5-trithianes can be resolved (see Tables IV and V, and Figure III), indicating that these isomeric trithianes also exist in the chair conformation. The reverse order of chemical shift for axial and equatorial protons in these *o*-halophenyl analogs is a coincidence caused by the secondary deshielding of axial protons by the axial *o*-halophenyl group. In the *o*-iodophenyl case (Figure IV) this reverse order may be observed in carbon disulfide, but is magnified in deuteriochloroform (See Table V).

It is immediately apparent from an examination of Tables VI and VII that the deshielding effect of the *ortho*-halogen on adjacent trithiane ring protons is ab-normally large. A comparison of chemical shifts of methyl protons in *ortho*- and *para*-halotoluenes (13) shows that an *ortho*-halogen exerts a modest deshielding effect of from 4 to 8 cps, from the resonance of toluene methyl protons, whereas the *ortho*-halophenyl groups on the trithiane ring exert a deshielding effect of from 27-42 cps. on adjacent axial trithiane ring protons (Table VI, Column 4). The effect of an axial *o*-halophenyl group on its adjacent

equatorial trithiane ring proton is nearly identical (Table VII, Column 3). One must conclude from these observa-tions that a restriction of rotation of aryl groups is occur-ring, which forces the *o*-halogen into a plane with the adjacent proton, where the full anisotropic effect of an *ortho*-halophenyl group in eclipsed configuration is exerted. This restriction to rotation is caused by a steric and/or electronic repulsion of the sulfur atoms in the trithiane ring, forcing the *ortho*-halogen into a position as remote as possible.

The transannular effect of an axial *ortho*-halophenyl group on axial protons of the trithiane ring is in agreement with these conclusions. Note that the difference between the chemical shifts of axial and equatorial protons in the α-*o*-halophenyl trithianes (Table VII, Column 4, $\Delta\Delta$a-e) is + 15 cps. for the three halogens, chlorine, bromine and iodine. (It is -15 cps. for the unsubstituted phenyl group) (Table V). This is consistent with a configuration in which the halogen-substituted axial aromatic ring is restricted in rotation, with *o*-halogen at a remote position from the surface of the trithiane ring (*i.e.*, eclipsed over the equatorial proton) and thus exerts a similar anisotropic effect for all three halogen substitutions.

Such considerations may account in part for the anomolous position of fluorine in this series. The much smaller size of the fluorine atom could decrease the steric repulsions, allowing some relaxation of restriction to rotation, this in turn would be reflected in a decrease in the deshielding component of the aromatic ring, both on adjacent and transannular trithiane ring protons. These are the effects observed (See Table VI, Column 4; and Table VII, Columns 3 and 4).

Most of the required halobenzaldehydes were commer-cially available, but both *o*- and *p*-iodobenzaldehyde had to be synthesized. These have both been prepared from the corresponding iodotoluenes (14, 15) by *alpha*-bromina-tion, with or without activating light, followed by a Sommelet reaction on the resultant crude iodobenzyl bromides. We have found that *N*-bromosuccinimide provides a fast and convenient source of the crude iodobenzyl bromides, and these are conveniently converted to the corresponding iodobenzaldehydes by the modified Sommelet reaction (14) in yields comparable or better than those previously reported.

EXPERIMENTAL

analyses were performed by Midwest Michrolab, Inc., Indianapolis, Indiana.

Preparation of Crude 2,4,6-Triaryltrithianes.

Six grams of p-chlorobenzaldehyde (Eastman Kodak) dissolved in 70 ml. of a mixture of ethyl acetate and ethanol (8:2) was maintained at $0° \pm 2°$ while dry hydrogen sulfide and dry hydrogen chloride were bubbled into the solution with continuous stirring for 5 hours. The mixture was allowed to stand overnight at refrigerator temperature, and the solid product (5.3 g.) was collected and washed with cold ethyl acetate. The filtrate was evaporated under a stream of nitrogen to a small volume and additional hydrogen sulfide and hydrogen chloride were passed through the filtrate to precipitate a second crop (1.2 g.). After filtration, air was drawn through the solid for a short time and the sintered glass funnel of dried solid stirred in an evacuated desicator to remove excess hydrogen chloride and hydrogen sulfide. In this way 6.5 g. (97%) of crude 2,4,6-tris(p-chlorophenyl)-1,3,5-trithiane was obtained. Similar treatment of 7.5 g. of m-chlorobenzaldehyde (Fluka-Switzerland) gave 7.64 g. (91%) of crude product. Starting with 5 g. of o-chlorobenzaldehyde (Eastman Kodak) in 60 ml. of absolute ethanol the yield of crude trithiane was 5.1 g. (93%).

The same technique was applied for the preparation of the other crude mixtures of 2,4,6-triaryltrithianes reported in Tables I and II. The required aldehydes, except o- and p-iodobenzaldehyde, were obtained from commercial sources, and purified before use.

Separation of α- and β-Triaryltrithianes by Column Chromatography.

Silica gel G (100-200 mesh) (120 g.) was dried and activated by heating overnight; then, after cooling, it was placed in a beaker and mixed with 12% ether in cyclohexane. The resulting slurry was transferred to a column and excess solvent was allowed to drain. One gram of crude tris(p-chlorophenyl)-trithiane was dissolved in benzene in a mortar and a small amount of silica gel was added. The resulting mixture was stirred well and left to dry under a stream of nitrogen. The dry material was ground well in the mortar, and transferred as dry powder to the top of the column. The material was covered with a thin band of silica gel and sand at the very top. (This packing of the column was the standard technique applied for all halophenyltrithianes). The column was developed with 12% ether in cyclohexane under pressure. The 10 ml. fractions which were collected by an automatic fraction collector were subjected to thin layer chromatography. Fractions containing only α- or only β-isomer were combined. (After the appearance of the fractions with pure β-isomer, the fraction collector was stopped and the residual β-isomer was flushed out with benzene in which the material was more soluble). The combined fractions of α- or β-isomer were evaporated separately on a rotary evaporator connected to an aspirator in a pre-weighed flask. From the weight of the flask containing each dried isomer, the yield of crude α- and β-isomers were obtained. In the present case, 0.6165 g. (62%) of crude α-2,4,6-tris(p-chlorophenyl)-1,3,5-trithiane and 0.3832 (38%) of crude β-isomer were obtained.

Each crude isomer was washed into a separate centrifuge tube quantitatively with benzene. The benzene was evaporated in a stream of nitrogen, and each isomer was washed with a small amount of cyclohexane, which extracted selectively the colored material present in both isomeric preparations. These cyclohexane extracts were transferred to smaller centrifuge tubes. The residues in the main centrifuge tubes were recrystallized from an ethanol-benzene mixture and the crystalline products showed one spot on

T.L.C. for each isomer. In checking the purity of each of these isomers on T.L.C., both copper-silver spray (8) and iodine vapors were used for spot detections. Analytical samples were recrystallized from absolute ethanol. The volume of the cyclohexane extracts in the small centrifuge tubes was reduced under a stream of nitrogen until a small new crop of trithiane was separated which, after separation, was washed with small amounts of cyclohexane. After repeated runs using the same process, the combined cyclohexane extracts yielded a reddish oil. The material balance was followed for tris(p-chlorophenyl)trithianes, tris(m-chlorophenyl)trithianes, and the tris(p-bromophenyl)trithianes, all separated in the same way, except that 10% diethyl ether in cyclohexane was used to develope the columns in the latter instances. The results of these studies are tabulated in Table VIII.

Crude tris(m-bromophenyl)trithiane and tris(m- and p-iodophenyl)trithianes were separated by column chromatography, using 12-15% ether-cyclohexane, and the α- and β-isomers were recrystallized to purity from ethanol. Because of the good agreement between the ratio of isomers found by nmr and by actual column separation in the chloro and bromo cases, the iodophenyltrithianes were recrystallized to purity without material balance, and are reported in Table II.

Separation of Isomeric Tris(o-halophenyl)trithianes by Thick Film.

Silica gel G (Merck) and an adjustable DESAGA applicator were used to prepare plates of 1.75 mm. thickness. The crude tris(o-halophenyl)trithiane was dissolved in hot benzene and spotted in a linear narrow strip of twenty centimeters at the origin. The technique of uni-dimentional multipass chromatography (8) was applied and iodine vapors were used for the detection of the isomeric compounds. (The iodine vapor treatment was as short as possible.) The solvent used for this preparative T.L.C. was either 8% ether in cyclohexene or 10-15% benzene in cyclohexene. Each plate yielded 10-20 mg. of each isomer. The yields and physical properties of the isomeric products are listed in Tables I and II.

p-Iodobenzaldehyde.

In a 500 ml. two-necked, round bottom flask equipped with two reflux condensers, one of the condensers being of the large, funnel-mouthed variety, were refluxed 125 ml. of dry thiophene-free benzene, 72.7 g. of p-iodotoluene (0.33 mole) and 0.67 g. of benzoyl peroxide. Through the large condenser a mixture of 60 g. (0.3 mole) of N-bromosuccinimide and 0.67 g. of benzoyl peroxide were added over a period of 15 minutes, keeping the mixture at constant reflux. After the addition was complete, the mixture was cooled in an ice bath. The succinimide was removed by suction filtration, and washed with 80 ml. of low boiling petroleum ether. The washings were added to the benzene solution and the mixture was poured directly into a cold solution of 50 g. of hexamethylenetetramine in 650 ml. of chloroform. The resulting mixture was allowed to stand overnight, and the hexaminium salt was collected on a Büchner funnel, washed with a small amount of chloroform and dried in air. Addition of petroleum ether to the filtrate yielded a second crop of hexaminium salt.

The hexaminium salt was dissolved in a mixture of 100 ml. of glacial acetic acid and 300 ml. of water and heated under reflux for 1.5 hours. After cooling, the mixture was diluted with water and extracted several times with ether. The ethereal extracts were washed several times with a solution of sodium carbonate, followed with water, dried, and

evaporated under a stream of nitrogen and the resulting product, after recrystallization either in petroleum ether or water-ethanol mixture, yielded 40.2 g. (52% overall) of crude p-iodobenzaldehyde, m.p. 74-78°, which upon further recrystallization from ethanol-water yielded 28 g. (36%), m.p. 78° (15) which showed one peak on v.p.c., using two different columns.

o-Iodobenzaldehyde.

Similar treatment of 36.3 g. of o-iodotoluene (Eastman Kodak) gave in the final step 11.5 g. (30% overall) of o-iodobenzaldehyde. The purification of this aldehyde was achieved by distillation *in vacuo*. The pure product melted at 37° (b.p. 129°/14 mm.) (14) and showed one component on v.p.c.

REFERENCES

(1) Contribution No. 1684 from the Chemistry Laboratories of Indiana University, supported in part by a grant from Mead-Johnson and Company, Evansville, Indiana. Taken from the Ph.D. thesis of M.P.G., Indiana University, 1963.

(2) E. Campaigne, *Chem. Rev.*, 39, 1 (1946).

(3) N. F. Moerman and E. H. Wibenga, *Z. Krist*, 97, 323 (1937).

(4) K. E. Calderbank and R. J. W. Lefevre, *J. Chem. Soc.*, 199 (1949).

(5a) K. Hayaski, *J. Chem. Soc., Japan.*, 74, 386 (1953); (b) *ibid.*, 76, 284 (1955).

(6) O. Hassel and H. Viervoll, *Acta Chem. Scand.*, 1, 149 (1949).

(7a) E. Campaigne, N. F. Chamberlain and B. E. Edwards, *J. Org. Chem.*, 27, 135 (1962); (b) *ibid.*, 27, 4718 (1962).

(8) E. Campaigne and M. Georgiadis, *ibid.*, 28, 1044 (1963).

(9) E. Campaigne and W. M. Budde, *Proc. Indiana Acad. Sci.* 58, 111 (1948).

(10) J. A. Stanfield and L. B. Reynolds, Jr., *J. Am. Chem. Soc.*, 74, 2878 (1952).

(11a) E. Worner, *Chem. Ber.*, 29, 139 (1896); (b) C. L. Jackson and J. H. White, *ibid.*, 11, 1042 (1878).

(12) L. M. Jackman, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", Macmillan, New York, 1959, p. 127.

(13) *cf.*, Sadtler NMR Spectra numbers 51, 161, 163, 173, 273 and 905. Sadtler Research Laboratories, Philadelphia, Pa.

(14) S. J. Angyal, "Organic Reactions", Vol. VIII, John Wiley and Sons, Inc., 1954, p. 197.

(15) J. W. Baker and H. B. Hopkins, *J. Chem. Soc.*, 1096 (1949).