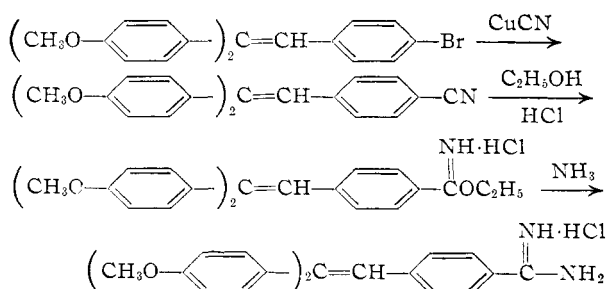# Amidines of Certain Substituted Triphenylethylenes

BY ROBERT E. ALLEN,[1] EDWARD L. SCHUMANN, WILLIAM C. DAY AND M. G. VAN CAMPEN, JR.[1]
RECEIVED SEPTEMBER 9, 1957

The conversion of certain bromo substituted triphenylethylenes via cyano- and ethyl imidate hydrochloride derivatives to the corresponding guanyl (amidino) substituted triphenylethylenes has been accomplished. Unsubstituted amidines, N-alkyl-, N,N-dialkyl- and N,N'-dialkylamidines were prepared and the amidine group was incorporated into various heterocyclic substituents. Structural modifications of the triphenylethylene moiety gave rise to amidine derivatives of triphenylethane, triphenylhaloethylene and 9-benzalfluorene. When cis-trans isomerism was possible, separation of isomers could be effected by fractional crystallization of the intermediate nitriles. A number of the amidines exhibited anti-inflammatory and antifungal activities.

Numerous examples of substituted di- and triphenylethylenes have exhibited estrogenic properties.[2] In contrast to the estrogenic activity of the halotriphenylethylene derivatives previously prepared in our laboratories,[3] the guanyl (amidino) derivatives described in the present work have shown antiinflammatory activity in addition to the microbiological effects previously reported for diamidinostilbene derivatives.[4]
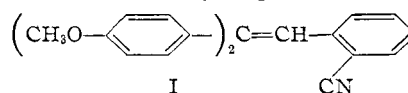
The general method for the preparation of amidines of substituted triphenylethylenes is

$$\left(CH_3O-\underset{}{\bigcirc}-\right)_2 C{=}CH-\bigcirc-Br \xrightarrow{CuCN}$$

$$\left(CH_3O-\bigcirc-\right)_2 C{=}CH-\bigcirc-CN \xrightarrow[HCl]{C_2H_5OH}$$

$$\left(CH_3O-\bigcirc-\right)_2 C{=}CH-\bigcirc-\overset{NH\cdot HCl}{\overset{\|}{C}}OC_2H_5 \xrightarrow{NH_3}$$

$$\left(CH_3O-\bigcirc-\right)_2 C{=}CH-\bigcirc-\overset{NH\cdot HCl}{\overset{\|}{C}}-NH_2$$
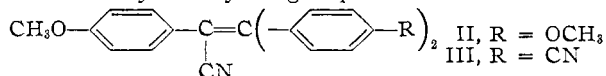
Triphenylethylenes substituted with one or more bromine atoms were prepared by allowing an appropriately substituted benzophenone to react with variously substituted benzylmagnesium halides followed by dehydration of the resulting carbinol. The corresponding nitriles were obtained by refluxing the bromo derivatives with cuprous cyanide in quinoline. The preparation of amidines in which one or two of the remaining benzene nuclei were substituted with chlorine presented some difficulty, which was encountered in the conversion of the bromo derivatives to the cyano derivatives. For example, when 1,1-bis-(p-chlorophenyl)-2-(p-bromophenyl)-ethylene was treated with the usual excess of cuprous cyanide, the product, the 1,1-bis-(p-chlorophenyl)-2-(p-cyanophenyl)-ethylene, was contaminated apparently with by-products in which some replacement of chlorine by cyano groups had occurred. This contamination was minimized by employing approximately equimolar quantities of the reactants.

In the conversion of nitriles to ethyl imidate hydrochlorides by the action of ethanolic hydrogen chloride, yields were increased when a 10:1 molar

ratio of ethanol to nitrile was employed instead of the usual 2 or 3:1 ratio. In several instances the yield was increased from about 40% to nearly quantitative when the molar ratio was increased to 10:1. The nitrile group in three compounds failed to react with ethanolic hydrogen chloride, e.g.

$$\left(CH_3O-\bigcirc-\right)_2 C{=}CH-\underset{CN}{\bigcirc}$$
$$\text{I}$$

and the ethylenic cyano group in

$$CH_3O-\bigcirc-\underset{CN}{\overset{}{C}}{=}C\left(-\bigcirc-R\right)_2 \quad \begin{array}{l} \text{II, R} = OCH_3 \\ \text{III, R} = CN \end{array}$$

This may have been due, in part, to steric effects, since it has been reported that most o-substituted arylnitriles fail to react with alcoholic hydrogen chloride.[5] However Compound I, when treated with diethylaminomagnesium bromide, gave the o-N,N-diethylguanyl derivative (compound 16, Table V).

The ethyl imidate hydrochlorides reacted readily with ammonia to give the corresponding amidine hydrochlorides in good yields. Several monoalkylated amidines were prepared by substituting methyl- or ethylamine for ammonia. An N,N'-diethylamidine was obtained by allowing the ethyl imidate free base to react under pressure with excess ethylamine. This product was shown to be different from the N,N-diethylamidine derived from the same parent nitrile (compounds 27 and 26, Table V). The latter amidine was prepared by the reaction of the nitrile with diethylaminomagnesium bromide. Amidines, in which one or both of the nitrogen atoms were part of nitrogen heterocycles, were obtained by the condensation of ethyl imidates with piperidine or with 1,2- or 1,3-diaminoalkanes or by condensation of the amidine with ethyl acetoacetate. A hydroxamidine (from the condensation of the nitrile with hydroxylamine) reacted with acetic anhydride to produce an oxadiazole (compound 36, Table V). The reaction between ethyl imidates and dialkylaminoalkylamines produced N-dialkylaminoalkylamidines (compounds 18, 19 and 48, Table V).

Of the triphenylethylenes in which geometric isomerism was possible, some were successfully separated into cis and trans isomers. This was accomplished by fractional crystallization of the intermediate nitriles. Ethyl imidates and amidines derived from these isomeric nitriles differed from each other in melting point and solubility.
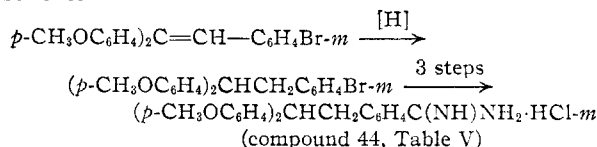
(1) Cutter Laboratories, Berkeley, California.

(2) J. Grundy, Chem. Revs., 57, 281 (1957).

(3) C. R. Thompson and H. W. Werner, Proc. Soc. Exptl. Biol. Med., 77, 494 (1951); R. S. Shelton, M. G. Van Campen, Jr., D. F. Meisner, S. M. Parmerter, E. R. Andrews, R. E. Allen and K. K. Wyckoff, THIS JOURNAL, 75, 5491 (1953).

(4) S. Bance, H. J. Barber and A. M. Woolman, J. Chem. Soc., 1 (1943).

(5) A. Pinner, Ber., 23, 2917 (1890).

The triphenylethylene moiety was modified in three ways. First, amidines of substituted triphenylethanes were prepared according to the scheme

$$p\text{-}CH_3OC_6H_4)_2C=CH—C_6H_4Br\text{-}m \xrightarrow{[H]}$$

$$(p\text{-}CH_3OC_6H_4)_2CHCH_2C_6H_4Br\text{-}m \xrightarrow{\text{3 steps}}$$

$$(p\text{-}CH_3OC_6H_4)_2CHCH_2C_6H_4C(NH)NH_2\cdot HCl\text{-}m$$

(compound 44, Table V)

The hydrogenation of the ethylene was stopped near the point of the theoretical uptake of hydrogen, since further hydrogenation removed bromine as evidenced by the analysis of the product isolated and the detection of hydrogen bromide. Second, amidines of substituted triphenylhaloethylenes were prepared by treatment of the intermediate nitriles with chlorine or bromine, and the resulting cyano-substituted triphenylhaloethylenes were carried through the usual sequence of reactions. Finally, another series of amidines was prepared in which the triphenylethylene nucleus was replaced by the structurally similar 9-benzalfluorene moiety.

The biological effects of these amidines will be reported elsewhere.

Experimental[6]

Benzophenones.—4,4'- and 2,4'-dichloro-, 4,4'-bis-(dimethylamino)-, 4,4'-dimethoxy-, 4,4'-dimethyl- and 4-bromobenzophenone were obtained from commercial sources. The substituted benzophenones listed in Table I were prepared by well known Friedel–Crafts procedures. 4,4'-Dibromobenzophenone (compound 5) was prepared from bromobenzene by the procedure given for the preparation of benzophenone.[7] The other benzophenones were prepared by the reaction of a halobenzoyl chloride with benzene or a substituted benzene in the presence of anhydrous aluminum chloride. In method A carbon disulfide was the solvent; in method B an excess of benzene or the substituted benzene was the solvent.

(2)[8] 3-Bromo-4'-methoxybenzophenone.[9]—In small portions, 62 g. (0.5 mole) of anhydrous aluminum chloride was added in 20 minutes to a stirred mixture of 106 g. (0.485 mole) of 3-bromobenzoyl chloride, 130 g. (1.2 moles) of anisole and 500 ml. of carbon disulfide. The mixture was heated to reflux for three hours. The carbon disulfide was removed by distillation, benzene (800 ml.) was added and the mixture poured onto a slurry of ice (800 g.) and 37% hydrochloric acid (50 ml.). The benzene extract was washed with 10% hydrochloric acid, water, 5% sodium hydroxide solution and again with water. After removal of the benzene and excess anisole by distillation under reduced pressure the product was crystallized from methanol; yield 120 g. (85%), m.p. 80–81°.

Anal. Calcd. for $C_{14}H_{11}BrO_2$: C, 57.53; H, 3.70; Br, 27.14. Found: C, 57.76; H, 3.81; Br, 27.45.

Bromo-substituted Triphenylethylenes (Table II). (2)[8] 1,1-Bis-(p-methoxyphenyl)-2-(p-bromophenyl)-ethylene (Method C).—A solution of 150 g. (0.6 mole) of p-bromobenzyl bromide in 1400 ml. of dry ether was added over a
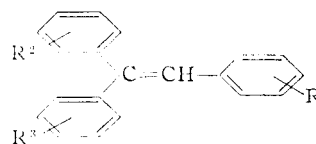
(6) All melting points are corrected.

(7) C. S. Marvel and W. M. Sperry, "Organic Syntheses," Coll. Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 95.

(8) This is the number of the compound in the appropriate table.

(9) This compound apparently has not been reported previously in the literature.

period of two hours to a stirred suspension of 14.6 g. (0.6 atom) of magnesium turnings in 100 ml. of dry ether cooled in an ice-bath. The Grignard solution, which titrated 0.428 mole, was added in 20 minutes to a hot solution of 90 g. (0.37 mole) of 4,4'-dimethoxybenzophenone in 800 ml. of dry benzene. After allowing the mixture to stand overnight, it was treated with 500 ml. of 10% hydrochloric acid, the solvent was removed and the residual oil was stirred rapidly with 400 ml. of 85% phosphoric acid on a steam-bath for four hours. Water was added and the product was extracted with chloroform, washed free of acid and the solvent was removed. The residue was taken up in 200 ml. of acetone from which 80 g. of crystals separated after being allowed to stand at room temperature for a day. After two recrystallizations, 61 g. of white crystals was obtained, m.p. 113–114°. The mother liquors were evaporated and the residues were distilled to give 53 g. of a yellow glass, b.p. 245–250° (0.5 mm.), which crystallized from acetone to give 27 g. of the product, m.p. 112–113°, an over-all yield of 60%.

(10) 1-(p-Bromophenyl)-1-phenyl-2-(p-chlorophenyl)-ethylene (Method D).—The procedure is the same as described in method C except that the Grignard reagent is prepared at the temperature of refluxing ether. From 120 g. (0.75 mole) of p-chlorobenzyl chloride, 18.2 g. (0.75 atom) of magnesium and 150 g. (0.575 mole) of 4-bromobenzophenone there was obtained 180 g. (85% yield) of an oily product boiling at 214° (0.5 mm.). Attempts to crystallize the material were unsuccessful.

(15) 1,1-Bis-(p-bromophenyl)-2-(p-methoxyphenyl)-ethylene (Method E).—To a stirred suspension of 36 g. each of magnesium turnings and powder in 800 ml. of dry ether was added a solution of 102 g. (0.65 mole) of p-methoxybenzyl chloride in 800 ml. of dry ether over a period of four hours or at a rate to ensure gentle refluxing. The Grignard reagent, which titrated 0.59 mole, was added in 30 minutes to a stirred solution of 143 g. (0.42 mole) of 4,4'-dibromobenzophenone in 400 ml. of dry benzene while heating on a steam-bath. The mixture was stirred and heated two hours, then worked up and the product dehydrated as in method C. The product was dissolved in 1500 ml. of methanol–acetone (2:1) from which was obtained 107 g. of white crystals, m.p. 97–98°, a yield of 57%.

(22) 9-(p-Bromobenzal)-fluorene (Method F).—A mixture of 25.6 g. (0.154 mole) of fluorene and 24.5 g. (0.45 mole) of sodium methoxide in 300 ml. of ethanol was stirred for 15 minutes. A solution of 28.5 g. (0.154 mole) of p-bromobenzaldehyde in 200 ml. of ethanol was added with stirring and the mixture was allowed to stand at room temperature for a day. An excess of 5% hydrochloric acid was added and the precipitated solid was washed with water. The product was crystallized from ethyl acetate–chloroform to give 37 g. (72% yield) of yellow crystals, m.p. 147–148°.

(18) 2,2-Bis-(p-bromophenyl)-1-(p-methoxyphenyl)-bromoethylene (Method G).—To a solution of 107 g. (0.24 mole) of 1,1-bis-(p-bromophenyl)-2-(p-methoxyphenyl)-ethylene (compound 15) in 250 ml. of carbon tetrachloride was added 38.4 g. (0.24 mole) of bromine in 100 ml. of carbon tetrachloride over a period of three hours while stirring and exposing to a source of ultraviolet light. The solvent was removed and the residue was dissolved in hot methanol

Table II

Bromo-substituted Triphenylethylenes

No.	R'	R²	R³	Method	M.p., °C.	Yield, %	Sol-vent	Formula	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found	Bromine, % Calcd.	Found
1	H	m-Br	H	D	a	99		C20H15Br						
2[b]	p-Br	OCH3[c]	OCH3	C	113–114	78	d	C22H19BrO2	66.85	66.99	4.85	4.96	20.22	19.95
3	m-Br	OCH3	OCH3	C	e	72		C22H19BrO2	66.85	66.97	4.85	4.68	20.22	19.96
4	o-Br	OCH3	OCH3	C	122–123	68	f	C22H19BrO2	66.85	66.53	4.85	5.46	20.22	19.54
5	OCH3	p-Br	OCH3	E	100–102	70	g	C22H19BrO2	66.85	66.97	4.85	4.84	20.22	20.41
6	OCH3	m-Br	OCH3	E	101–102[h]	38	i	C22H19BrO2	66.85	66.90	4.85	4.40	20.22	20.19
7	p-Br	CH3	CH3	C	102–103[j]	74	k	C22H19Br	72.72	72.97	5.27	5.34	22.00	22.06
8[l]	p-Br	p-Cl	p-Cl	C	121–122	58	d	C20H13BrCl2	59.44	59.51	3.24	3.40		
9	p-Br	o-Cl	p-Cl	C	m	60								
10	p-Cl	p-Br	H	C	n	85								
11	p-Br	OCH3	p-Cl	C	o	49								
12	p-Br	CH3	p-Cl	C	91–93[p]	79		C21H16BrCl	65.76	65.98	4.20	4.37		
13[q]	p-Br	N(CH3)2	N(CH3)2	C	161–162	40	r	C24H25BrN2	68.40	68.00	5.98	5.88	6.65[s]	6.84
14[t]	H	p-Br	p-Br	E	136–137	76	d	C20H14Br2	58.00	57.99	3.41	3.50	38.59	38.48
15	OCH3	p-Br	p-Br	E	97–98	57	r	C21H16Br2O	56.78	56.79	3.63	3.71	35.99	35.82
16	p-Br	p-Br	OCH3	C	113–115[u]	44	k	C21H16Br2O	56.78	56.94	3.63	3.63	35.99	35.88
17	p-Br	p-Br	OCH3	C	120–121[v]	29	g	C21H16Br2O	56.78	56.84	3.63	3.85	35.99	36.01
18[w]	OCH3	p-Br	p-Br	G	142–143	77	f	C21H15Br3O	48.23	48.07	2.89	2.95		
19[x]	p-Br	p-Br	p-Br	C	104–105[y]	40	k	C20H13Br3	48.72	48.93	2.65	2.73	48.64	49.21

Bromo-substituted Triphenylethanes

No.	R'	R²	R³	Method	M.p., °C.	Yield, %	Sol-vent	Formula	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found	Bromine, % Calcd.	Found
20	p-Cl	p-Br	H	H[z]		100								
21	m-Br	OCH3	OCH3	H		100		C22H21BrO2	66.51	65.08	5.33	5.25	20.12	23.81

Bromo-substituted Fluorenes
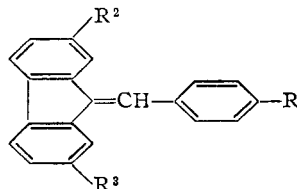
No.	R'	R²	R³	Method	M.p., °C.	Yield, %	Sol-vent	Formula	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found	Bromine, % Calcd.	Found
22	Br	H	H	F	147–148[aa]	72								
23	Br	Cl	Cl	F[bb]	218	81		C20H11BrCl2	59.74	59.50	2.76	2.96		
24	OCH3	Br	H	F[cc]	92–94	52		C21H15BrO	69.43	69.05	4.16	4.26	22.00	22.28

[a] B.p. 170° at 0.5 mm. [b] W. Tadros, Y. Akhnookh and G. Aziz, *J. Chem. Soc.*, 186 (1953), report m.p. as 107°. [c] All OCH3, CH3 and (CH3)2N groups situated in the p-position. [d] Acetone. [e] B.p. 228–230° at 0.4 mm. [f] Ethanol-chloroform. [g] Methanol-butanone. [h] B.p. 220–224° at 0.5 mm. [i] Crystallizes slowly from ligroin-ether. [j] B.p. 209–215° at 0.5 mm. [k] Ethanol. [l] W. Tadros, Y. Akhnookh and G. Aziz (footnote b) report m.p. as 118°. [m] B.p. 225–230° at 0.5 mm.; compound was not analyzed. [n] B.p. 214° at 0.5 mm.; compound was not analyzed. [o] B.p. 233° at 0.3 mm.; compound was not analyzed. [p] B.p. 213° at 0.2 mm. [q] W. Tadros and A. Latif, *J. Chem. Soc.*, 3823 (1952), report m.p. as 159°. [r] Methanol-acetone. [s] N analysis. [t] A. Schönberg, J. M. Robson, W. Tadros and H. A. Fahim, *J. Chem. Soc.*, 1327 (1940), report m.p. as 133–134°. [u] Lower-melting geometric isomer. [v] Higher-melting geometric isomer; mixed with compound 16 the m.p. was 96–105°. [w] Bromoethylene derived from compound 15. [x] W. Tadros, Y. Akhnookh and G. Aziz (footnote b) report m.p. as 101°. [y] B.p. 255–265° at 0.3 mm. [z] Hydrogenated compound 10, Table II; the oily product was not analyzed. [aa] A. Sieglitz, *Ber.*, 53, 1232 (1920), report m.p. as 144°. [bb] Replaced fluorene with 2,7-dichlorofluorene; recrystallized from toluene. [cc] Used 2-bromofluorene and anisaldehyde in place of fluorene and bromobenzaldehyde; recrystallized from isopropyl alcohol–ethyl acetate.

and chloroform from which separated 97 g. (77% yield) of white, fluffy needles, m.p. 142–143°.
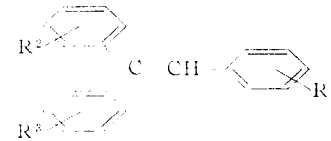
Bromo-substituted Triphenylethanes (Table II). (21) 1,1-Bis-(p-methoxyphenyl)-2-(m-bromophenyl)-ethane (Method H).—A mixture of 40 g. (0.10 mole) of 1,1-bis-(p-methoxyphenyl)-2-(m-bromophenyl)-ethylene (compound 3), 0.6 g. of platinum oxide and 100 ml. each of ethanol and ethyl acetate was hydrogenated at 3 atm. and 65°. In 75 minutes the uptake of hydrogen had exceeded the theoretical amount by 10%. The solvent and catalyst were removed, but attempts to crystallize the residual oil were fruitless. The oil was analyzed without further purification.

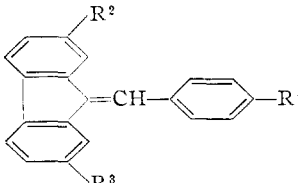**Cyano-substituted Triphenylethylenes (Table III). (16)[8] 1,1-Bis-(p-cyanophenyl)-2-(p-methoxyphenyl)-ethylene (Method J).**—A mixture of 227 g. (0.51 mole) of 1,1-bis-(p-bromophenyl)-2-(p-methoxyphenyl)-ethylene (compound 15, Table II), 137 g. (1.53 mole) of cuprous cyanide and one liter of 90% quinoline was refluxed 2.5 hours. The mixture was cooled and poured into 1500 ml. of concentrated hydrochloric acid, cooled in a Dry Ice–acetone-bath. The mixture was extracted five times with 200-ml. portions of chloroform, the chloroform extracts were washed with 200 ml. of concentrated hydrochloric acid, once with water and dried over magnesium sulfate. The solution was reduced in volume to 300 ml. and then diluted with a liter of hot methanol; the 150 g. of tan crystals which separated was recrystallized from ethanol and chloroform (10:1) to give 130 g., m.p. 151–152°.

Ethyl Imidate Hydrochlorides of Triphenylethylenes (Table IV). (15)[8] 1,1-Bis-(p-ethoxycarbiminophenyl)-2-(p-methoxyphenyl)-ethylene Dihydrochloride (Method K).—

TABLE III

CYANO-SUBSTITUTED TRIPHENYLETHYLENES

No.	R'	R²	R³	M.p., °C.	Yield, %	Solvent	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
1[a]	H	m-CN	H	135-137	23	b	$C_{21}H_{15}N$	89.66	89.76	5.37	5.48	4.98	4.75
2[c]	H	m-CN	H	168-169	26	d	$C_{21}H_{15}N$	89.66	89.51	5.37	5.34	4.98	4.99
3	p-CN	OCH₃[t]	OCH₃	113[e]	79	f	$C_{23}H_{19}NO_2$	80.92	81.22	5.61	5.88	4.10	4.05
4	m-CN	OCH₃	OCH₃	96-97	77	f	$C_{23}H_{19}NO_2$	80.92	80.94	5.61	5.50	4.10	4.22
5	o-CN	OCH₃	OCH₃	127-128	92	g	$C_{23}H_{19}NO_2$	80.92	81.05	5.61	5.72	4.10	4.29
6	OCH₃	p-CN	OCH₃	122-123	53	f	$C_{23}H_{19}NO_2$	80.92	80.81	5.61	5.63	4.10	4.12
7	OCH₃	m-CN	OCH₃	113-114	37	f	$C_{22}H_{19}NO_2$	80.92	80.83	5.61	5.70	4.10	4.11
8	p-CN	CH₃	CH₃	127-128	88	b	$C_{23}H_{19}N$	89.28	89.35	6.18	6.14	4.53	4.50
9	p-CN	p-Cl	p-Cl	117-118	55	f	$C_{21}H_{13}Cl_2N$	72.02	71.40	3.74	3.83	4.00	4.34
10	p-CN	o-Cl	p-Cl	u									
11[e]	p-Cl	p-CN	H	171-172	26[h]	d	$C_{21}H_{14}ClN$	79.87	77.33	4.47	4.14	4.44	4.18
12	p-CN	OCH₃	p-Cl	122-128	52	f	$C_{22}H_{16}ClNO$	76.41	76.09	4.66	4.91	4.05	4.55
13	p-CN	CH₃	p-Cl	118-123	77	b	$C_{22}H_{16}ClN$	80.11	76.47	4.89	4.67	4.25	3.41
14	p-CN	N(CH₃)₂	N(CH₃)₂	156-157	53	d	$C_{25}H_{25}N_3$	81.72	81.32	6.86	6.82	11.44	11.54
15	H	p-CN	p-CN	168-170[i]	63	b	$C_{22}H_{14}N_2$	86.25	85.86	4.61	4.74	9.14	8.87
16	OCH₃	p-CN	p-CN	151-152	88	f	$C_{23}H_{16}N_2O$	82.12	82.15	4.79	4.62	8.33	8.39
17[j]	p-CN	p-CN	OCH₃	90-93	43	f	$C_{23}H_{16}N_2O$	82.12	82.16	4.79	4.79	8.33	8.49
18[k]	p-CN	p-CN	OCH₃	134-136	41	f	$C_{23}H_{16}N_2O$	82.12	82.39	4.79	4.81	8.33	8.29
19[l]	OCH₃	p-CN	p-CN	164	28	m	$C_{24}H_{15}N_3O$	79.76	79.71	4.18	4.38	11.63	11.62
20[n]	p-CN	OCH₃	OCH₃	135-136	88	f	$C_{23}H_{18}BrNO_2$	65.73	65.70	4.32	4.65	3.33	3.24
21[o]	OCH₃	p-CN	OCH₃	152-153	45	b	$C_{23}H_{18}ClN_2O$	73.50	73.54	4.83	4.87	3.73	3.85
22	p-CN	p-CN	p-CN	232	97	g	$C_{23}H_{13}N_3$	83.38	83.30	3.95	3.87	12.67	12.80

CYANO-SUBSTITUTED TRIPHENYLETHANES

No.	R'	R²	R³	M.p., °C.	Yield, %	Solvent	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
23	p-Cl	p-CN	H	150-158	15	g	$C_{21}H_{16}ClN$	79.38	79.28	5.08	4.93	4.41	4.58
24	m-CN	OCH₃	OCH₃	p	82		$C_{23}H_{21}NO_2$	80.44	79.19	6.16	6.26	4.08	2.66

CYANO-SUBSTITUTED FLUORENES

No.	R'	R²	R³	M.p., °C.	Yield, %	Solvent	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
25	CN	H	H	151-152	68	d	$C_{21}H_{13}N$	90.30	90.21	4.69	4.87	5.01	5.07
26	CN	Cl	Cl	190-215	p								
27[a]	OCH₃	CN	H	139-140	24	d	$C_{22}H_{15}NO$	85.40	85.37	4.89	5.09	4.53	4.56
28[c]	OCH₃	CN	H	206-207	31	r	$C_{22}H_{15}NO$	85.40	85.40	4.89	5.07	4.53	4.78

[a] Lower-melting geometric isomer. [b] Ethanol. [c] Higher-melting geometric isomer. [d] Ethanol-chloroform. [e] R. Neher and K. Miescher, *Helv. Chim. Acta,* **29,** 449 (1946), report m.p. as 113-115°. [f] Methanol. [g] Methanol-chloroform. [h] Lower-melting geometric isomer was not isolated in pure form, m.p. 124-130°, but the yield of combined *cis* and *trans* forms was 77%. [i] W. Tadros, Y. Akhnookh and G. Aziz, *J. Chem. Soc.,* 186 (1953), report m.p. as 151°. [j] Lower-melting geometric isomer derived from compound 17, Table II. [k] Higher-melting geometric isomer derived from compound 16, Table II. [l] Cyanoethylene derived from compound 18, Table II. [m] Methanol-ethyl acetate. [n] Bromoethylene derived from compound 3, Table III, by bromination according to method G. [o] Chloroethylene derived by chlorination of compound 6, Table III, according to method G. [p] B.p. 232-234° at 0.4 mm.; could not be purified further. [q] Compound could not be separated from unreacted bromo compound. [r] Benzene. [s] Method J was used in the preparation of all nitriles using the corresponding bromotriarylethylenes of Table II with the exception of compounds 20 and 21; only slight excesses of CuCN were used in the preparations of compounds 9 through 13, 23 and 26. [t] All OCH₃, CH₃ and (CH₃)₂ N groups situated in the *p*-position. [u] Compound was impure but was used to prepare compound 9, Table V.
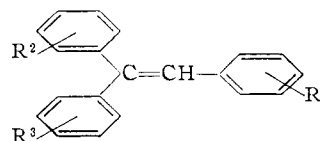
The following procedure is representative of the preparation of any bis-ethyl imidate dihydrochloride. A solution of 80 g. (0.234 mole) of 1,1-bis-(*p*-cyanophenyl)-2-(*p*-methoxyphenyl)-ethylene (compound 16, Table III) in one liter of dry benzene and 48 ml. of absolute ethanol was cooled to 6° and maintained at this temperature while the solution was saturated with anhydrous hydrogen chloride. After standing at room temperature for six days, the precipitated yellow solid was collected on a filter and dried in a vacuum oven at 56° until free of solvent and excess hydrogen chloride. The product weighed 116 g. (99% yield), m.p. 148° dec.
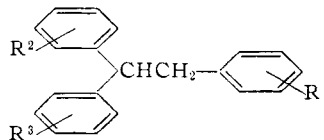
(3) 1,1-**Bis-(*p*-methoxyphenyl)-2-(*p*-ethoxycarbimino-phenyl)-ethylene Hydrochloride (Method L).**—The following procedure is typical of the preparation of any monoethyl
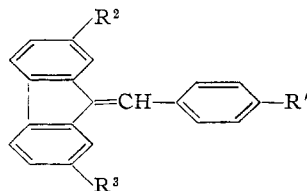
TABLE IV

ETHYL IMIDATES OF TRIPHENYLETHYLENES

No.	R'	R²	R³	M.p., °C.ᵃ	Yield, %	Formula	Chlorine, % Calcd.	Foundᵇ
1ᶜ	H	m-IEᵗ	H	142	43	$C_{23}H_{21}NO·HCl$	9.74	9.49
2ᵈ	H	m-IE	H	117	81	$C_{23}H_{21}NO·HCl$	9.74	9.59
3	p-IE	OCH₃ᵘ	OCH₃	131	90	$C_{25}H_{25}NO_3·HCl$	8.36	8.24
4	m-IE	OCH₃	OCH₃	140	80	$C_{25}H_{25}NO_3·HCl$	8.36	8.66
5	OCH₃	p-IE	OCH₃	120	90	$C_{25}H_{25}NO_3·HCl$	8.36	8.64ᵉ
6	OCH₃	m-IE	OCH₃	119	46	$C_{25}H_{25}NO_3·HCl$	8.36	8.75ᶠ
7	p-IE	CH₃	CH₃	148	90	$C_{25}H_{25}NO·HCl$	9.05	9.25
8	p-IE	p-Cl	p-Cl	129	94	$C_{23}H_{19}Cl_2NO·HCl$	8.19	7.94
9	p-IE	o-Cl	p-Cl	ᵍ				
10ʰ	p-Cl	p-IE	H	174	87	$C_{23}H_{20}ClNO·HCl$	8.90	8.45
11	p-IE	OCH₃	p-Cl	117	72	$C_{24}H_{22}ClNO_2·HCl$	8.28	8.65
12	p-IE	CH₃	p-Cl	127	86	$C_{24}H_{22}ClNO·HCl$	8.60	8.76
13	p-IE	N(CH₃)₂	N(CH₃)₂	160	100	$C_{27}H_{31}N_3O·HCl$	7.88ⁱ	7.72
14	H	p-IE	p-IE	139	88	$C_{26}H_{26}N_2O_2·2HCl$	15.04	14.76ʲ
15	OCH₃	p-IE	p-IE	148	99	$C_{27}H_{28}N_2O_3·2HCl$	14.15	14.07ᵏ
16ˡ	p-IE	p-IE	OCH₃	137	85			
17ᵐ	p-IE	p-IE	OCH₂	131	88	$C_{27}H_{28}N_2O_3·HCl$	14.15	13.88ⁿ
18ᵒ	OCH₃	p-IE	p-IE		92	$C_{28}H_{27}N_3O_3·2HCl$	13.47	11.80
19ᵖ	p-IE	OCH₃	OCH₃	144	99	$C_{25}H_{24}BrNO_2·HCl$	7.05	6.63
20�q	OCH₃	p-IE	OCH₃	167	94	$C_{25}H_{24}ClNO_3·HCl$	7.74	6.91
21	p-IE	p-IE	p-IE	100	100	$C_{29}H_{31}N_3O_3·3HCl$	18.37	19.50

No.	R'	R²	R³	M.p., °C.ᵃ	Yield, %	Formula	Chlorine, % Calcd.	Foundᵇ
22	p-Cl	p-IE	H	166	84	$C_{23}H_{22}ClNO·HCl$	8.86	8.97
23	m-IE	OCH₃	OCH₃	127	59	$C_{25}H_{27}NO_3·HCl$	8.33	8.33

No.	R'	R²	R³	M.p., °C.ᵃ	Yield, %	Formula	Chlorine, % Calcd.	Foundᵇ
24	IE	H	H	263	94	$C_{23}H_{19}NO·HCl$	9.80	10.30
25ʳ	OCH₃	IE	H	140	99	$C_{24}H_{21}NO_2·HCl$	9.05	9.78
26ˢ	OCH₃	IE	H	133	100	$C_{24}H_{21}NO_x·HCl$	9.05	9.23

ᵃ All compounds melted with decomposition. ᵇ These values were obtained by titration with AgNO₃ using dichloro-fluorescein indicator. ᶜ Higher-melting geometric isomer derived from comp. 1, Table III. ᵈ Lower-melting geometric isomer derived from comp. 2, Table III. ᵉ Calcd.: N, 3.30. Found: N, 3.35. ᶠ Calcd.: N, 3.30. Found: N, 3.72. ᵍ Compound fused on standing. ʰ The ethyl imidate derived from impure lower-melting nitrile isomer decomposed at 161°. ⁱ Compound forms an unstable trihydrochloride; the Cl value is for the stable monohydrochloride. ʲ Calcd.: N, 5.94. Found: N, 5.93. ᵏ Calcd.: N, 5.59. Found: N, 5.61. ˡ Higher-melting geometric isomer derived from comp. 17, Table III. ᵐ Lower-melting geometric isomer derived from comp. 18, Table III. ⁿ Calcd.: N, 5.59. Found: N, 5.77. ᵒ Derived from comp. 19, Table III; the ethylenic CN group did not react. ᵖ Bromoethylene derived from comp. 20, Table III. q Chloroethylene derived from comp. 21, Table III. ʳ Higher-melting geometric isomer derived from comp. 27, Table III.
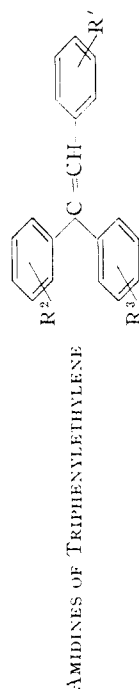
ˢ Lower-melting geometric isomer derived from comp. 28, Table III. ᵗ IE = —$\overset{\overset{\text{NH·HCl}}{\|}}{C}$OC₂H₅. ᵘ All OCH₃, CH₃ and (CH₃)₂N groups situated in the p-position.

imidate hydrochloride. A solution of 39 g. (0.114 mole) of 1,1-bis-(p-methoxyphenyl)-2-(p-cyanophenyl)-ethylene (compound 3, Table III) in 60 ml. (1.03 moles) of absolute ethanol and 250 ml. of dry benzene was saturated at 0° with anhydrous hydrogen chloride, then allowed to stand at room temperature for three days. The solvent was removed by water-pump vacuum at a temperature not exceeding 40°. The residue was triturated with dry ether to induce crystallization and the product was dried in a vacuum oven at 55° until free of excess hydrogen chloride. The product weighed 43.5 g. (90% yield), m.p. 131° dec.

Amidine Hydrochlorides of Triphenylethylenes (Table V). (3)⁸ 1,1-Bis-(p-methoxyphenyl)-2-(p-guanylphenyl)-ethylene Hydrochloride (Method M).—This procedure is illustrative of the manner in which most of the amidines were prepared. Liquid ammonia was added to a suspension of 68 g. (0.16 mole) of 1,1-bis-(p-methoxyphenyl)-2-(p-ethoxy-carbiminophenyl)-ethylene hydrochloride (compound 3,
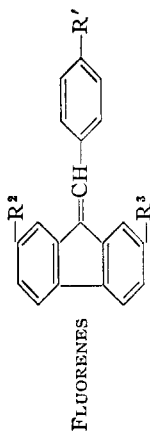
TABLE V

AMIDINES OF TRIPHENYLETHYLENE

No.	R'	R³	Method	M.p., °C	Yield, %	Formula of base	C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found
1	H	m-C(NH)NH$_2$	M[e]	238–239	84	$C_{21}H_{18}N_2$	75.33	75.58	5.72	5.74	8.37	8.10
2	H	m-C(NH)NH$_2$	M[e]	234 d.	89	$C_{21}H_{18}N_2$	75.33	75.03	5.72	5.60	8.37	8.31
3	p-C(NH)NH$_2$	OCH$_3$	M[c]	252	96	$C_{23}H_{22}N_2O_2$	69.95	70.21	5.87	5.93	7.10	7.20
4	m-C(NH)NH$_2$	OCH$_3$	M[p]	232–233	75	$C_{23}H_{22}N_2O_2$	69.95	69.76	5.87	6.09	7.10	7.11
5	OCH$_3$	p-C(NH)NH$_2$	M[p]	226 d.	87	$C_{23}H_{22}N_2O_2$	69.95	69.67	5.87	5.87	7.10	7.06
6	OCH$_3$	m-C(NH)NH$_2$	M[c]	208 d.	53	$C_{23}H_{22}N_2O_2$	69.95	70.02	5.87	5.81	7.10	7.11
7	p-C(NH)NH$_2$	CH$_3$	M[h]	314	88	$C_{22}H_{22}N_2$	76.12	76.18	6.39	6.33	7.72	7.86
8	p-C(NH)NH$_2$	p-Cl	M[i]	306–307	96	$C_{21}H_{16}Cl_2N_2$	62.47	62.15	4.25	4.43	6.94	6.91
9	p-C(NH)NH$_2$	o-Cl	M[i]	315	j	$C_{21}H_{16}Cl_2N_2$	62.47	62.49	4.25	4.40	6.94	7.02
10	p-Cl	p-C(NH)NH$_2$	M[c]	290	100[k], 95[l]	$C_{21}H_{17}ClN_2$	68.31	68.22	4.91	4.95	7.59	7.68
11	p-C(NH)NH$_2$	OCH$_3$	M[m]	277–279	39	$C_{22}H_{19}ClN_2O$	66.17	65.84	5.05	5.13	7.02	7.09
12	p-C(NH)NH$_2$	CH$_3$	M[m]	305–306	76	$C_{22}H_{19}ClN_2$	68.95	68.58	5.26	5.22	7.31	7.37
13	p-C(NH)NH$_2$	N(CH$_3$)$_2$	M[m]	173 d.	92	$C_{25}H_{28}N_4$	71.32	71.49	6.94	6.86	13.30	13.44
14	p-C(NH)NH$_2$	OH	X[c]	232 d.	95	$C_{23}H_{18}N_2O_2$	68.75	68.57	5.22	5.44	7.64	7.40
15	p-C(NEt)NH$_2$	OCH$_3$	P[p]	247–248	79	$C_{25}H_{26}N_2O_2$	70.99	70.79	6.44	6.34	6.62	6.57
16	o-C(NH)N(Et)$_2$	OCH$_3$	N	221–222	61	$C_{27}H_{30}N_2O_2$	71.90	72.05	6.93	6.95	6.21	6.13
17	p-C(NOH)NH$_2$	OCH$_3$	O	184–185 d.	76	$C_{21}H_{22}N_2O_3$	67.23	67.24	5.64	5.62	6.82	6.63
18	p-C(NH)NH-C$_2$H$_4$N(Et)$_2$	OCH$_3$	Q[p]	239 d.	54	$C_{29}H_{35}N_3O_2$	65.64	65.32	7.03	6.91	7.92	7.80
19	p-C(NH)NHCH(CH$_2$)C$_6$H$_4$N(Et)$_2$	OCH$_3$	Q[q,c]	140 d.	77	$C_{32}H_{41}N_3O_2$	67.11	66.86	7.57	7.42	7.34	7.08
20	p-C(NH)NHCOC$_6$H$_4$-2,5-OH, OCH$_3$	CH$_3$	P[p,g]	220 d.	63	$C_{31}H_{29}N_3O_3$	70.52	70.47	5.73	5.75	7.96	7.62
				Bis- and Trisamidines								
21	H	p-C(NH)NH$_2$	M[w]	238 d.	65	$C_{22}H_{20}N_4$	63.92	63.19	5.37	5.55	13.56	13.68
22	OCH$_3$	p-C(NH)NH$_2$	M[q]	235 d.	93	$C_{23}H_{22}N_4O$	62.30	62.54	5.46	5.45	12.63	12.55
23	p-C(NH)NH$_2$	OCH$_3$	M[c]	210 d.	69	$C_{23}H_{22}N_4O$	62.30	62.16	5.46	5.91	12.63	12.24
24	p-C(NH)NH$_2$	p-C(NH)NH$_2$	M[q]	275 d.	59	$C_{23}H_{22}N_6$	54.18	54.43	5.34	5.43	16.48	16.34
25	p-C(NCH$_3$)NH$_2$	OCH$_3$	P[u,i]	279 d.	74	$C_{25}H_{26}N_4O$	63.70	63.58	5.99	6.14	11.88	11.72
26	p-C(NH)N(Et)$_2$	OCH$_3$	N[v]	128–129	94	$C_{31}H_{38}N_4O$	77.14	77.30	7.94	8.02	11.61	11.53
27	p-C(NEt)NHEt	OCH$_3$	R	210 d.	63	$C_{31}H_{38}N_4O$	67.00	67.18	7.26	7.39	10.08	10.13
				Cyclic Amidines								
28	p-Cl	p-C(NH)NC$_5$H$_{10}$	M[w,e]	225	76	$C_{26}H_{25}ClN_2$	71.38	71.55	5.99	6.07	6.41	6.58
29	OCH$_3$	p-C(NH)NC$_5$H$_{10}$	M[x]	245	80	$C_{28}H_{30}N_2O_2$	72.63	72.46	6.75	6.76	6.05	5.90
30	N(CH$_3$)$_2$	p-C(NH)NC$_5$H$_{10}$	M[y,c]	152 d.	64	$C_{30}H_{36}N_4$	73.67	73.81	7.63	7.59	11.46	11.39
31	OCH$_3$	p-2-Imidazolinyl	S	261–262	63	$C_{25}H_{24}N_2O_2$	71.33	71.33	5.99	6.03	6.66	6.53
32	CH$_3$	p-2-Imidazolinyl	S[z,h]	268–269	50	$C_{26}H_{24}N_2$	77.22	77.11	6.48	6.61	7.21	7.21
33	p-Cl	p-2-Imidazolinyl	S[aa]	282	49	$C_{24}H_{19}Cl_2N_2$	64.27	63.09	4.46	4.39	6.52	6.51

[a] Hydrochloride.

TABLE V (*Continued*)

No.	R'	R²	Method	M.p. °C	Yield %	Formula of base	Hydrochloride[a] Carbon % Calcd.	Found	Hydrogen % Calcd.	Found	Nitrogen % Calcd.	Found
34	p-2-4H pyrimidyl	OCH₃	T	238	87	C₂₆H₂₆N₂O₂	71.78	71.40	6.26	6.32	6.44	6.40
35	p-2(6-OH,4-CH₃-pyrimidyl)	OCH₃	V[bb]	218–219	58	C₂₇H₂₄N₂O₃	76.38	76.20	5.70	5.62	6.60	6.78
36	p-3(5-CH₃-1,2,4-oxadiazolyl)	OCH₃	W	114–115	71	C₂₅H₂₂N₂O₃	75.35	75.00	5.57	5.52	7.03	6.75
37	OCH₃	p-2-Imidazolinyl	U	255 d.	91	C₂₇H₂₆N₄O	65.45	65.66	5.70	6.13	11.31	11.20
38	OCH₃	p-2(6-OH,4-CH₃-pyrimidyl)	V	310 d.	60	C₃₁H₂₆N₄O₃	74.09	74.10	5.22	5.56	11.15	11.28
				SUBSTITUTION AT THE ETHYLENE								
39	OCH₃	p-C(NH)NH₂	M[cc]	135	93	C₂₃H₂₁ClN₂O₂	64.34	64.23	5.17	5.19	6.53	6.65
40	p-C(NH)NH₂	OCH₃	M[dd,m]	236–237	93	C₂₃H₂₁BrN₂O₂	58.30	58.35	4.68	4.77	5.91	6.05
41	p-C(NH)NH₂	OCH₃	M[ee,g]	245 d.	81	C₂₄H₂₁N₅O	61.54	61.64	4.95	4.89	14.95	14.70
				ETHANES								
42	p-Cl	p-C(NH)NH₂	M[ff]	274	77	C₂₁H₁₉ClN₂	67.93	67.76	5.43	5.51	7.55	7.39
43	p-Cl	p-C(NH)NC₆H₁₀	aa	258	73	C₂₆H₂₇ClN₂	71.05	71.01	6.42	6.25	6.38	6.80
44	m-C(NH)NH₂	OCH₃	M[hh]	200 d.	90	C₂₃H₂₄N₂O₂	69.60	69.58	6.35	6.30	8.93	9.07
				FLUORENES								
45	-C(NH)NH₂	H	M[ii]	308	75	C₂₁H₁₆N₂	75.78	75.66	5.15	5.14	8.42	8.28
46	OCH₃	-C(NH)NH₂	M[jj,p]	130 d.	87	C₂₂H₁₈N₂O	72.83	72.96	5.28	5.21	7.72	7.83
47	-C(NH)NH₂	Cl	M[kk,i]	315		C₂₁H₁₄Cl₂N₂	62.79	62.65	3.76	3.75	6.98	6.99
48	-C(NH)NH-C₂H₄N(C₂H₅)₂	H	Q[ll]	297 d.	82	C₂₇H₂₉N₃	69.22	68.94	6.67	6.67	8.97	8.93

(Fluorene structure: benzylidene-fluorene bearing R' on the para position of the CH-phenyl, and R², R³ on the fluorene rings.)

[a] Except where stated the hydrochloride was isolated and analyzed; most bisamidines were isolated as the dihydrochloride. [b] Higher-melting geometric isomer derived from compound 1, Table IV; soluble in water, 1:1000. [c] Obtained by trituration of residue with dry ether. [d] Lower-melting geometric isomer derived from compound 2, Table IV; soluble in water, 1:100. [e] Free base melts at 132°. [f] All OCH₃, CH₃, OH and N(CH₃)₂ groups are located in the p-position. [g] Recrystallized from ethanol. [h] Recrystallized from ethanol–ethyl acetate. [i] The ethyl imidate·HCl prepared from the corresponding nitrile, being unstable, was not isolated so that no yield of amidine was possible. [k] Higher-melting geometric isomer derived from compound 10, Table IV; insoluble in warm water. [j] Lower-melting (245°) geometric isomer, soluble in warm water. *Anal.* Found: C, 68.12; H, 5.06; N, 7.58. [m] Recrystallized from chloroform–ethyl acetate. [n] Free base decomposes at 200°. [o] Isolated as the dihydrochloride. [p] Recrystallized from isopropyl alcohol–ethyl acetate. [q] Replaced the β-diethylaminoethylamine of method Q with 5-diethylamino-2-aminopentane. [r] Replaced the ethylamine of method P with a molar equivalent of 5-methoxysalicylhydrazide. [s] This is the higher-melting geometric isomer derived from compound 17, Table IV; a lower-melting isomer (196° d.) was derived from compound 16, Table IV. [t] Isolated as the trihydrochloride monohydrate. [u] Replaced the ethylamine of method P with methylamine. Replaced the nitrile of method N with compound 16, Table III and doubled the quantity of (C₂H₅)₂NMgBr; without converting to the dihydrochloride salt the product was crystallized from ligroin; analysis is on the free base; the dihydrochloride melts at 215°. [w] Treated compound 10, Table IV, with an equivalent of piperidine. [x] Replaced ammonia with excess piperidine; recrystallized from water and dried at 100° *in vacuo.* [v] Treated compound 13, Table IV, with an equivalent of piperidine. [z] Treated compound 7, Table IV, with ethylenediamine. [aa] Treated compound 8, Table IV, with ethylenediamine; recrystallized from methanol–water and dried at 120° *in vacuo.* [bb] Treated compound 3, Table V, with ethyl acetoacetate; the product isolated as the free base from ethanol–chloroform. [cc] Replaced compound 3 with compound 20, Table IV. [dd] Replaced compound 3 with compound 19, Table IV. [ee] Replaced compound 3 with compound 18, Table IV. [ff] Replaced compound 3 with compound 25, Table IV; washed product with water and dried at 100°. [gg] Same procedure as for 42 but replaced ammonia with piperidine. [hh] Replaced compound 3 with compound 26, Table IV. [ii] Replaced compound 3 with compound 24, Table IV. [jj] Replaced compound 3 with compound 22, Table V; recrystallized from methanol–isopropyl alcohol. [kk] Ethyl imidate derived from compound 24, Table IV. [ll] Ethyl imidate derived from compound 24, Table III, was not isolated but was treated with ammonia.

Table IV) in 150 ml. of ethanol until an excess was evident. The solution was heated to reflux for two hours, then concentrated to a small volume, cooled and diluted with dry ether. The precipitated product, weighing 60.5 g. (96% yield), melted with decomposition at 252° and required no further purification.

(16) 1,1-Bis-(p-methoxyphenyl)-2-(o-N,N-diethylguanyl-phenyl)-ethylene Hydrochloride (Method N).—To the Grignard reagent (91% by titration) prepared from 6.5 g. (0.06 mole) of ethyl bromide in 150 ml. of ether and 1.46 g. (0.06 atom) of magnesium turnings in 50 ml. of ether was added a solution of 40 g. (0.055 mole) of ethylamine in 30 ml. of ether. After the mixture was refluxed an hour, a solution of 13.6 g. (0.04 mole) of 1,1-bis-(p-methoxyphenyl)-2-(o-cyanophenyl)-ethylene (compound 5, Table III) in 100 ml. each of dry benzene and ether was added over a period of 50 minutes. The mixture was refluxed six hours, treated with 500 ml. of cold 10% sodium hydroxide solution and filtered. The organic layer was washed with water, dried over magnesium sulfate and the solvent was removed. The residue was dissolved in ethanol, acidified with alcoholic hydrogen chloride and the ethanol was removed. After triturating the residue repeatedly with dry ether, the tan crystalline product was dried in a vacuum oven at 55° overnight. The product weighed 11 g. (61% yield), m.p. 221–222°.

(17) 1,1-Bis-(p-methoxyphenyl)-2-(p-N-hydroxyguanyl-phenyl)-ethylene Hydrochloride (Method O).—A solution of hydroxylamine in methanol was prepared from 0.12 mole each of hydroxylamine hydrochloride and potassium hydroxide according to the directions in reference 10. A mixture of this solution and 20 g. (0.059 mole) of 1,1-bis-(p-methoxyphenyl)-2-(p-cyanophenyl)-ethylene (compound 3, Table III) in 175 ml. of methanol was refluxed four hours, then cooled. The tan precipitate weighed 16.7 g. (76% yield), m.p. 200° dec. *Anal.* Calcd. for $C_{23}H_{22}N_2O_3$: C, 73.77; H, 5.92; N, 7.48. Found: C, 73.87; H, 6.10; N, 7.45. The hydrochloride salt, prepared as in method N, was recrystallized from methanol–ethyl acetate to give yellow platelets, decomposing at 184–185°.

(15) 1,1-Bis-(p-methoxyphenyl)-2-(p-N-methylguanyl-phenyl)-ethylene Hydrochloride (Method P).—A solution of 10 g. (0.025 mole) of 1,1-bis-(p-methoxyphenyl)-2-(p-guanyl-phenyl)-ethylene hydrochloride (compound 3, Table V) and 7.5 g. of ethylamine in 50 ml. of ethanol was refluxed for six hours. The excess amine and ethanol were removed and the residue was recrystallized from ethanol to give 8.4 g. (79% yield) of yellow crystals, m.p. 247–248°.

(18) 1,1-Bis-(p-methoxyphenyl)-2-[p-(N-β-diethylamino-ethyl)-guanylphenyl]-ethylene Dihydrochloride (Method Q).—A mixture of 23 g. (0.054 mole) of 1,1-bis-(p-meth-oxyphenyl)-2-(p-ethoxycarbiminophenyl)-ethylene hydrochloride and 6.4 g. (0.055 mole) of β-diethylaminoethyl-amine in 50 ml. of ethanol was allowed to stand at room temperature overnight, was then refluxed 15 minutes and the solvent removed. A chloroform solution of the residue was shaken with a slight excess of 10% sodium hydroxide solution, twice with water, then dried over magnesium sulfate. The solution was rendered slightly acidic with alcoholic hydrogen chloride, the chloroform was removed and the residue was crystallized from isopropyl alcohol–ethyl acetate. Yellow crystals weighing 15.5 g. (54% yield) were obtained, m.p. 239° dec.

(27) 1,1-Bis-[p-(N,N'-diethyl)-guanylphenyl]-2-(p-methoxyphenyl)-ethylene Dihydrochloride (Method R).—A solution of 10 g. (0.02 mole) of 1,1-bis-(p-ethoxycarbimino-phenyl)-2-(p-methoxyphenyl)-ethylene dihydrochloride (compound 15, Table IV) in 60 ml. of chloroform (0°) was shaken with 16 ml. of cold (0°) 10% sodium hydroxide solution, then dried over anhydrous sodium sulfate. The solution was evaporated to dryness in a pressure bottle, the contents were chilled, 4.5 g. (0.1 mole) of ethylamine was added and the stoppered bottle was warmed in a water-bath

at 65° for six hours, with occasional shaking. The excess amine was removed and an alcoholic solution of the residue was acidified with alcoholic hydrogen chloride. After removal of the alcohol, the gummy residue was triturated with dry ether until crystalline to give 7 g. (63% yield) of product, which decomposed at 210°.

(31) 1,1-Bis-(p-methoxyphenyl)-2-[p-(2-imidazolinyl)-phenyl]-ethylene Hydrochloride (Method S).—A mixture of 9.6 g. (0.0226 mole) of compound 3 (Table IV) and 3.4 g. (0.056 mole) of ethylenediamine in 25 ml. of ethanol was refluxed three hours, the solvent was removed and the residue was washed with water. A methanol solution of the residue was rendered acidic with alcoholic hydrogen chloride. Addition of butanone gave yellow platelets weighing 7 g. (63% yield), m.p. 261–262°.

(34) 1,1-Bis-(p-methoxyphenyl)-2-[p-2(1,4,5,6-tetrahy-dropyrimidyl)-phenyl]-ethylene Hydrochloride (Method T).—The ethyl imidate free base obtained from 15 g. (0.035 mole) of the hydrochloride (compound 3, Table IV), according to the procedure of method R, was refluxed in a solution of 2.62 g. (0.035 mole) of 1,3-diaminopropane in 50 ml. of ethanol for one day. The solution was acidified with alcoholic hydrogen chloride, the solvent was removed and the residue crystallized from methanol–ethyl acetate to give 13.2 g. (87% yield) of yellow crystals, m.p. 238–240°.

(37) 1,1-Bis-[p-(2-imidazolinyl)-phenyl]-2-(p-methoxy-phenyl)-ethylene Dihydrochloride (Method U).—A mixture of 10 g. (0.02 mole) of compound 15 (Table IV) and 6 g. (0.10 mole) of ethylenediamine in 25 ml. of ethanol was refluxed a day, diluted with water and the precipitate was converted to the dihydrochloride salt in ethanol. Dry ether was added to the ethanol solution to precipitate the product which weighed 9 g. (91% yield) and decomposed at 225°.

The same product could be prepared by refluxing the free base of compound 22 (Table V) with two equivalents of ethylenediamine in ethanol for six hours. The dihydro-chloride of the product was crystallized from isopropyl alcohol.

(38) 1,1-Bis-[p-(4-methyl-6-hydroxy-2-pyrimidyl)-phenyl]-2-(p-methoxyphenyl)-ethylene (Method V).—A mixture of 20 g. (0.045 mole) of compound 22 (Table V), 14.3 g. (0.11 mole) of ethyl acetoacetate, and 18 ml. of 25% sodium hydroxide (0.112 mole) in 60 ml. of ethanol was refluxed four hours then diluted with water. The yellow precipitate was collected, converted to its hydrochloride salt in ethanol, then precipitated by the addition of dry ether. The hydrochloride lost hydrogen chloride on standing, so the product was suspended in water, and 25% sodium carbonate solution was added until the supernatant solution was basic. The free base was washed with water, ethanol and ether to give 13.5 g. (60% yield) which decomposed at 310°.

(36) 1,1-Bis-(p-methoxyphenyl)-2-[p-3-(5-methyl-1,2,4-oxadiazolylphenyl)]-ethylene (Method W).—A mixture of 12.2 g. (0.033 mole) of the free base of compound 17 (Table V) and 7 g. (0.068 mole) of acetic anhydride was heated at 130° for 30 minutes. A chloroform solution of the mixture was washed with dilute sodium bicarbonate solution, dried over magnesium sulfate and the solvent was removed. The residue was crystallized from benzene–methanol to give 9.2 g. (71% yield), m.p. 114–115°.

(14) 1,1-Bis-(p-hydroxyphenyl)-2-(p-guanylphenyl)-ethylene Hydrochloride (Method X).—A mixture of 8 g. (0.02 mole) of compound 3 (Table V) and 11.5 g. (0.10 mole) of pyridine hydrochloride was heated at 190–200° for a period of six hours. The reaction mixture was diluted with water, extracted with chloroform, whereupon three layers were formed. The chloroform layer was discarded and the two remaining layers were extracted with isoamyl alcohol. The alcohol solution was washed with water, the isoamyl alcohol was removed under vacuum and the residue was triturated with dry ether. The yellow crystalline product weighed 7.0 g. (95% yield), m.p. 232° dec.

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(10) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., p. 67.