A New Synthesis for a Highly Halogenated Styrene

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A novel styrene derivative containing a high halogen content has been prepared by a three-step synthesis starting from ethylbenzene and dichlorotetrafluoroacetone. This provides a potential means of incorporating halogen into polymers by copolymerization. Attempts to use hexachloroacetone or hexafluoroacetone to make similar styrene derivatives failed. Hexachloroacetone did not react with ethylbenzene and 4-(1-chloroethyl)phenyl-bis(trifluoromethyl)carbinol failed to dehydrochlorinate.

Condensation of perhaloacetones with aromatic compounds has been described as a route to a variety of haloalkyl-substituted aromatic compounds (*1–13*). Hexafluoroacetone was reacted with ethylbenzene essentially as described by Farah *et al.* (*7*) using aluminum chloride as catalyst to give 60 to 75% of 4-ethylphenyl-bis(trifluoromethyl)carbinol (**I**), together with 6% of 1-ethyl-2,4-bis(2-hydroxy-1,1,1,3,3,3-hexafluoro-2-propyl)benzene. Similarly, the reaction of dichlorotetrafluoroacetone and ethylbenzene produced 4-ethylphenyl-bis(chlorodifluoromethyl)carbinol (**II**). Hexafluoroacetone condensed readily with ethylbenzene at −70° and dichlorotetrafluoroacetone gave best yields at 25°. Other variables such as catalyst concentration from 10 to 100% of the ketone, excess ethylbenzene up to threefold, use of carbon disulfide as a solvent, starting with the aluminum chloride in the ketone rather than the ethylbenzene, has little effect on the yield.

The effect of substituents on the reactivity of the aromatic compounds in these condensations was confirmed (*6–8*) since condensation was faster with ethylbenzene and slower with chlorobenzene than with benzene. No reaction was observed with nitrobenzene. Attempts to utilize hexachloroacetone in the condensation with aromatic compounds were not successful, but 4-chlorobenzoic acid was isolated from the reaction of hexachloroacetone with chlorobenzene in the presence of aluminum chloride at 130°. This is probably formed either by condensation followed by loss of both trichloromethyl groups or by Friedel-Crafts reaction of fragments from hexachloroacetone breakdown.

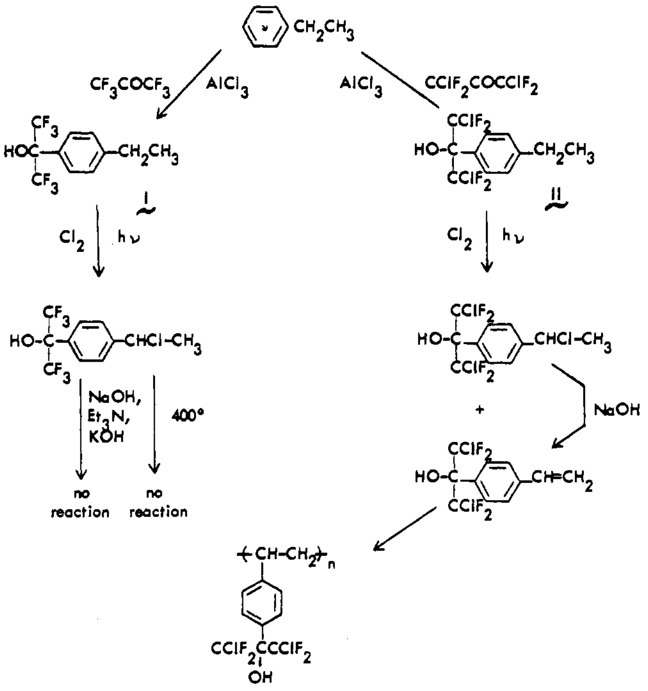
Chlorination of **I** and **II** were carried out in carbon tetrachloride at 60° to 65° with a 100-W mercury vapor lamp. **I** gave 47.4% of 4-(1-chloroethyl)phenyl-bis(trifluoromethyl)carbinol, and **II** gave 29.7% of 4-(1-chloroethyl)phenyl-bis(chlorodifluoromethyl)carbinol, and 17.6% of 4-vinylphenyl-bis(chlorodifluoromethyl)carbinol.

Dehydrochlorination of 4-(1-chloroethyl)phenyl-bis(chlorodifluoromethyl)carbinol with NaOH in 50% ethanol at 40° to 50° gave 36.7% of 4-vinylphenyl-bis(chlorodifluoromethyl)carbinol, although titration of aliquots for chloride ion indicated nearly complete reaction after 90 minutes.

For no immediately obvious reason, 4-(1-chloroethyl)-phenyl-bis(trifluoromethyl)carbinol was not dehydrochlorinated by NaOH, 50% excess, in hot 50% ethanol, KOH in refluxing butanol, anhydrous triethylamine at 90° for 17 hours, powdered KOH in mineral oil at 150°, nor pyrolysis at 400°. The desired product has been obtained by pyrolysis of the corresponding compounds with bromine or acetate in place of the chlorine and by thermal dehydrogenation of **I** (*13*).

On standing, 4-vinylphenyl-bis(chlorodifluoromethyl)-carbinol polymerized. The polymer was dissolved in hot methylene chloride and added slowly to an excess of hexane to remove the remaining monomer and give finely divided particles of polymer. The polymer, which could be fused to a brittle plaque, had a reduced viscosity of 1.80 indicating a rather low molecular weight.

SCHEME I



EXPERIMENTAL

4-Ethylphenyl-bis(trifluoromethyl)carbinol (I). The procedure of Farah *et al.* (*7*) was followed. Distillation was used to separate 51 grams (74.4%) of **I**, bp 76°/10 mm, n_D^{20} 1.4272; ir (neat) 2.80 (hindered OH), 3.37, 3.43, 3.5 (CH_3 and CH_2), 7.9, 8.2, 8.9 (CF and/or COH), 5.2, 5.6, 12.2, 12.5 (1,4 disub. arom.); nmr ($CDCl_3$) δ1.24 (t, 3, CH_3), 2.71 (m, 2, CH_2), 3.52 (s, 1, OH), 7.1–8.0 (A-B, 4, ArH); and 6.5 grams (6%) of 1-ethyl-2,4-bis(2-hydroxy-1,1,1,3,3,3-hexafluoro-2-propyl)benzene, bp 100°–102°/2 mm, n_D^{20} 1.4108; ir (neat) 2.80 (hindered OH), 3.37, 3.42, 3.50 (CH_3 and CH_2), 7.9, 8.2, 8.9 (CF and/or COH), 11.90 (substituted arom.); nmr ($CDCl_3$) δ1.24 (t, 3, CH_3), 3.08 (m, 2, CH_2), 3.49 (s, 2, OH), 7.2–8.1 (m, 3, ArH).

Anal. Calcd. for $C_{11}H_{10}F_6O$: C, 48.54; H, 3.70; mol wt 272.19. Found: C, 48.64; H, 3.99; mol wt 270.

Anal. Calcd. for $C_{14}H_{10}F_{12}O_2$: C, 38.37; H, 2.30; mol wt 438.22. Found: C, 38.58; H, 2.81; mol wt 440.

4-Ethylphenyl-bis(chlorodifluoromethyl)carbinol (II). For the preparation of **II** various conditions were tried. The best was the addition of 26.5 grams of ethylbenzene to 50 grams of 1,3-dichloro-1,1,3,3-tetrafluoroacetone containing 6.5 grams of $AlCl_3$. The mixture was stirred for 3 hours at room temperature and worked up by extraction and distillation to give 40 grams of **II**, bp 92°–93°/2.5 mm, n_D^{20} 1.4790; ir (neat) 2.8 (hindered OH), 3.38, 3.43, 3.5 (CH_3 and CH_2), 8.4, 8.7, 9.0 (CF and/or COH), 5.22, 5.55, 12.3, 12.48 (1,4 disub. arom.), 13.3, 13.95 (CCl); nmr ($CDCl_3$) δ1.23 (t, 3, CH_3), 2.69 (m, 2, CH_2), 3.89 (s, 1, OH), 7.1–7.9 (A-B, 4, ArH).

Anal. Calcd. for $C_{11}H_{10}Cl_2F_4O$: C, 43.30; H, 3.30; Cl, 23.24; mol wt 305.10. Found: C, 43.35; H, 3.82; Cl, 23.53; mol wt 301.

4-(1-Chloroethyl)phenyl-bis(trifluoromethyl)carbinol. A 115-gram portion of **I** in 500 ml of CCl_4 was chlorinated with 23.5 grams of chlorine over 0.75 hour at 60° to 76° using a 100-W Hanovia mercury vapor lamp. The mixture was separated by distillation to give 61 grams (47.4%) of 4-(1-chloroethyl)phenyl-bis(trifluoromethyl)carbinol, bp 65°–66°/1.0 mm, n_D^{20} 1.4520; ir (neat) 2.8 (hindered OH) 3.33, 3.39, 7.25 (CH_3 and CHCl), 8.20, 9.0 (CF and/or COH), 5.2, 5.53, 11.95 (1,4 disub. arom.) 12.57 (CCl); nmr ($CDCl_3$) δ1.77 (d, 3, CH_3), 5.08 (m, 1, CHCl), 3.50 (s, 1, OH), 7.47 (d, 2, ArH by CHCl), 7.86 [d, 2, ArH by $C(CF_3)_2OH$].

Anal. Calcd. for $C_{11}H_9ClF_6O$: C, 43.09; H, 2.96; Cl, 11.56. Found: C, 43.43; H, 3.04; Cl, 11.38.

4-(1-Chloroethyl)phenyl - bis(chlorodifluoromethyl)carbinol. In a manner similar to that described above, 60 grams of **II** was reacted with 12.6 grams of chlorine. The mixture was separated by distillation to give 17 grams of **II**, 10.5 grams (17.6%) of 4-vinylphenyl-bis(chlorodifluoromethyl)-carbinol, bp 76–80°/0.5–1.0 mm, n_D^{20} 1.4991, and 17.5 grams (29.7%) of 4-(1-chloroethyl)phenyl-bis(chlorodifluoromethyl)-carbinol, bp 112°/1.0 mm, n_D^{20} 1.4995; ir (neat) 2.80 (hindered OH), 3.32, 3.40, 7.26 (CH_3 and CHCl), 8.4, 8.7, 9.0 (CF and/or COH), 5.2, 5.5, 12.1 (1,4 disub. arom.), 13.2, 13.9 (CCl); nmr ($CDCl_3$) δ1.77 (d, 3, CH_3), 5.08 (m, 1, CHCl), 3.80 (s, 1, OH), 7.3–7.9 (A-B, 4, ArH).

Anal. Calcd. for $C_{11}H_9Cl_3F_4O$: Cl, 31.32. Found: Cl, 31.39.

4-Vinylphenyl-bis(chlorodifluoromethyl)carbinol. 4-(1-Chloroethyl)phenyl-bis(chlorodifluoromethyl)carbinol, 46 grams, was added to 6 grams of NaOH in 225 ml of 50% ethanol. The mixture was heated to 40–50° and the extent of reaction was followed by the titration of aliquots. After 90 minutes the ethanol was distilled at 10 mm Hg pressure and the remaining mixture was extracted with ether. Distillation was used to separate 15 grams (36.7%) of 4-vinylphenyl-bis(chlorodifluoromethyl)carbinol, bp 75–77°/0.5 mm, n_D^{20} 1.5118; ir (neat) 2.80 (hindered OH), 3.22, 3.27 (=CH— and $=CH_2$), 6.15 (conjugated C=C), 8.40, 8.7, 9.04 (CF and/or COH), 10.1, 10.9 ($—CH=CH_2$), 5.23, 5.5, 12.45 (1,4 disub. arom.), 13.05, 13.8 (CCl); nmr ($CDCl_3$) δ3.8 (s, 1, OH), 5.3 and 5.8 (m, 2, $=CH_2$), 6.7 (m, 1, =CH—), 7.2–7.7 (m, 4, ArH).

Anal. Calcd. for $C_{11}H_8Cl_2F_4O$: C, 43.60; H, 2.66; Cl, 23.40. Found: C, 43.31; H, 2.96; Cl, 23.18.

LITERATURE CITED

(1) Allied Chemical Corp., Belgian Patent **649,989** (November 3, 1964).
(2) Allied Chemical Corp., Belgian Patent **657,707** (April 26, 1965).
(3) E. I. du Pont de Nemours and Co., British Patent **975,846** (May 2, 1962).
(4) E. I. du Pont de Nemours and Co., French Patent **1,394,897** (April 9, 1965).
(5) England, D.C., French Patent **1,325,204** (April 26, 1963).
(6) Farah, B.S., Gilbert, E.E., Fitt, M., Otto, J.A., Sibilia, J.P., *J. Org. Chem.* **30**, 1003 (1965).
(7) Farah, B.S., Gilbert, E.E., Sibilia, J.P., *Ibid.*, **30**, 998 (1965).
(8) Gilbert, E.., Jones, E.S., Sibilia, J.P., *Ibid.*, **30**, 1001 (1965).
(9) Gitel, P.O., Yakubovich, A. Ya., Ginsburg, V.A., Russian Patent **154,271** (October 1963); *CA* **60**, 4060a (1964).
(10) Knunyants, I.L., Chen, Tsin-Yun, Gambaryan, N.P., *Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk* **1960**, 686.
(11) Knunyants, I.L., Chen, Tsin-Yun, Gambaryan, N.P., Rokhlin, E.M., *Zhur. Vsesoyuz. Khim. Obshchestva im. D.I. Mendeleeva* **5**, 114 (1960); *CA* **54**, 20962 (1960).
(12) Knunyants, I.L., Gambaryan, N.P., Chen Ching-Yun, Rokhlin, E.M., *Izvest. Akad. Nauk SSSR, Otdel. Khim, Nauk* **1962**, 684.
(13) Middleton, W.J., U.S. Patent **3,179,640** (Apr. 20, 1965).

RECEIVED for review February 20, 1970. Accepted June 15, 1970.

Some 2,5- and 5,6-Dihalonicotinic Acids and Their Precursors

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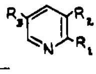
The preparation of several new 2,5- and 5,6-dihalonicotinic acids (2,5- and 5,6-dihalo-3-pyridinecarboxylic acids) by oxidation of the corresponding dihalo-3-picolines is described. Experimental and spectral data for the acids and their precursors are presented.

The pharmacological significance of nicotinic acid (niacin) has been recognized for decades (*4*). Since introduction of halogen atoms into biologically active compounds often increases activity, and since relatively few dihalonicotinic acids have been reported, we were prompted to prepare several 2,5- and 5,6-dihalonicotinic acids incorporating bromine, chlorine, and fluorine in a variety of combinations.

A recent note (*2*) described the synthesis of 3-bromo-2-chloro-5-methylpyridine (Ib) and 3-bromo-2-fluoro-5-methylpyridine (Ic) via diazotization of 2-amino-3-bromo-5-methylpyridine (Ia) in hydrochloric and fluoboric acid, respectively. We now observe that diazotization of Ia as the hydrobromide perbromide using the procedure of Craig (*1*) provides 2,3-dibromo-5-methylpyridine (Id) in adequate yield.

The extension of this preparative scheme to the synthesis of the analogous 2,5-dihalo-3-picolines has been equally successful. Diazotization of 2-amino-3-methyl-5-bromopyridine (Ie), available by bromination of 2-amino-3-methylpyridine, in hydrochloric, fluoboric, and hydrobromic acids, provides substantial yields of the 2-chloro- (If), 2-fluoro- (Ig), and 2-bromo- (Ih) derivatives, respectively.



I

	R_1	R_2	R_3
a.	NH_2	Br	CH_3
b	Cl	Br	CH_3
c.	F	Br	CH_3
d.	Br	Br	CH_3
e.	NH_2	CH_3	Br
f.	Cl	CH_3	Br
g.	F	CH_3	Br
h.	Br	CH_3	Br

II

	R_1	R_2	R_3
a.	Cl	Br	CO_2H
b.	F	Br	CO_2H
c.	Br	Br	CO_2H
d.	Cl	CO_2H	Br
e.	F	CO_2H	Br
f.	Br	CO_2H	Br

Permanganate oxidation of all the dihalo-3-picolines mentioned above led to the corresponding dihalonicotinic acids, IIa through IIf. The rather low yields are not surprising, in view of a previous report (*3*) which indicates