heating and stirring were continued at 170–180° for 0.5 hr. The liquid product was then poured into a 1-l. beaker and allowed to cool. The crude solid was dissolved in ether, petroleum ether was added, and the mixture was concentrated and then cooled. There was obtained 131 g. of product, m.p. 148–150°, and from the mother liquor 45 g. of crude product, m.p. 80–100°, lit.[2] m.p. 151–152°.

B. With Catalyst.—The above procedure was repeated with 186 g. (2 moles) of aniline containing 5 g. of p-toluenesulfonic acid. Ketone (365 g., 2.2 moles) was added at 170–180° over 1.75 hr. There was little difficulty with sublimation during the reaction. Recrystallization of the crude product gave 291 g. of solid, m.p. 149–151°, and from the mother liquor 130 g. of crude product.

C. With Catalyst and Solvent.—Into a solution of 46.6 g. (0.5 mole) of aniline and 1 g. of p-toluenesulfonic acid dissolved in 100 ml. of xylene heated to 100° was bubbled 88 g. (0.53 mole) of hexafluoroacetone over 0.5 hr. The temperature rose to 133° and was maintained at 130–135° by heating during the addition and for 1 hr. afterward. The mixture was cooled and filtered to give 103 g. crude product, m.p. 110–140°, and from the mother liquor 16 g. of the low-melting isomer, m.p. 85–90°, was isolated.

Recrystallization of the main fraction gave 78 g. of product, m.p. 150–151°.

Preparation and Rearrangement of the Aniline–Hexafluoroacetone Adduct.—Into 18.6 g. (0.2 mole) of aniline at room temperature was bubbled 35 g. (0.2 mole) of hexafluoroacetone with stirring and cooling at 25–50°. The solid which separated was filtered and recrystallized from ether–petroleum ether to give 17.9 g. of adduct, m.p. 65–68°. The adduct (13.0 g.) was heated at 130–150° for 1.5 hr., cooled, and filtered. Recrystallization from ether–petroleum ether gave 5.5 g. of 1-(2-hydroxyhexafluoro-2-propyl)-4-aminobenzene, m.p. 150–152°.

Reaction of Aniline with Tetrafluorodichloroacetone.—Aniline (23.3 g., 0.25 mole) and p-toluenesulfonic acid (1.9 g.) were mixed, and 55 g. (0.27 mole) of sym-tetrafluorodichloroacetone was added dropwise. The temperature rose spontaneously to 83° and was maintained at 80–100° by heating during the addition, which took 0.75 hr. The mixture was refluxed for an additional hour after the addition was complete, at which time the pot temperature was 135°. After cooling, hexane was added, the mixture was chilled, and the solid was filtered. Recrystallization from ether–hexane gave 37.1 g. of product, m.p. 149–150°. Omission of the catalyst in this experiment gave an intractable tar.

# Perhalo Ketones. VII. Phenolic Derivatives of the Perhaloacetones

BASIL S. FARAH, EVERETT E. GILBERT,[1] MORTON LITT, JULIAN A. OTTO, AND JOHN P. SIBILIA

General Chemical Research Laboratory, Allied Chemical Corporation, Morris Township, New Jersey 07960

Thirty new carbinols have been prepared by condensation of tetrafluorodichloro-, pentafluoromonochloro-, and hexafluoroacetones with various mono- and dihydric phenols and with phenolic ethers. Several acidic catalysts were employed, the choice of which determines whether orientation of the entering 2-hydroxyperhalo-2-propyl group is *ortho* or *para* to the phenolic group. An n.m.r. study of nine of the compounds indicated that electron-donating hydroxyl and alkyl groups largely neutralize the electron-withdrawing effect of the entering highly fluorinated alkyl group.

The present study was undertaken as part of a general program on reactions and derivatives of hexafluoroacetone and the analogous perhalogenated fluorochloro ketones.[2] Brief reports on the reaction of three phenolic compounds with two of these ketones have already appeared.[3,4] Knunyants and co-workers[3] showed that phenol reacts with hexafluoroacetone at 2:1 molar ratio at 100° for 10 hr. in the presence of a large quantity of anhydrous HF to form a "bisphenol" derivative as follows. Only the 2:1 product was iso-

$$2C_6H_5OH + (F_3C)_2CO \xrightarrow{HF} (HOC_6H_4)_2C(CF_3)_2 + H_2O$$
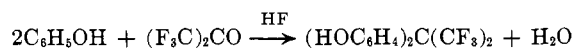
lated, although the 1:1 compound, $HOC_6H_4C(CF_3)_2OH$, was postulated as the intermediate. England, in a patent[4] published after completion of the present study, showed that *ortho* 1:1 and 1:2 products, respectively, resulted by heating phenol or hydroquinone with hexafluoroacetone at 150–200° in a bomb for 8 hr. without a catalyst. With AlCl₃ as catalyst, the 2-hydroxyhexafluoro-2-propyl moiety was introduced *para* in diphenyl ether; with the same catalyst, tetrafluorodichloroacetone likewise substituted *para* to the hydroxyl group in 2-ethylphenol.

The present study has generally confirmed the above observations and, at the same time, has substantially broadened the scope of the reaction as ap-

plied to hexafluoroacetone (Table I) and tetrafluorodichloroacetone (Table II); both reacted at 1:1 molar ratio with a series of phenols and phenolic ethers. Although these ketones will effect *ortho* substitution of phenol when heated with it under pressure without solvent or catalyst, we have found that operation at atmospheric pressure with xylene as reaction solvent and toluenesulfonic acid as catalyst is more convenient and rapid and yields a purer product. This catalyst preferentially forms the *ortho* derivatives, except when available *ortho* positions are blocked or when formation of the *ortho* compound is sterically somewhat unfavorable, as in 2-*t*-butylphenol. Boron trifluoride, on the other hand, forms only the *para* isomer, which upon prolonged standing with excess phenol yields the same 2:1 "bisphenol" product earlier noted with anhydrous HF.[3] Aluminum chloride was found to give *para,para'* substitution of diphenyl ether, as observed by England. However, this catalyst induced *ortho* substitution of phenol by hexafluoroacetone in the present study, although England noted *para* substitution of 2-ethylphenol using AlCl₃ with tetrafluorodichloroacetone. The reason for this difference in orientation is not clear, since the reaction conditions were similar, and, as indicated in Table II, the chlorinated ketone is sterically capable of substitution in a position *ortho* to the phenolic group. Aluminum chloride catalysis in the usual sense is probably not involved here, since phenols react easily with AlCl₃, forming phenoxides.[5]

Although phenols undergo uncatalyzed condensation with anhydrous hexafluoroacetone, no reaction occurs

(1) To whom inquiries should be addressed.

(2) Perhalo Ketones. VI: E. E. Gilbert, E. S. Jones, and J. P. Sibilia, *J. Org. Chem.*, **30**, 1001 (1965).

(3) I. L. Knunyants, C. Ching-Yun, N. P. Gambaryan, and E. M. Rokhlin, *Zh. Vses. Khim. Obshchestva im. D. I. Mendeleeva*, **5**, 114 (1960); *Chem. Abstr.*, **54**, 20962 (1960).

(4) D. C. England, French Patent 1,325,204 (1963); *Chem. Abstr.*, **59**, 11339 (1963).

(5) G. A. Olah, "Friedel–Crafts and Related Reactions," Vol. 1, G. A. Olah, Ed., Interscience Publishers, Inc., New York, N. Y., 1963.

TABLE I
PHENOLIC AND PHENOLIC ETHER DERIVATIVES OF TETRAFLUORODICHLOROACETONE

Phenol used	Catalyst[a]	Time, hr.	Yield, %[b]	M.p., °C.[c]	Isomer[d]	%C Calcd	%C Found	%H Calcd	%H Found	%F[e] Calcd	%F[e] Found	%Cl Calcd	%Cl Found
Phenol	T	33–50	68–83	128–133	o[f]	36.8	36.8	2.1	2.2			24.2	24.0
Phenol	BF₃	...	12	146–150	p[g]					25.9	25.7		
2-Cresol	T	10	58	128–130	o[h]	39.0	39.0	2.6	2.9			23.1	22.8
3-Cresol	T	21	58	127–130	o[i]	39.0	39.0	2.6	2.5			23.1	23.1
4-Cresol	T	28	74	133–137	o[f]	39.0	39.0	2.6	2.8			23.1	23.0
2,6-Dimethylphenol	T	60	38	95	p[j]							22.1	22.7
2-Cyclohexylphenol	T	30	55	95–98	p[h]					20.2	21.2		
4-Cyclohexylphenol	T	5	70	202	o[j]					18.9	18.4		
2-Isopropylphenol	T	9	42	100–104	p[j]	43.0	42.6	3.6	3.4			21.2	21.0
3-Isopropylphenol	T	5	66	55–63	o[j,k]							21.2	20.6
2,6-Diisopropylphenol	T	40	88	125	p[h]	47.7	48.2	5.0	4.5			18.8	18.5
2-t-Butylphenol	T	6	36	144–149	p[j]							20.3	19.9
2-Methyl-6-t-butylphenol	T	7	79	135–143	p[h]	46.3	47.0	4.4	4.2			19.5	19.1
2,2-Bis(4-hydroxyphenyl)propane	T	...	09	(Paste)	o,o'[h]					24.3	24.6		
Diphenyl ether	AlCl₃	...	26	B.p. 205 (2 mm.)	p,p'[h]			1.8	1.9	26.8	25.7		
4-Chlorophenol	T	150	8	120–125	o[j]					23.2	23.5	32.5	32.5

[a] T = toluenesulfonic acid. [b] Based on ketone used. [c] Uncorrected. [d] Indicates position of the 2-hydroxyperhalo-2-propyl moiety with respect to the phenolic group. [e] By n.m.r. [f] Proved by hydrolysis to the carboxylic acid. [g] Proved by conversion to the "bisphenol." [h] Not proven experimentally. [i] 1-(2-Hydroxytetrafluorodichloro-2-propyl)-2-hydroxy-4-methylbenzene. [j] As indicated by n.m.r. [k] 1-(2-Hydroxytetrafluorodichloro-2-propyl)-2-hydroxy-4-isopropylbenzene.

TABLE II
PHENOLIC AND PHENOLIC ETHER DERIVATIVES OF HEXAFLUOROACETONE

Phenol used	Catalyst[a]	Time, hr.	Yield, %[b]	M.p., °C.[c]	Isomer[d]	C, % Calcd	C, % Found	H, % Calcd	H, % Found	F, %[e] Calcd	F, %[e] Found
Phenol	T	32	35	72–75[f]	o[g]	41.5	41.5	2.3	2.5	43.8	44.0
Phenol[h]	AlCl₃	6	62	70–72	o	...	...	...	...	...	...
Phenol	BF₃	10	75	127–130[i]	p[j]	...	...	...	...	43.8	44.0
Phenol[k]	BF₃	10	68	138–142	p[j]	...	...	...	...	34.3	34.7
2-Cresol	T	19	55	67–72	o[l]	43.7	43.3	2.9	3.9	41.5	40.0
3-Cresol	T	7	90	81–85	o[m,n]	43.7	43.5	2.9	3.1	41.5	42.0
4-Cresol	None	17	47	121–126	o[n]	43.7	43.1	2.9	3.3	41.5	42.0
4-Cresol	T	8	54	121–126	o	...	...	...	...	...	...
2,6-Dimethylphenol	T	28	85	93–104	p[g]	45.8	44.8	3.5	3.6	39.5	38.0
2-t-Butylphenol	T	10	52	63–71	p[l]	49.3	49.2	4.4	4.9	36.0	35.5
Resorcinol	T	..	91	144–147	..[l,n,o]	39.1	39.3	2.2	2.4	40.6	40.0
1-Naphthol	T	..	67	121–124	o[l]	...	...	...	...	36.8	34.9
1,5-Naphthalenediol	T	..	62	235–236	o[l]	...	...	...	...	46.3	46.5
2,2-Bis(4-hydroxyphenyl)propane	T	..	96	Oil	o[l]	...	...	...	...	28.9	29.0
Anisole (1:1)	AlCl₃	7	68	101–102	p[g]	...	...	...	...	41.6	41.9
Anisole (2:1)	AlCl₃	3	30	132–133	o,p[l]	...	...	...	...	51.0	51.0
Diphenyl ether	AlCl₃	..	70–97	B.p.[p] 155 (3 mm.)	p,p'[g]	...	...	...	...	45.6	45.8
Diphenyl sulfide	AlCl₃	..	87	B.p. 148 (1 mm.)	p,p'[g]	...	...	...	...	6.2[q]	6.0[q]

[a] T = toluenesulfonic acid. [b] Based on ketone used. [c] Uncorrected. [d] Indicates position of the 2-hydroxyhexafluoro-2-propyl moiety with respect to the phenolic group. [e] As determined by n.m.r. [f] Lit.[4] m.p. 77–79°. [g] Proved by hydrolysis to the acid. [h] A small yield of 2,4-bis(2-hydroxyhexafluoro-2-propyl)-1-phenol, m.p. 153–154°, was also formed. Anal. Calcd.: F, 53.6. Found: F, 53.2. The orientation of this compound was not proven experimentally. [i] Lit.[3] m.p. 122.5–123.5°. [j] Proven by conversion to the "bisphenol." [k] Pentafluoromonochloroacetone used. [l] Not proven experimentally. [m] 1-(2-Hydroxyhexafluoro-2-propyl)-2-hydroxy-4-methylbenzene. [n] As indicated by n.m.r. [o] 1-(2-Hydroxyhexafluoro-2-propyl)-2,4-dihydroxybenzene. [p] Lit.[4] b.p. 140° (0.9 mm.). [q] Analysis for sulfur.

upon refluxing with the milder ketone hydrate. The hydrate, on the other hand, does react with aromatic amines,[2] since they are more susceptible to electrophilic attack than phenols.

The following phenols appeared to react normally with tetrafluorodichloroacetone, but the products could not be obtained in analytically pure form: catechol, resorcinol, 2- and 4-phenylphenols, 4-methylmercaptophenol, 2-chlorophenol, and 4-nonylphenol.
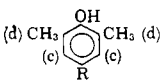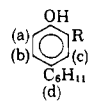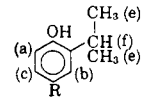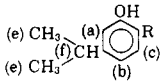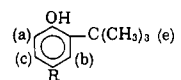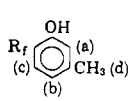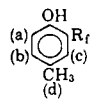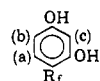
It was found that the 2-hydroxyperhalo-2-propyl groups in the phenolic derivatives could be hydrolyzed rapidly and generally in good yield to carboxyl groups.

This procedure, which provides a convenient, rapid, and general method for identifying these and other perhalo ketone derivatives, is discussed in detail in another publication from this laboratory.[6] The reaction is conducted at 175° for 4 hr. in diethylene glycol.

As indicated in Table III, n.m.r. structural studies were made on nine of the compounds cited in Tables I and II. Eight of these were 1,2,4-trisubstituted, the third substituent being an alkyl group in all cases except one in which it was chlorine. The ninth

(6) B. S. Farah, E. E. Gilbert, E. S. Jones, and J. A. Otto, J. Org. Chem.; 30, 1006 (1965).

TABLE III

N.M.R. DATA ON PHENOLIC DERIVATIVES OF PERHALO KETONES

Compd.[a]	Solvent[b]	Proton chemical shifts, p.p.m.					
		a	b	c	d	e	f
(structure: OH, (d)CH₃ CH₃(d), (c)(c), R)	CCl₄	...	...	7.23	2.24	...	...
(structure: OH, (a)(b) R (c), C₆H₁₁ (d))	CH₃OH	6.47 6.61	6.81[c] 6.95[c]	7.03	1.3[d]	...	...
(structure: CH₃(e), OH CH(f) CH₃(e), (a)(c)(b), R)	CH₃OH	6.63 6.77	7.17	7.17[c] 7.31[c]	...	1.12 1.24	e
(structure: OH, (e)CH₃ (a) R, (f)CH (c), (e)CH₃ (b))	CCl₄	6.68	6.68 6.82	7.27 7.41	...	1.13 1.25	2.77[f]
(structure: OH, (a)—C(CH₃)₃ (e), (c)(b), R)	CDCl₃	6.68 6.83	ca. 7.22	ca. 7.22[c] 7.22[c]	...	1.23	...
(structure: OH, (a)(b) R (c), Cl)	CCl₄	6.67 6.81	7.02[c] 7.16[c]	7.16	...	...	...
(structure: OH, R_f (a) (c) CH₃(d), (b))	CCl₄	6.63	6.63 6.77	7.18 7.32	2.20	...	...
(structure: OH, (a)(b) R_f (c), CH₃ (d))	CDCl₃	6.65 6.78	7.00[c] 7.13[c]	7.16	2.20	...	...
(structure: OH, (b)(c) (a) OH, R_f)	CH₃OH	6.91 7.07	6.08[c] 6.24[c]	6.15[c]	...	...	...

[a] R denotes the 2-hydroxytetrafluorodichloro-2-propyl moiety; R_f denotes the 2-hydroxyhexafluoro-2-propyl group. [b] Tetramethylsilane used as internal standard for the carbon tetrachloride and chloroform solutions, and as external standard for the methanol solutions. [c] These positions represent doublet centers with J_c = 2.5 c.p.s. [d] Band center of complex multiplet. [e] Solvent interference. [f] Septet.

compound contained two alkyl groups and was 1,2,4,6-tetrasubstituted. The trisubstituted compounds were characterized by their typical AB patterns for the two adjacent aromatic protons, with coupling constants between 8 and 10 c.p.s. In a number of cases, coupling of the order of 2.5 c.p.s. was observed between *meta* protons. Ring protons, except those *ortho* to the fluorinated hydroxyisopropyl group, were shifted to a higher field as a result of the electron-donating properties of the phenolic and alkyl groups. Values for the ring protons adjacent to the fluorinated group were close to those of benzene, indicating that the electron-withdrawing fluorinated group was neutralized by the electron-donating phenolic and alkyl groups. The ability of the 2-hydroxyperhalo-2-propyl moiety to withdraw electrons is apparently considerably reduced by the presence of its hydroxyl group.

Experimental

The following examples are typical of the procedure used.

4-Cresol with Hexafluoroacetone.—4-Cresol (27 g., 0.25 mole), xylene solvent (100 ml.), and *p*-toluenesulfonic acid (2 g.) were placed in a three-necked laboratory reaction flask equipped with mechanical stirrer, heater, Dry Ice–acetone reflux condenser, and gas inlet tube. The mixture was heated to 100° and hexafluoroacetone (b.p. −28°) was slowly admitted with efficient stirring as fast as reaction occurred; the presence of excess ketone was indicated by refluxing from the condenser. Twenty-seven grams (0.16 mole) of ketone reacted in 7.5 hr., after which heating was continued for 3 hr. at 100°. The reaction mixture was cooled and washed with water, and the xylene solvent was removed by distillation *in vacuo*. The residue, after recrystallization from hexane, melted at 121–126°. The yield was 20.5 g. (47% based on the amount of hexafluoroacetone used).

Phenol with Tetrafluorodichloroacetone.—Phenol (94 g, 1.0 mole), toluenesulfonic acid (4 g.), and xylene solvent (100 ml.) were heated to 135° with agitation in a three-necked laboratory reaction flask, and tetrafluorodichloroacetone (b.p. 45°) was added dropwise at such a rate that the temperature of the reaction mixture stayed in the range 110–135°. Introduction of 200 g. (1.0 mole) thus required 50 hr. After cooling, chloroform (400 ml.) and water (50 ml.) were added with stirring. The water layer was removed, thus removing the catalyst, and hexane (500 ml.) was added. The solid product, which separated upon cooling to 0°, was filtered, washed with cold hexane, and dried to constant weight. The yield was 246 g. (83% of theory). This crude product was light in color and melted at 128–135°. Omission of the xylene reaction solvent gave a 68% yield of a darker product which melted at 128–133° even after one recrystallization.