# REACTIONS OF PERFLUOROMETHACRYLIC ACID DERIVATIVES WITH HYDROXY AND MERCAPTO COMPOUNDS

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Previously it was shown that the acid fluoride and esters of perfluoromethacrylic acid (PFMA) react easily with alcohols to give addition products at the C = C bond [1-3]. Phenol and certain mercaptans react in a similar manner with the acid fluoride of PFMA under somewhat more drastic conditions [2]. At the same time, a PFMA dialkylamide easily gives the substitution products of the vinyl fluorine atom when reacted with alcohols [3]. It seemed of interest to study the reactions of PFMA derivatives with other hydroxy compounds, in particular with acids.

It proved that the methyl ester of PFMA (I) reacts easily with carboxylic acids ($CH_3CO_2H$ and $CF_3CO_2H$) to give addition products (II):

$$CF_2{=}C(CF_3)COOCH_3\ (I) + RCOOH \longrightarrow RCOOCF_2CH(CF_3)COOCH_3\ (II)$$

R = $CH_3$ (a), $CF_3$ (b)

This reaction is completely uncharacteristic for either $\alpha,\beta$-unsaturated carbonyl compounds [4] or perfluoroolefins [5] (perfluoroisobutylene when heated with AcOH does not react in the absence of a catalyst [6]). It is obvious that (I) is so electrophilic that even weakly nucleophilic carboxylic acids can react with it without a catalyst. However, phenol and pentafluorophenol do not react with ester (I) under the same conditions: this seems strange, since it is difficult to assume that the nucleophilicity of $CF_3CO_2H$ is greater than the nucleophilicity of phenol.

As was to be expected, HCl, which is practically devoid of nucleophilic properties, does not react with ester (I) in the absence of a base, and gives adduct (III) only in the presence of a catalytic amount of pyridine (the addition of HCl to perfluoroisobutylene also requires catalysis by a base [7]).

$$CF_2{=}C(CF_3)COOCH_3\ (I) + HCl \xrightarrow[C_5H_5N]{} ClC(F)(CF_3)CHCOOCH_3\ (III)$$

The dimethylamide of PFMA (IV) behaves like ester (I) in the reactions with carboxylic acids (AcOH, $CF_3CO_2H$, benzoic acid), and readily forms the addition products (V).

$$CF_2{=}C(CF_3)CON(CH_3)_2\ (IV) + RCOOH \longrightarrow RCOOC(F)(CF_3)CHCON(CH_3)_2\ (V)$$

R = $CH_3$ (a), $CF_3$ (b), $C_6H_5$ (c)

In contrast to ester (I), amide (IV) also react with phenols ($C_6H_5OH$ and $C_6F_5OH$), but much more slowly than with carboxylic acids. The "vinyl" substitution products are formed with the unsubstituted phenol [cis form (VI) and trans form (VII)]; substantial amounts of $\alpha$-hydrohexafluoroisobutyric acid

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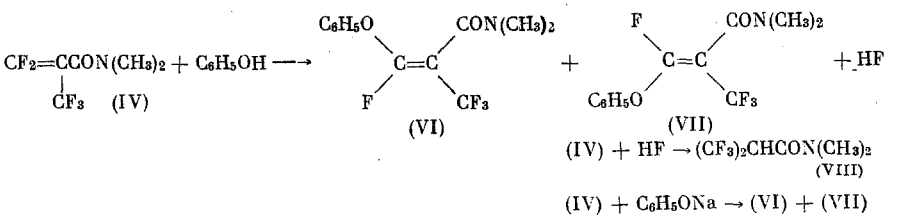
TABLE 1. Reaction of Perfluoromethacrylic Acid Dimethylamide (IV) with Hydroxy and Mercapto Compounds

| Hydroxy or mercapto compound | | Time for half reaction of amide (IV), h | Composition of formed mixture (amount, mole %) | | | |
|---|---|---|---|---|---|---|
| | | | addition product | substitution products | | α-hydrohexafluoroisobutyric acid dimethylamide (VIII) |
| formula | $pK_a$ | | | cis isomer | trans isomer | |
| $CH_3COOH$ | 4,7 [8] | <0,2 | (Va) (100) | — | — | — |
| $C_6H_5SH$ | 8,0 [8] | 5—10 | — | (XIIIa) (~55) | (XIVa) (~15) | (~30) |
| $C_6F_5OH$ | 5,5 [9] | 15—20 | (IX) (~80) | (X) (~5) | (XI) (~5) | (~10) |
| $C_6H_5CH_2SH$ | ~12 * | 30—40 | — | (XIIIб) (~45) | (XIVб) (~10) | (~45) |
| $C_6H_5OH$ | 9,9 [8] | ~100 | — | (VI) (~15) | (VII) (~50) | (~35) |
| $(CF_3)_2CHOH$ | 9,3 [10] | >800 | — | — | — | — |

* The $pK_a$ of ethyl mercaptan is given [8].

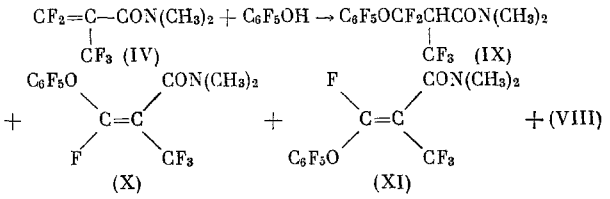
dimethylamide (VIII) are formed here, evidently by the addition of the liberated HF to the starting amide (IV). The substitution products (VI) and (VII) were also obtained by the reaction of amide (IV) with sodium phenoxide.



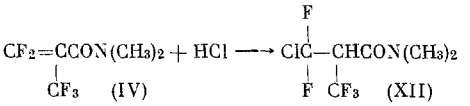
$(IV) + HF \rightarrow (CF_3)_2CHCON(CH_3)_2$ (VIII)

$(IV) + C_6H_5ONa \rightarrow (VI) + (VII)$

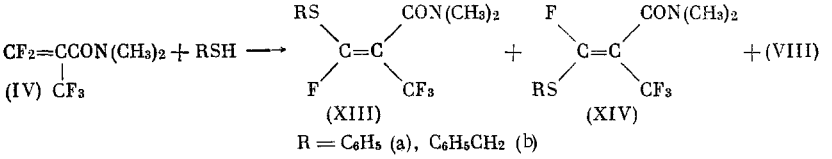
A stronger acid, namely pentafluorophenol, reacts with amide (IV) more rapidly than does phenol. Here the main product is the addition product (IX), while the substitution products (X) and (XI) are formed in small amounts (Table 1).



Hexafluoroisopropyl alcohol, whose acidity is close to that of phenol, does not react with dimethylamide PMFA. At the same time amide (IV), in contrast to ester (I), easily reacts with HCl without a catalyst in a nonpolar solvent (hexane) to give the addition product at the C = C bond (XII). Apparently, the basicity of the amide function is sufficient for the partial bonding of a proton; as a result, on the one hand, the amide (IV) molecule is activated, and, on the other hand, the nucleophilic $Cl^{\ominus}$ anion appears in the mixture. It is possible that the basicity of the amide function also plays an important role when a PFMA dialkylamide is reacted with carboxylic acids and with phenols.



The thiols, thiophenol and benzyl mercaptan, react quite slowly with amide (IV) (PhSH reacts more rapidly than $PhCH_2SH$) and form only the substitution products, (XIII) and (XIV), and α-hydrohexafluoroisobutyric acid dimethylamide (VIII).



R = $C_6H_5$ (a), $C_6H_5CH_2$ (b)

TABLE 2. NMR Spectra of Compounds $F^A$ / $YC^b$—$CHCOX$ / $F$ $CF_3$

| Compound | X | Y | Solvent | PMR spectrum[a] δ, ppm | | | PMR spectrum[a] J, Hz | | $^{19}F$[b] NMR spectrum chemical shift, ppm | | | $^{19}F$[b] NMR spectrum J, Hz | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | X | Y | CH | CH—$CF_3$ | CH—$CF_2$ | $CF_3$ | $F^A$ | $F^B$ | $CF_3$—CH | $CF_3$—$CF_2$ | $CF_2$—CH | $F^A$—$F^B$ |
| (IIa) | $OCH_3$ | $CH_3COO$ | — | 3,61 | 1,95 | 4,20 | 8,2 | 10,0 | —12,5 | —5,86 d. q.[c] | | 8,1 | 10,1 | 10,1 | — |
| (IIb) | $OCH_3$ | $CF_3COO$ | $CF_3COOH$ | 3,52 | — | 4,00 | 7,4 | 9,8 | —12,1[d] | —5,26 d. q.[c] | | 7,3 | 9,7 | 9,7 | — |
| (III) | $OCH_3$ | Cl | $CH_3CN$ | 3,43 | — | 3,91 m | — | — | —13,7 | —26,38 | —20,12 | 7,4 | 10,8 | 10,8 | 173 |
| (Va) | $N(CH_3)_2$ | $CH_3COO$ | $CH_3CN$ | 2,80 + 2,95 | 2,00 | 4,70 | 7,8 | 9,8 | —14,3 | —6,45 | —7,30 | 7,8 | 9,9 | 9,9 | 155 |
| (Vb) | $N(CH_3)_2$ | $CF_3COO$ | $CF_3COOH$ | 2,84 + 3,00 | — | 4,46 | 7,5 | 9,6 | —14,0[d] | —6,3[e] | | 7,4 | 9,7 | 9,7 | — |
| (Vc) | $N(CH_3)_2$ | $C_6H_5COO$ | $C_6H_6$ | 2,83 + 3,02 | 7,1—7,9 | 5,17m | — | — | —14,8 | —9,1 d. q.[c] | | 7,3 | 9,9 | 9,9 | — |
| (IX) | $N(CH_3)_2$ | $C_6F_5O$ | $CH_3CN$ | 2,74 + 2,95 | — | 4,70 | 7,5 | 7,4 | —13,4[f] | —7,4 m | | 7,4 | 8,8 | — | — |
| (XII) | $N(CH_3)_2$ | Cl | $CH_3CN$ | 2,85 + 3,00 | — | 4,75 | 7,2 | 9,9 | —14,7 | —24,41 | —28,39 | 7,1 | 9,7 | 9,9 | 165 |
| (XV) | $N(CH_3)_2$ | $CH_3COS$ | $CH_3CN$ | 2,78 + 2,95 | 2,15 | 4,90 | 7,7 | 13,1 | —15,8 | —1,48 | —5,41 | 7,6 | 10,1 | 13,2 | 242 |

*a) $CH_3CO$ s, $C_6H_5$ m, $OCH_3$ s, $N(CH_3)_2$ two s, CH t. q. b) $CF_3$ d. t, $F^A$ and $F^B$ (AB system with splitting into d. q); $C_6F_5$ in compound (IX) = three multiplets at ~ 74, ~ 79, and ~ 85 ppm. c) $F^A$ and $F^B$ are equivalent. d) Signals from $CF_3CO$ group: (IIb) — 1.0 s, (Vb) — 0.8 s. e) Multiplet (center of AB portion of ABMX, system). f) Broad signal due to additional splitting.

TABLE 3. $^{19}F$ NMR Spectra of Compounds YCF = $\overset{|}{C}CON(CH_3)_2$ ($CF_3$)

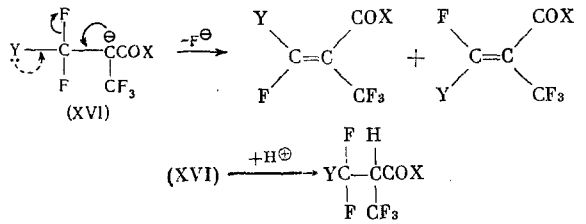
| Y | cis Isomer | | | | trans Isomer | | | |
|---|---|---|---|---|---|---|---|---|
| | Compound | chemical shift, ppm | | J, Hz | Compound | chemical shift, ppm | | J, Hz |
| | | $CF_3$* | CF* | | | $CF_3$* | CF* | |
| $C_6H_5O$ | (VI) | −20,7 | −5,2 | 16,1 | (VII) | −20,3 | −7,1 | 12,1 |
| $C_6F_5O$ | (X) | −19,1† | — | 16,6 | (XI) | −18,2† | — | 11,5 |
| $C_6H_5S$ | (XIIIa) | −20,0 | −2,5 | 16,2 | (XIVa) | −21,6 | −6,5 | 12,2 |
| $C_6H_5CH_2S$ | (XIIIb) | −20,4 | −2,3 | 16,4 | (XIVб) | −23,9 | −4,1 | 12,9 |

* $CF_3$, d, CF q.
† The signals are broad due to additional couplings.

Thioacetic acid reacts easily with amide (IV), but here a mixture of products was obtained, from which we were able to isolate the thiolacetyl derivative (XV) in low yield.

$$CF_2{=}C(CF_3)CON(CH_3)_2\ (IV) + CH_3COSH \longrightarrow CH_3COSC(F)(CF_3)CH(F)CON(CH_3)_2\ (XV)$$

The reaction rate of the PFMA derivatives with nucleophiles as a function of the character of the latter does not lend itself to simple treatment. For dimethylamide (IV) the reaction rate with nucleophiles decreases in the following order: RCOOH ($pK_a$ 0.2-4.7) > AlkOH ($pK_a \sim 18$) > $C_6H_5SH$ ($pK_a$ 8.0) > $C_6F_5OH$ ($pK_a$ 5.5) > $C_6H_5CH_2SH$ ($pK_a \sim 12$) > $C_6H_5OH$ ($pK_a$ 9.9) ≫ $(CF_3)_2CHOH$ ($pK_a$ 9.3). As can be seen, this order in no way coincides with the order of change in the acidity. It is possible that the reaction mechanism changes when the nature of the nucleophile changes substantially. Depending on the acidity of the reagent, in the case of dimethylamide (IV) the basic properties of the amide function ("intramolecular basic catalysis") can exert a variable effect. In any case, these problems require further study. The same can also be said concerning the reasons for the different direction of the reactions of PFMA derivatives with nucleophiles. The great tendency of amide (IV) to give substitution products is probably also related to the basic properties of the amide function (cf. [3]). In addition, the +M effect of the Y substituent should play an important role in the formation of the substitution products, since it facilitates the cleavage of $F^{\ominus}$ anion from the intermediately formed particle, for example, from carbanion (XVI). If the +M effect is small, a large amount (or even exclusively) of the addition product is formed due to attack by the proton on the carbanion center. When reacted with carboxylic acids (Y = RCOO), both ester (I) and amide (IV) give only addition products, which is evidently explained by the electron-withdrawing effect of the RCO group.



Previously it was shown that when perfluoroisobutylene is reacted with AcOH in the presence of $Et_3N$ it gives the decomposition products of the intermediately formed adduct, namely $CH_3COF$ and $(CF_3)_2CHCOF$ [6]. It proved that the addition products of carboxylic acids to PFMA derivatives when heated [and adduct (Vb) also at room temperature] also decompose in a similar manner into two acid fluorides: RCOF and (XVII). These transformations represent a convenient method for the preparation of trifluoromethylmalonic acid derivatives that contain one acid fluoride function.

$$RCOOCF_2CH(CF_3)COX \longrightarrow RCOF + FCOCH(CF_3)COX$$

(IIa), (Va, b) (XVII)

X = $OCH_3$ (XVIIa), $N(CH_3)_2$ (XVIIb)

## EXPERIMENTAL METHOD

The PMR spectra were taken on a Perkin–Elmer R-12 spectrometer (60 MHz) using TMS as the external standard, while the $^{19}F$ NMR spectra were taken on Hitachi (56.46 MHz) and Perkin–Elmer R-20 (56.46 MHz) spectrometers using $CF_3COOH$ as the external standard. The chemical shifts are given in parts per million from TMS and $CF_3COOH$, respectively. The NMR spectra of the obtained compounds are given in Tables 2 and 3. The IR spectra were taken by L. P. Volkova on a UR-20 spectrometer (as a thin layer).

Methyl Ester of α-Hydro-β-acetoxypentafluoroisobutyric Acid (IIa). To 5.7 g of the methyl ester of PFMA (I) was added 1.8 g of AcOH in drops. When exothermic reaction had ceased the mixture was distilled to give 4.6 g (61%) of ester (IIa), bp 48-49° (3 mm). Found: C 33.89; H 2.86; F 38.01%. $C_7H_7F_5O_4$. Calculated: C 33.62; H 2.82; F 37.98%.

α-Hydro-β-acetoxypentafluoroisobutyric Acid N,N-Dimethylamide (Va). The same as the preceding, from 5.7 g of PFMA dimethylamide (IV) and 2.3 g of AcOH we obtained 6.6 g (89%) of amide (Va), bp 86-87° (2 mm). Found: C 36.41; H 3.90; F 37.43; N 5.33%. $C_8H_{10}F_5NO_3$. Calculated: C 36.51; H 3.83; F 36.10; N 5.32%. Infrared spectrum ($\nu$, $cm^{-1}$); 1675 (C = O), 1800 (C = O).

Methyl Ester of α-Hydro-β-trifluoroacetoxypentafluoroisobutyric Acid (IIb). Excess $CF_5COOH$ was added to a small amount of methyl ester (I). Via the $^1H$ and $^{19}F$ NMR spectra it was found that the starting ester (I) is converted completely to the addition product (IIb) in ~ 0.5 h. A solution of ester (IIb) in $CF_3COOH$ is stable at ~ 20°.

α-Hydro-β-trifluoroacetoxypentafluoroisobutyric Acid N,N-Dimethylamide (Vb). Amide (Vb) was obtained in a similar manner (without isolation) from the PFMA dimethylamide (IV). Amide (Vb) when kept at ~ 20° for a day decomposes almost completely into $CF_3COF$ [$^{19}F$ NMR spectrum: −1.7 d ($CF_3$); − 92.0 g (COF), $J_{CF_3-COF}$ = 6.5 Hz] and the acid fluoride of the N,N-dimethylamide of trifluoromethylmalonic acid (XVIIb) (data of $^1H$ and $^{19}F$ NMR spectra).

α-Hydro-β-benzoyloxypentafluoroisobutyric Acid N,N-Dimethylamide (Vc). A solution of excess benzoic acid in benzene was added to a small amount of dimethylamide (IV). After several hours at ~20° it was found via the NMR spectra that amide (IV) is converted completely to the addition product (Vc). The latter product is stable at ~ 20°.

α-Hydro-β-chloropentafluoroisobutyric Acid N,N-Dimethylamide (XII). Excess dry HCl was passed slowly into a mixture of 3.9 g of dimethylamide (IV) and 4 ml of hexane. The precipitate of amide (XII) obtained on conclusion of exothermic reaction weighed 2.8 g (69%), mp 68-69° (from hexane). Found: C 29.93; H 2.96; F 39.74; N 5.56%. $C_6H_7ClF_5NO$. Calculated: C 30.08; H 2.95; F 39.65; N 5.85%.

Methyl Ester of α-Hydro-β-chloropentafluoroisobutyric Acid (III). Excess dry HCl was passed into a solution of a small amount of methyl ester (I) in a hexane–benzene mixture (no reaction according to the NMR spectrum); then one drop of pyridine was added and HCl was passed in again, after which the solvents were vacuum-distilled, and the residue proved to be almost pure ester (III) (identified by the NMR spectra).

α-Trifluoromethyl-β-fluoro-β-phenoxyacrylic Acid N,N-Dimethylamides (VI) and (VII). With stirring, 2.3 g of dry sodium phenoxide was gradually added at ~ 20° to a solution of 3.4 g of dimethylamide (IV) in 25 ml of abs. ether; the mixture was stirred for another 1.5 h, and the precipitate was filtered. Distillation of the filtrate gave 3.5 g (76%) of a mixture of crude unsaturated amides (VI) and (VII), bp 118-120° (2 mm). PMR spectrum: 2.48 and 2.66, two s [$(CH_3)_2N$, cis isomer (VI)]; 2.58 and 2.69, two s [$(CH_3)_2N$, trans isomer (VII)], ~ 6.9 m ($C_6H_5$).

α-Hydro-β-pentafluorophenoxypentafluoroisobutyric Acid N,N-Dimethylamide (IX). A mixture of 1.8 g of dimethylamide (IV), 1.5 g of pentafluorophenol, and 2.5 ml of benzene was refluxed for 2.5 h. Distillation gave 2.0 g (68%) of crude addition product (IX), bp 115° (1 mm). The product is contaminated with amides (X) and (XI) (NMR spectra).

α-Hydro-β-thiolacetylpentafluoroisobutyric Acid N,N-Dimethylamide (XV). To 6.3 g of dimethylamide (IV) was added 2.4 g of thioacetic in drops. When exothermic reaction had ceased the mixture was distilled to give 1.6 g (18%) of amide (XV), bp 92-93° (3 mm). Found: C 34.41; H 3.54; F 34.13; N 5.43%. $C_8H_{10}F_5NC_2S$. Calculated: C 34.41; H 3.61; F 34.02; N 5.02%. Infrared spectrum ($\nu$, $cm^{-1}$) 1670 (C = O), 1720 (C = O).

Reaction of Dimethylamide (IV) with Hydroxy and Mercapto Compounds. A solution of equimolar amounts of the reactant and dimethylamide (IV) in a little benzene was kept at ~20°. To approximately determine the half-reaction times of the starting amide (IV) the reaction products were analyzed via the $^{19}F$ NMR spectra; then the mixtures were kept until the conversion of amide (IV) was almost complete, and the compositions of the formed mixtures were determined (see Table 1).

Acid Fluoride of Acid Methyl Ester of Trifluoromethylmalonic Acid (XVIIa). The methyl ester of α-hydro-β-acetoxypentafluoroisobutyric acid (IIa) (2.3 g) was refluxed for 10 min using an air condenser (bath temperature ~0.5 g (~90%) of $CH_3COF$. Distillation of the residue gave 1.5 g (87%) of acid fluoride (XVIIa), bp 121-123°. Found: C 32.57; H 2.14; F 41.36%. $C_5H_4F_4O_3$. Calculated: C 31.93; H 2.14; F 40.41%. PMR spectrum: 3.56 s ($CH_3O$); 4.31 q (CH), $J_{CH-CF_3}$ = 7.7 Hz. $^{19}F$ NMR spectrum: −11.4 d.d ($CF_3$); −123.4 q (COF), $J_{CF_3-COF}$ = 9.9, $J_{CF_3-CH}$ = 7.7 Hz.

Acid Fluoride of N,N-Dimethylamide of Trifluoromethylmalonic Acid (XVIIb). In a similar manner, from 4.4 g of α-hydro-β-acetoxypentafluoroisobutyric acid dimethylamide (Va) after 40 min (bath temperature 145-150°) we obtained ~1 g (~95%) of $CH_3COF$ [PMR spectrum: 1.74 d ($CH_3$), $J_{CH_3-COF}$ = 7.5 Hz. $^{19}F$ NMR spectrum: −127.1 q (COF), $J_{COF-CH_3}$ = 7.5 Hz] and 1.8 g (54%) of acid fluoride (XVIIb), bp 79-80° (1 mm). Found: C 35.76; H 3.89; F 38.03; N 6.78%. $C_6H_6F_4NO_2$. Calculated: C 35.83; H 3.51; F 37.79; N 6.96%. PMR spectrum (in $CH_3CN$): 2.87 and 3.04, two s [$(CH_3)_2N$; 5.23 d.q (CH), $J_{CH-COF}$ = 3.6, $J_{CH-CF_3}$ = 7.2 Hz. $^{19}F$ NMR spectrum (in $CH_3CN$): −11.7 d.d ($CF_3$); −119.7 d.q (COF), $J_{CF_3-CH}$ = 7.2, $J_{CF_3-COF}$ = 11.3, $J_{COF-CH}$ = 3.6 Hz.

## CONCLUSIONS

1. Perfluoromethacrylic acid derivatives (methyl ester and dimethylamide) easily add carboxylic acids at the C=C bond to give comparatively stable α-hydro-β-acyloxypentafluoroisobutyric acid derivatives. These adducts when heated are cleaved to the corresponding acyl fluoride and α-hydro-α-fluorocarbonyltrifluoropropionic acid derivative.

2. Hydrogen chloride adds to the perfluoromethacrylic acid dimethylamide to give the α-hydro-β-chloropentafluoroisobutyric acid derivative. The perfluoromethacrylic acid ester reacts in a similar manner only in the presence of a base.

3. The perfluoromethacrylic acid dimethylamide when reacted with phenol, thiophenol, and benzyl mercaptan gives the substitution products of the vinyl fluorine atom (mixture of cis and trans isomers), while with pentafluorophenol it gives a mixture of substitution and addition products.

4. The reaction rate of the perfluoromethacrylic acid dimethylamide with nucleophiles decreases in the order: RCOOH > AlkOH > $C_6H_5SH$ > $C_6F_5OH$ > $C_6H_5CH_2SH$ > $C_6H_5OH$ ≫ $(CF_3)_2CHOH$.

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