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Catalysts for Promoting Direct Esterification of Fluoroalcohols

▶ **Esters derived from $H(CF_2)_nCH_2OH$ and $F(CF_2)_nCH_2OH$ alcohols and hydrocarbon carboxylic acids have exceptional stability to oxidation, hydrolysis, and pyrolysis. Suitable solvents and solvent combinations permit direct esterification of these alcohols with a variety of acid catalysts.**

FLUOROALCOHOLS, $F(CF_2)_nCH_2OH$, have been generally regarded as "difficultly esterifiable alcohols" (*1*, *8*, *10*). Presumably $H(CF_2)_nCH_2OH$ alcohols behave similarly, as they have similar structures and comparable acidities. It has been reported that direct esterification of $F(CF_2)_3CH_2OH$ and hydrocarbon carboxylic acids in the presence of acid catalysts does not proceed at a practicable rate, but that esterification does proceed by refluxing the fluoro alcohol with the appropriate acid chloride (*8*). The use of catalytic amounts of aluminum chloride greatly accelerates the latter reaction (*10*). $F(CF_2)_nCH_2OH$ has been esterified with acrylic acid, using large quantities of trifluoroacetic anhydride (*1*, *4*). Methanesulfonic acid anhydride has also been reported to resemble trifluoroacetic anhydride in promoting esterification reactions (*7*).

Esters derived from $H(CF_2)_nCH_2OH$ and $F(CF_2)_nCH_2OH$ alcohols and hydrocarbon carboxylic acids are of interest for a variety of applications because of their exceptional stability to oxidation, hydrolysis, and pyrolysis (*5*). Because larger amounts of these materials are needed to determine their usefulness for specific applications, simpler methods for their production are desired.

To facilitate discussion the same abbreviated names for fluoroalcohols and their esters are employed here as in an earlier report (*5*). Thus $H(CF_2)_nCH_2OH$ alcohols are designated as ψ'-alkyl alcohols and $F(CF_2)_nCH_2OH$ alcohols as ϕ'-alkyl alcohols. Bis (ψ'-amyl) glutarate and bis(ϕ'-butyl) glutarate refer to glutaric acid diesters of $H(CF_2)_4CH_2OH$ and $F(CF_2)_3CH_2OH$, respectively.

Experiments with Acid Catalysts

Esters have been prepared directly from both classes of fluoroalcohols and a variety of hydrocarbon carboxylic acids, using *p*-toluenesulfonic acid as a catalyst (*5*). Along with relative slowness, this process poses purification problems. The removal of ψ'-alkyl *p*-toluenesulfonates (tosylates) obtained as by-products in direct esterifications is unusually difficult because of their high boiling points, and their unexpected resistance to pyrolysis and hydrolysis (*6*). Properties of ψ'-heptyl tosylate, a representative member of this class, are summarized in Table I. It distills at between 290° and 300° C. at 760 mm. with slight decomposition and is hydrolyzed only about 5% after 24 hours' reflux with a stoichiometric quantity of 10% sodium hydroxide. As the tosylate ester boils at 126° C. at 0.5 mm., repeated distillations are required to remove it from the desired bis(ψ'-heptyl) 3-methylglutarate boiling at 150° C. at 0.5 mm.

Studies were therefore undertaken to determine whether alkanesulfonic acid catalysts would promote faster esterifications and permit easier purifications. Table II shows that in the preparation of bis(ψ'-amyl) glutarate and phthalate, ethanesulfonic acid offered only small gains in speed over the *p*-toluenesulfonic acid. By contrast methanesulfonic acid gave a five- or sixfold increase in esterification rate. Properties of ψ'-heptyl methanesulfonate and ψ'-heptyl ethanesulfonate are given in Table I. Unlike the heat-labile alkyl alkanesulfonates, fluoroalkyl alkanesulfonates are stable thermally and show little tendency toward olefin or ether formation. They are resistant to attack by 10% aqueous sodium hydroxide at 100° C. or by reagents such as $H(CF_2)_nCH_2ONa$. In contrast, *n*-alkyl alkanesulfonates undergo facile hydrolysis with aqueous caustic and react by familiar displacement reactions to give symmetrical ethers (*12*). Resistance to hydrolysis of the ψ'-heptyl alkanesulfonates resembles that of phenyl methanesulfonate (*9*).

Under experimental conditions both alkanesulfonic acids formed esters with the fluoroalcohols. For example, ethanesulfonic acid reacted directly with ψ'-heptyl alcohol in refluxing carbon tetrachloride (see Table II). Although these esters could be removed by distillation with less difficulty than the tosylate ester, such methods are not amenable to plant production.

Studies were therefore made to determine the usefulness of sulfuric, phosphoric, and formic acids as esterifica-

Table I. Hydrocarbon Sulfonic Acid Esters of ψ′-Heptyl Alcohol

Compound	Formula	Boiling Point				Melting Point,	
		° C.	Mm.	n_{D}^{20}	d_4^{20}	° C.	AR_{F}[a]
ψ′-Heptyl *p*-toluenesulfonate[b]	$C_{14}H_{10}F_{12}O_3S$	126	0.5	1.4123	1.592	*ca.* 33	1.19
ψ′-Heptyl methanesulfonate[c]	$C_8H_6F_{12}O_3S$	146 92	20.0 1.0	1.3490	1.7372	−4	1.118
ψ′-Heptyl ethanesulfonate[d]	$C_9H_8F_{12}O_3S$	100	0.3	1.3540	1.6695	−9	1.111

[a] Atomic refractivity of fluorine calculated by subtracting atomic constants by Vogel (*14*) and the —O—SO_2 group refractivity (*13*) of 10.5 from observed Lorentz-Lorenz molecular refraction.
[b] Properties as reported in (*7*).
[c] Prepared by refluxing CH_3SO_2Cl and $H(CF_2)_6CH_2OH$ for 100 hours in a stream of nitrogen.
[d] Prepared as indicated in Table II.

Table II. Effect of Catalyst on Direct Esterification of Fluoroalcohols

	Reactants		Catalyst			Reflux Time[a],	Esterification Water, Ml.		Yield[b],
Ester	Acid, mole	Alcohol, mole	Compound	Grams	Solvent	Hours	Found	Theory	%
Bis(φ′-butyl) 3-methylglutarate	0.10	0.25	H_2SO_4	1.0	CCl_4/C_6H_6	8–12	3.7	3.6	80.0
	1.00	2.20	*p*-$CH_3C_6H_4SO_3H$	2.0	$CCl_4/C_6H_5CH_3$	48	36.4	36.0	82.8
Bis(φ′-hexyl) 3-methylglutarate	0.10	0.25	H_2SO_4	1.0	$CCl_4/C_6H_5CH_3$	8–12	4.3	3.6	78.0
	0.06	0.16	*p*-$CH_3C_6H_4SO_3H$	2.0	$CCl_4/C_6H_5CH_3$	48	2.2	2.2	84.2
Bis(ψ′-propyl) 3-methylglutarate	0.20	0.45	H_2SO_4	1.0	C_6H_6	8–10	8.7	7.2	86.5
Bis(ψ′-amyl) glutarate	0.10	0.25	None	None	CCl_4	3	0	3.6	..
	0.10	0.25	H_2SO_4	1.0	CCl_4	7–10	3.9	3.6	81.3
	0.60	1.40	$C_2H_5SO_3H$	2.6	CCl_4	40	21.6	21.6	81.2
	0.10	0.25	CH_3SO_3H	2.0	C_6H_6	9–12	3.6	3.6	82.5
	0.60	1.40	*p*-$CH_3C_6H_4SO_3H$	2.0	$C_6H_5CH_3$	48	21.6	21.6	92.1
Bis(ψ′-amyl) phthalate	0.10	0.25	H_2SO_4	1.0	CCl_4	24	3.7	3.6	93.8
	0.10	0.25	H_2SO_4	3.0	CCl_4	24	4.0	3.6	[c]
	0.10	0.25	H_2SO_4	0.1	CCl_4	72	3.5	3.6	[c]
	0.10	0.25	H_3PO_4	1.0	CCl_4	72	2.5	3.6	[c]
	0.60	1.40	$C_2H_5SO_3H$	6.0	CCl_4	146	21.6	21.6	81.3
	0.63	1.56	*p*-$CH_3C_6H_4SO_3H$	2.0	$C_6H_5CH_3$	196	20.2	22.7	78.0
Tris(ψ′-amyl) tricarballylate	0.15	0.55	H_2SO_4	1.0	CCl_4	24	7.4	8.1	74.8
	0.46	1.48	*p*-$CH_3C_6H_4SO_3H$	2.0	$C_6H_5CH_3$	196	23.0	24.9	76.0
Bis(ψ′-heptyl) 3-methylglutarate	0.10	0.25	H_2SO_4	1.0	$C_6H_5CH_3$	4	3.6	3.6	79.2
	0.10	0.25	H_2SO_4	1.0	$C_6H_5CH_3$	1–2[d]	3.6	3.6	78.0
	0.60	1.30	*p*-$CH_3C_6H_4SO_3H$	2.0	$C_6H_5CH_3$	48	21.0	21.6	87.2
ψ′-Nonyl 2-ethylhexanoate	0.10	0.15	H_2SO_4	1.0	$C_6H_5CH_3$	6	1.9	1.8	76.8
	0.60	0.45	*p*-$CH_3C_6H_4SO_3H$	2.0	$C_6H_5CH_3$	88	7.8	8.1	94.0
ψ′-Heptyl ethanesulfonate	0.23	0.30	.....	..	CCl_4	100	4.1	4.2	48.0

[a] Minimum time required to establish constant volume reading of aqueous layer.
[b] Yields of distilled ester are based on limiting reactant.
[c] Distillations were not made to determine yield.
[d] Reaction mixture was stirred.

Table III. Effect of Solvent on Direct Esterification of Fluoroalcohols

	Reactants		Catalyst			Reflux Time[a],	Esterification Water, Ml.		Yield
Ester	Acid, mole	Alcohol, mole	Compound	Grams	Solvent	Hours	Found	Theory	%
Bis(φ′-butyl) 3-methylglutarate	0.10	0.25	H_2SO_4	1.0	C_6H_6	3	[b]	3.6	[c]
	0.10	0.25	H_2SO_4	1.0	$C_6H_5CH_3$	3	[b]	3.6	[c]
	0.10	0.25	H_2SO_4	1.0	CCl_4	3	[b]	3.6	[c]
	0.10	0.25	H_2SO_4	1.0	$CHCl_3$	20	4.0	3.6	33
	0.10	0.25	H_2SO_4	1.0	$CHCl_3/CCl_4$	40	3.8	3.6	60
	0.10	0.25	H_2SO_4	1.0	CCl_4/C_6H_6	8–12	3.7	3.6	80
	1.00	2.20	*p*-$CH_3C_6H_4SO_3H$	2.0	$CCl_4/C_6H_5CH_3$	48	36.4	36.0	82.8
Bis(φ′-hexyl) 3-methylglutarate	0.10	0.25	H_2SO_4	1.0	CCl_4	16	3.7	3.6	71.0
	0.10	0.25	H_2SO_4	1.0	$CCl_4/C_6H_5CH_3$	8–12	4.3	3.6	78.0
Bis(ψ′-propyl) 3-methylglutarate	0.20	0.45	H_2SO_4	1.0	CCl_4	3	[b]	3.6	[c]
	0.20	0.45	H_2SO_4	1.0	$CHCl_3$	28	8.0	7.2	64.0
	0.20	0.45	H_2SO_4	1.0	$CHCl_3/CCl_4$	40	8.0	7.2	79
	0.20	0.45	H_2SO_4	1.0	CCl_4/C_6H_6	12–18	8.7	7.2	[c]
	0.20	0.45	H_2SO_4	1.0	C_6H_6	8–10	8.7	7.2	86.5
Bis(ψ′-amyl) glutarate	0.10	0.25	H_2SO_4	1.0	CCl_4	7–10	3.9	3.6	81.3
	0.10	0.25	CH_3SO_3H	2.0	$C_6H_5CH_3$	8–9	3.6	3.6	82.5
Bis(ψ′-amyl) phthalate	0.10	0.25	H_2SO_4	1.0	CCl_4	24	3.7	3.6	93.8
Bis(ψ′-heptyl) 3-methylglutarate	0.10	0.25	H_2SO_4	1.0	$C_6H_5CH_3$	4	3.6	3.6	79.2
	1.50	3.20	H_2SO_4	6.0	$C_6H_5CH_3$	10[d]	54.0	54.0	88.7
	0.20	0.50	H_2SO_4	2.0	$ClCH_2CH_2Cl$	24[d]	7.2	7.2	90.5
	2.60	5.50	H_2SO_4	5.0	$ClCH_2CH_2Cl$	40[d]	93.7	94.0	93.0
ψ′-Nonyl 2-ethylhexanoate	0.10	0.15	H_2SO_4	1.0	$C_6H_5CH_3$	6	1.9	1.8	76.8

[a] Minimum time required to establish a constant volume reading of the aqueous layer collected in the water trap.
[b] Azeotropic removal and collection of water could not be accomplished with this solvent system, using 12-inch Vigreux column condenser and appropriate water traps.
[c] Distillations were not made to determine yields.
[d] Reaction mixture was stirred.

tion catalysts. These acids were chosen because previous work showed that their ψ'-alkyl esters underwent facile hydrolysis with dilute caustic solution. Experiments with sulfonic acid catalysts indicated that esterification rates were fastest when the hydrocarbon substituent was small. On this basis it was reasoned that sulfuric acid would give faster esterification rates. The data of Table II fully substantiate this hypothesis. As a catalyst sulfuric acid promoted esterifications six to 14 times faster than did *p*-toluenesulfonic acid or ethanesulfonic acid. Comparable reaction rates were observed for the esterification of ψ'-amyl alcohol and glutaric acid, using either methanesulfonic acid or sulfuric acid as catalysts. Since sulfuric acid is insoluble in the reaction mixtures listed in Table II, the rate of esterification can be accelerated by stirring to increase the surface contact between the liquid phases.

It was observed that both ψ'-alkyl and ϕ'-alkyl alcohols reacted with sulfuric acid to form esters. The reaction of ψ'-alkyl alcohols with sulfuric acid and sulfur trioxide to form unsymmetrical ψ'-alkyl sulfates has been reported (*2*). Slow reaction of ϕ'-alkyl alcohols with sulfuric acid has also been noted (*11*). Sulfuric acid esters of fluoroalcohols were readily decomposed and the acid was removed from the reaction mixture by washing with dilute caustic solution.

Phosphoric acid (85%) promoted esterification at about the same rate as *p*-toluenesulfonic acid, but was less efficient than sulfuric acid. The difficulty of maintaining formic acid in the reaction mixture made it appear unpromising as an esterification catalyst for the acids investigated. However, formate esters of fluoroalcohols may be prepared by methods resembling those used in the preparation of *n*-alkyl formates. For example, ψ'-heptyl formate was obtained in 87% yield by filtering and distilling a previously refluxed mixture of formic acid (1.0 mole), ψ'-heptyl alcohol (0.5 mole), and 100 grams of anhydrous copper sulfate. Here, formic acid acts as a catalyst for its own esterification and water is removed by chemical means.

Effect of Solvents

Experimental results with different solvents are summarized in Table III. In all esterifications a 12-inch Vigreux column was used between the pot and the condenser. Appropriate traps were employed to collect and measure the esterification water and to return the condensed solvent phase. Neither benzene nor carbon tetrachloride was effective in removing water from esterifications containing ϕ'-butyl alcohol, but for different reasons. Benzene (boiling point 80° C.) was ineffective because the dense alcohol (boiling point 97–98° C.) accumulated in the hydrocarbon layer and reversed the density relationship between that layer and the aqueous layer. ϕ'-Butyl alcohol was moderately soluble in refluxing carbon tetrachloride but only slightly soluble in the cooled condensate. Two mutually saturated phases separated in the trap—a wet fluoroalcohol layer above and a carbon tetrachloride layer below. As water is moderately soluble in the fluoroalcohol, this prevented the isolation of water.

After the failure to remove esterification water with benzene or carbon tetrachloride, the esterification of ϕ'-butyl alcohol was tried with a mixture of the two solvents. Water was effectively separated with this solvent combination (30 to 70% by volume carbon tetrachloride) and a good yield of bis (ϕ'-butyl) 3-methylglutarate was obtained. With this mixed solvent system the necessary density relationship between the aqueous and nonaqueous phase is maintained throughout the reaction. The ϕ'-butyl alcohol is continuously extracted from the upper aqueous phase by the condensing benzene-carbon tetrachloride solution. A carbon tetrachloride–toluene solution is equally effective for the esterification of ϕ'-butyl alcohol. The same combination of solvents was also effective in removing water from esterification with ϕ'-hexyl and ϕ'-octyl alcohols.

In contrast to the ϕ'-butyl alcohol (boiling point 97–98° C.), ψ'-propyl alcohol (boiling point 109° C.) may be readily esterified using benzene (boiling point 80° C.) as a solvent for the azeotropic removal of water. Higher ψ'-alkyl alcohols may be esterified using carbon tetrachloride, ethylene dichloride, benzene, or toluene (see Table III). In general, aromatic solvents gave faster esterifications than did the chlorinated solvents. Sulfuric acid–catalyzed esterifications produced high yields of esters with either class of solvent. Some charring of the reaction mixture was observed in the presence of aromatic solvents, but this discoloration was readily removed by distillation. Charring was greatly reduced or eliminated when chlorinated solvents were used. Undoubtedly many other solvents and solvent combinations can be obtained for the satisfactory esterification of ψ'- and ϕ'-alkyl alcohols.

Small amounts of ψ'-alkyl *p*-toluenesulfonates cause a substantial decrease in the electrical resistivity of bis(ψ'-alkyl) esters of hydrocarbon carboxylic acids (*3*). Esters prepared using aromatic solvents and sulfuric acid also have comparatively low resistivities (*3*). Under comparable conditions esters prepared using chlorinated solvents have higher resistivities (*3*). On the basis of these data, the sulfuric acid catalyst should be used with solvents which resist sulfonation, if fluoro esters of higher purity are desired.

Conclusions

Direct esterification of $H(CF_2)_nCH_2OH$ and $F(CF_2)_nCH_2OH$ with hydrocarbon carboxylic acids has been accomplished with a variety of acid catalysts. In the approximate order of their increasing catalytic activity, they are phosphoric acid, *p*-toluenesulfonic acid, ethanesulfonic acid, methanesulfonic acid, and sulfuric acid. A side reaction between fluoroalcohols and sulfonic acid catalysts produces thermally and hydrolytically stable sulfonate esters which are difficult to separate from the product. Analogous side reactions occur with fluoroalcohols and the sulfuric acid catalyst. However, the sulfate esters of fluoroalcohols undergo facile hydrolysis with dilute caustic solution and the acid is readily removed from the product.

Earlier efforts at the direct esterification of $F(CF_2)_3CH_2OH$ probably failed because unusual solubility and density phenomena prevented the effective removal of water. Suitable solvents and solvent combinations are given for the esterification of fluoroalcohols of the general formulas, $H(CF_2)_nCH_2OH$, where *n* is 2 or more, and $F(CF_2)_nCH_2OH$, where *n* is 3 or more.

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