♣Reactions of Glycerol Derivatives with N,N-Diethyl-1,1,2,3,3,3-hexafluoropropanamine

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ABSTRACT

Fluorination of mono- and disubstituted glycerols with N,N-diethyl-1,1,2,3,3,3-hexafluoropropanamine (PPDA) was attempted. Instead of the expected fluoroglycerol derivative from a disubstituted glycerol, the major product was the fluorinated propyl ester. Thus, 2,3-dibromopropyl 2,3,3,3-tetrafluoropropionate was isolated in 52% yield from the reaction of 2,3-dibromo-1-propanol with PPDA. With a monosubstituted glycerol, a cyclic adduct was obtained. Thus, 4-allyloxymethyl-2-diethylamino-2-(1,2,2,2-tetrafluoroethyl)-1,3-dioxolane was isolated in 68% yield from 3-allyloxy-1,2-propanediol and PPDA. Shielding by the bromine atoms in the former reaction and intramolecular nucleophilic attack by the vicinal hydroxyl group in the latter reaction are possible explanations for the reaction results.

INTRODUCTION

Fluorinated compounds have been used widely in biochemical investigation and surface active agents. Recently, we have reported that 1,1,2,3,3,3-hexafluoropropyldiethylamine (PPDA) is useful as a fluorinating agent for fatty alcohols (1,2) and diols (3). However, the reaction of glycerine derivatives with PPDA is not well known. On examination of this reaction, we found that cyclic adducts of PPDA or 2,3,3,3-tetrafluoropropionates are obtained in moderate yields from a variety of glycerine derivatives and PPDA.

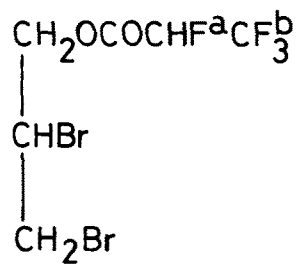
EXPERIMENTAL

Reaction of 2,3-Dibromo-1-propanol (I) with PPDA

A solution of PPDA (4.0 g, 18 mmol) in dry tetrahydrofuran (10 mL) was added dropwise into a solution of 2,3-dibromo-1-propanol (I) (2.18 g, 10 mmol) in tetrahydrofuran (10 mL) at room temperature. After having been stirred for 6 hr at 40-50 C, the reaction mixture was left overnight. It was then added to water (50 mL) and the oily product was extracted with diisopropyl ether. The ether extract was washed with water, dried over anhydrous sodium carbonate, filtered, and evaporated to remove the solvent. The residue was distilled with a small spinning type column to give the following fractions: (i) 90-98 C/19 mmHg, 1.3 g; (ii) 98-99 C/19 mmHg, 2.3 g.

Analysis of fraction (i) indicated that it was a mixture of N,N-diethyl-2,3,3,3-tetrafluoropropioamide (70%), an unidentified product (5%), unreacted (I) (7%) and 2,3-dibromopropyl 2,3,3,3-tetrafluoropropionate (II) (20%). Fraction (ii) was a mixture of the amide (2%), an unidentified product (1%), unreacted (I) (7%) and 2,3-dibromopropyl 2,3,3,3-tetrafluoropropionate (II) (90%). These compositions were determined by gas chromatography. [Shimadzu GC-3BF, column Silicone DC 200 (10%) on Celite 545 (3m), temperature 150 C, carrier gas N_2, 40 mL min^{-1}.] Fraction (ii) was redistilled to give 1.8 g (yield 52%) of pure (II) boiling at 98 C/19 mmHg as an oil. IR (cm^{-1}): 1780, 1220, 1150; ^1H NMR (δ, ppm): 3.73 (2H, t, J = 4.5 Hz, $-CH_2Br$), 4.1-4.6 (1H, m, $-CHBr$), 4.71 (2H, d, J = 4.2 Hz, $-O-CH_2-$), 5.17 (1H, dq, $J_{HF(a)}$ = 46.0 Hz, $J_{HF(b)}$ = 6.6 Hz, CHF); ^{19}F NMR (δ, ppm) ($CDCl_3$): signal of F(b) was recognized at 2.9 downfield from the external standard of CF_3COOH (d, d, $J_{F(a)F(b)}$ = 12.4 Hz, $J_{HF(b)}$ = 6.6 Hz, CF_3^*) (*two overlapped signals were detected which may be due to diastereomers, though they were not isolated by usual experimental methods). Signal of F(a) was recognized at 124.2 upfield from the external standard of CF_3COOH (d, q, $J_{HF(a)}$ = 46.0 Hz, $J_{F(a)F(b)}$ = 12.4 Hz, CHF(a)).

Other disubstituted glycerine derivatives were treated with PPDA in the same manner, and the results are listed in Table I.

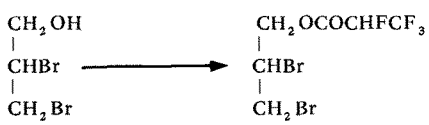


(II)

SCHEME 1

TABLE I

Fluorination of Disubstituted Glycerols



Glycerol derivatives	Product boiling point °C	Yield %[a]
1,3-Dibromo-2-propanol	93-95 at 18 mmHg[b]	52%
2,3-Dichloro-1-propanol	93-94 at 33 mmHg	62%
1,3-Dichloro-2-propanol	88-89 at 18 mmHg	53%
2,3-Dibromo-1-propanol	98-99 at 19 mmHg	52%
2,2-Dimethyl-1,3-dioxolan-4-methanol	92-96 at 22 mmHg	49%

[a]The yield was calculated as isolated yield.

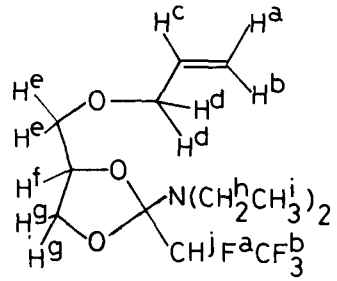
[b]The separation of products was done by spinning band fractionating column (Taika Co. Ltd.).

Reaction of Glycerol α-Monoallylether (III) with PPDA

A solution of PPDA (4.46 g, 20 mmol) in dry tetrahydrofuran (10 mL) was added dropwise into a solution of glycerol α-monoallylether (III) (2.64 g, 20 mmol) in tetrahydrofuran (10 mL) at room temperature. After stirring for 6 hr at 40-50 C, the reaction mixture was left overnight. The reaction mixture was treated in a manner similar to that mentioned above, and the following fractions were gained: (1) 126-132 C/24 mmHg, 1.2 g; (2) 132-134 C/24 mmHg, 4.8 g.

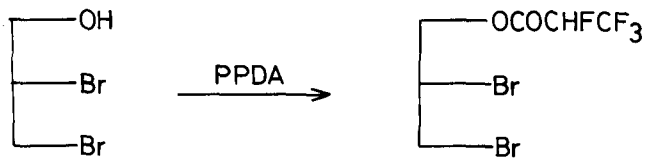
Fraction (i) was a mixture of N,N-diethyl-2,3,3,3-tetrafluoropropioamide (30%), an unidentified product (7%), unreacted (III) (3%) and 4-allyloxymethyl-2-diethylamino-2-(1,2,2,2-tetrafluoroethyl)-1,3-dioxolane (IV) (60%). Fraction (ii) was a mixture of unreacted (III) (10%) and compound (IV) (90%). These compositions were determined by gas chromatography (130 C). Fraction (ii) was redistilled to give 3.9(g) of pure (IV), boiling at 133-134 C/24 mmHg. IR(cm^{-1}): 1200, 1150, 1090. Pure (IV), 4.3 g, was obtained from the fraction (i) (0.4 g) and from the fraction (ii) (3.9 g). The yield of IV was 68%. ^1H NMR (δ, ppm): 1.05 (6H, t, J = 7.2 Hz, Hi), 2.82 (4H, q, J = 7.2 Hz, Hh), 3.52 (2H, q, J = 4.7 Hz, He), 3.70-4.40 (3H, m, Hf and Hg), 4.00 (2H, d, d, J_{cd} = 5.0 Hz, J_{bd} = 1.2 Hz, Hd), 4.83 (1H, d, q, $J_{HF(a)}$ = 43.8 Hz, $J_{HF(b)}$ = 6.0 Hz, Hj), 5.20 (1H, dm, J_{ac} = 9.0 Hz, Ha), 5.26 (1H, dm, J_{bc} = 20.4 Hz, Hb), 5.80 (1H, ddt, J_{bc} = 20.4 Hz, J_{ac} = 9.0 Hz, J_{cd} = 5.0 Hz, Hc). ^{19}F NMR (δ, ppm) ($CDCl_3$): signal of F(b) (multiplet) was recognized at +4.5 downfield from the external standard of CF_3COOH. Signal of F(a) (multiplet) was recognized at 126.5 upfield from the external standard of CF_3COOH.

Other monosubstituted glycerine derivatives were reacted with PPDA in the same manner, and the results are listed in Table II.

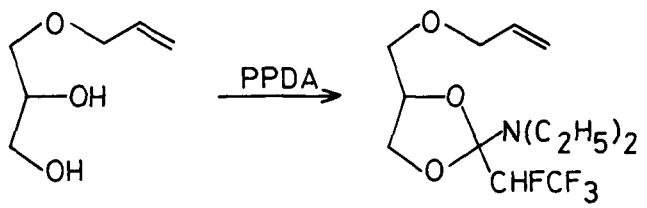


(IV)

SCHEME 2



(I) SCHEME 3 (II)



(III) SCHEME 4 (IV)

RESULTS AND DISCUSSION

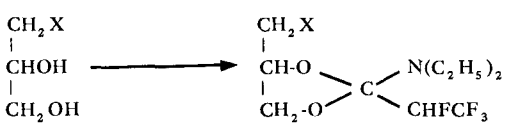
Convenient fluorination of standard alcohols (2) and higher fatty alcohols (1) with PPDA was reported recently. This paper concerns attempted fluorination of monosubstituted glycerols and disubstituted glycerols.

2,3,3,3-Tetrafluoropropionate esters were obtained from the reaction of disubstituted glycerols with PPDA. For example, 2,3-dibromopropyl 2,3,3,3-tetrafluoropropionate (II) was obtained from 2,3-dibromo-1-propanol (I) and PPDA. A cyclic adduct of PPDA was produced from the reaction of monosubstituted glycerol with PPDA. For example, 4-allyloxymethyl-2-diethylamino-2-(1,2,2,2-tetrafluoroethyl)-1,3-dioxolane (IV) was obtained from glycerol α-monoallylether and PPDA.

Other esters and cyclic ethers were prepared in moderate yields and the results are listed in Tables I and II. The foregoing observations indicate that the reaction of PPDA with

TABLE II

Fluorination of Monosubstituted Glycerines

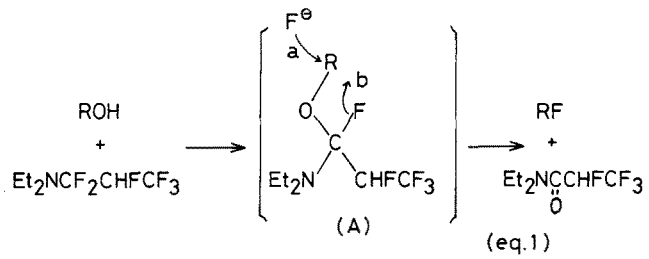


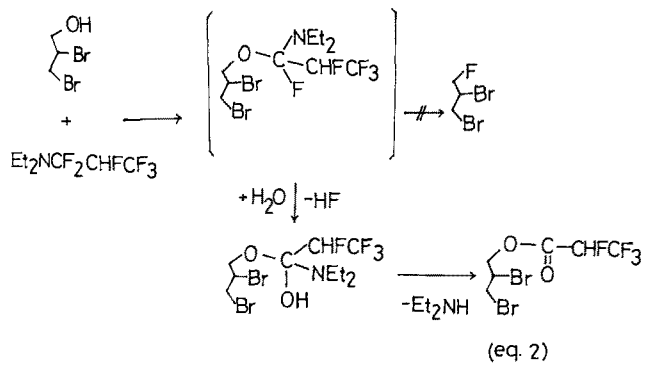
Glycerine derivatives	Product boiling point °C	Yield %[a]
α-Monoacetin	135-140 at 22 mmHg[b]	24
α-Guaiacol glycerine ether	*[c]	67
Glycerol α-monochlorohydrine	105-106 at 22 mmHg	44
Glycerol monoallylether	132-134 at 24 mmHg	68
Monostearin	185-188 at 3 mmHg	50
Monoolein	187-190 at 3 mmHg	38

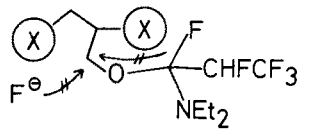
[a]The yield was calculated as isolated yield.

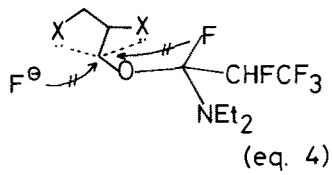
[b]The separation of products was done by spinning band fractionating column (Taika Co. Ltd.).

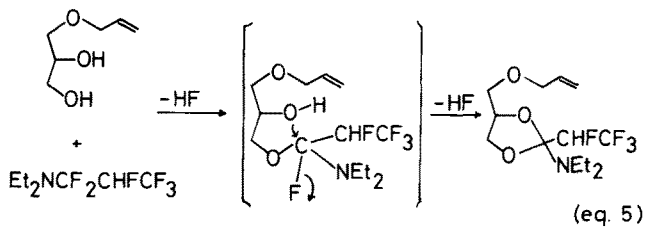
[c]The product was isolated by liquid chromatography using silica gel with n-hexane containing ethylacetate.











disubstituted glycerol yields esters, and reaction with monosubstituted glycerols yields 1,3-dioxane derivatives, in contrast with standard alcohols which give monofluorinated compounds.

The reason for the lack of monofluorinated compounds is proposed as follows. With standard alcohols (1), an alcohol reacts with PPDA to give an intermediate compound (A), which is subjected to subsequent inter-(a)- or intramolecular (b) nucleophilic attack by F^- to produce monofluorinated compounds (Equation 1). In the case of disubstituted glycerols, the carbon adjacent to hydroxyl group is "blocked" or "shielded" by two adjacent halogen atoms both sterically and electronically, which preclude subsequent nucleophillic attack of fluorine atom (Equation 2). Equations 3 and 4 show how the halogen atom blocks the carbon to be fluorinated. At the time of reaction termination by adding of water, the water attacks the intermediate to form the dibromopropyl ester by removing of hydrogen fluoride and diethylamine (Equation 2). On the occasion of monosubstituted glycerol, an intramolecular nucleophilic attack by the adjacent hydroxyl group occurs to give a stable five-membered ketal (Equation 5). Application of these new fluorine compounds as surfactants and others is now in progress at our laboratory.

ACKNOWLEDGMENT

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