CATALYTIC PHOSPHORYLATION OF POLYFLUOROALKANOLS

6. FORMATION OF α-POLYFLUOROALKYLBENZYL ETHERS DURING CATALYTIC PHOSPHORYLATION OF α-POLYFLUOROALKYLBENZYL ALCOHOLS

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Phosphorylation of unsubstituted α-polyfluoroalkylbenzyl alcohols, or their derivatives containing acceptor substituents in the aromatic ring, with excess $POCl_3$ in the presence of a catalyst gives α-polyfluoroalkylbenzyl dichlorophosphates [1,2]

$$RC_6H_4CH(R_F)OH + POCl_3 \xrightarrow[-HCl]{\text{Catalyst}} RC_6H_4CH(R_F)OPOCl_2$$
$$R = H,\ m\text{-}CF_3;\ R_F = CF_3,\ C_3F_7$$

On the other hand, phosphorylation of p-methyl-α-trifluoromethylbenzyl alcohol (I) under analogous conditions gives di-p-methyl-α-trifluoromethylbenzyl ether (II) instead of the expected dichlorophosphate [2, 3]. Ether formation has also been observed in an attempt to prepare bis(α-trifluoromethylbenzyl) chlorophosphate by phosphorylating α-trifluoromethylbenzyl alcohol (III) with $POCl_3$ under severe conditions [3]. It has been postulated that in both cases the ethers are formed as a result of alkylation of the α-polyfluoroalkylbenzyl alcohols by intermediate α-polyfluoroalkylbenzyl dichlorophosphates [2,3].

To check this hypothesis, we have synthesized α-trifluoromethylbenzyl dichlorophosphate (IV) and p-methyl-α-trifluoromethylbenzyl dichlorophosphate (V) and studied their reaction with α-polyfluoroalkylbenzyl alcohols, as well as certain other reactions which might take place under the conditions of catalytic phosphorylation.

Dichlorophosphate (IV) was prepared by catalytic phosphorylation of (III) with excess $POCl_3$ by the method described in [1,2]. However, catalytic phosphorylation is unsuitable for preparing (V): even under the mildest possible conditions (10-fold excess of $POCl_3$, 95°C, 8 h), only ether (II) and p-methyl-α-trifluoromethylbenzyl chloride (VI), the structure of which was confirmed by elementary analysis and NMR spectra, can be isolated from the reaction mixture. It should be noted that analysis of the reaction mixture by ^{19}F NMR showed that, besides the signals belonging to the ether (II) (two doublets at −2.41 and −2.20 ppm with J_{H-F} = 6.6 Hz) and chloride (VI) (doublet at −5.26 ppm with J_{H-F} = 6.8 Hz), there is a low-intensity doublet at −1.80 ppm with J_{H-F} = 6.0 Hz, which, as was shown subsequently, can be assigned to (V). The ratio of the integral intensities of the signals corresponding to these three compounds was 49:47:4

$$\underset{(I)}{4\text{-}CH_3C_6H_4CH(CF_3)OH} + POCl_3 \xrightarrow[-HCl]{CaCl_2,\ 95^\circ} \underset{(II)}{(4\text{-}CH_3C_6H_4CH(CF_3))_2O} + \underset{(VI)}{4\text{-}CH_3C_6H_4CHClCF_3} [+\underset{(V)}{4\text{-}CH_3C_6H_4CH(CF_3)OPOCl_2}]$$

We therefore employed phosphorylation in the presence of a tertiary amine to synthesize (V). Although phosphorylation of benzyl alcohols, including their α-alkyl derivatives, with $POCl_3$ under these conditions gives the corresponding chlorides [4], the presence of the strong electron-accepting α-CF_3 group made it possible to obtain the normal phosphorylation product, i.e. (V), the structure of which was confirmed by elementary analysis and NMR spectroscopy

$$(I) + POCl_3 \xrightarrow{(C_2H_5)_3N,\ 0^\circ} (V)$$

The dichlorophosphates (IV) and (V) were then reacted with an equimolar amount of the corresponding α-polyfluoroalkylbenzyl alcohol at elevated temperature. It was found that (IV) starts to react only at 160°C, where (V) reacts at a fairly fast rate at 95°C. Analysis of the reaction mixtures by TLC, GLC, and ^{19}F NMR

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TABLE 1. NMR and GLC Data for Di-α-trifluoromethylbenzyl Ethers of the Type p-$RC_6H_4\overset{*}{C}H(CF_3)-O-\overset{*}{C}H(CF_3)C_6H_4R$-p

Compound	R	Diastereomer	PMR spectrum (δ, ppm)			^{19}F NMR spectrum (ppm)	GLC	
			CH_3	CH	aromatic protons	CF_3 (content in mixture, %)	retention time, min	content in mixture, %
(II)	CH_3	A	2,28 s	4,44 q J_{H-F}=6,5 Hz	6,95–7,30 m	−2,17 d (57) J_{H-F}=6,6 Hz	9	56
		B	2,21 s	4,77 q J_{H-F}=6,5 Hz		−2,44 d (43) J_{H-F}=6,6 Hz	8	44
(VII)	H	A	–	4,55 q J_{H-F}=6,5 Hz	7,46 s*	−2,11 d (56) J_{H-F}=6,5 Hz	19	52
		B	–	4,88 q J_{H-F}=6,5 Hz	7,33 s*	−2,38 d (44) J_{H-F}=6,5 Hz	18	48

*Narrow, poorly resolved multiplet.

showed that the main products of this reaction are respectively di-α-trifluoromethylbenzyl ether (VII) and ether (II), together with small amounts of α-polyfluoroalkylbenzyl chlorides*

$$4\text{-}RC_6H_4CH(CF_3)OH + 4\text{-}RC_6H_4CH(CF_3)OPOCl_2 \xrightarrow[-HCl]{t^\circ} (4\text{-}RC_6H_4\underset{\displaystyle CF_3}{\underset{|}{C}}H)_2O + [PO_2Cl] [+ 4\text{-}RC_6H_4CHClCF_3]$$

[R = H (III), CH_3 (I) R = H (IV), CH_3 (V)

R = H (VII), CH_3 (II) R = H (VIII), CH_3 (VI)

In both cases, the ratio of ether to chloride, as determined by ^{19}F NMR, was ≈15:1. According to ^{19}F NMR and GLC data, the ratio of diastereomers in the benzyl ethers is different (Table 1), the major diastereomers being those with the CF_3 signal shifted to stronger field and having the longer retention time. It should be noted that the formation of different amounts of diastereomers has been reported before for the acylation of α-polyfluoroalkylbenzyl alcohols with the anhydrides of chiral carboxylic acid [6], but this is evidently the first time that stereospecific alkylation of α-polyfluoroalkylbenzyl alcohols by phosphorus acid esters containing a chiral center has been observed. The yield of the di-α-polyfluoroalkylbenzyl ethers after chromatographic purification and distillation was 44-48%.

It must be emphasized that the temperature at which alcohols (I) and (II) undergo alkylation corresponds in each case to the temperature conditions under which ethers are formed during catalytic phosphorylation of these alcohols. We have also shown that heating these alcohols and α-polyfluoroalkylbenzyl dichlorophosphates individually under the same conditions, including the presence of catalytic amounts of anhydrous $CaCl_2$, does not lead to the formation of benzyl ethers. Thus, the formation of ethers during the catalytic phosphorylation of α-polyfluoroalkylbenzyl alcohols is indeed due to alkylation of the alcohols by α-polyfluoroalkylbenzyl dichlorophosphates formed as intermediates in the course of the reaction.

In order to elucidate the route by which the chloride (VI) is formed during the catalytic phosphorylation of (I) or its alkylation by the corresponding dichlorophosphate, we studied the response of the alcohol and dichlorophosphate (V) to the action of dry HCl on heating. We found that (V) is completely decomposed within 2 h at 95°C, being converted (according to TLC, PMR, and ^{19}F NMR data) mainly to (VI),† whereas (I) does not react with HCl at this temperature. Consequently, (VI) is formed only due to cleavage of the C—O—P bond in the corresponding dichlorophosphate under the influence of HCl. As regards the traces of chloride (VIII) detected during the alkylation of alcohol (III) with dichlorophosphate (IV), it is probably reasonable to assume that (VIII) is formed by direct reaction between the dichlorophosphate and alcohol, since neither the alcohol nor the dichlorophosphate forms the chloride under the influence of HCl under these conditions (160°C, 2 h).

Thus, the introduction of a donor p-methyl group into the aromatic nucleus substantially changes the reactivity of dichlorophosphate (V) compared with its unsubstituted analog, as shown by its lower thermal stability and the considerably lower stability of its C—O—P bond with respect to the action of dry HCl. Since (V) is unstable under severe catalytic-phosphorylation conditions, it can be used as a phosphorylating agent only at low temperatures in the presence of an HCl acceptor. Indeed, reaction of methanol with (V) in the presence of triethylamine in CH_2Cl_2 at 0°C gives p-methyl-α-trifluoromethylbenzyl dimethyl phosphate (IX) in 55% yield

$$\underset{(V)}{4\text{-}CH_3C_6H_4C^*H(CF_3)OPOCl_2} + CH_3OH \xrightarrow{(C_2H_5)_3N,\ 0^\circ} \underset{(IX)}{4\text{-}CH_3C_6H_4C^*H(CF_3)O\overset{\displaystyle O}{\overset{\|}{P}}(OCH_3)_2}$$

The structure of (IX) was confirmed by elementary analysis and NMR spectroscopy. The PMR spectrum of (IX) indicates nonequivalence of the diastereotopic protons in the OCH_3 groups attached to the P atom. The magnetic nonequivalence of the protons in such groups has been observed before for certain other dimethyl phosphates [7] and phosphonates [8], but it is still noteworthy that this nonequivalence is quite great (~0.24 ppm), in spite of the considerable distance between the asymmetric center and the protons of the diastereotopic groups.

EXPERIMENTAL

The PMR and ^{19}F NMR spectra were recorded with a Perkin—Elmer R-20 instrument using CCl_4 solutions (HMDS as internal standard for PMR; CF_3COOH as external standard for ^{19}F NMR). The ^{31}P NMR

*α-Trifluoromethylbenzyl chloride (VIII) was identified by comparison with an authentic sample synthesized by reaction of (III) with PCl_5 [5].

†According to ^{19}F NMR data, only 1-2% of (VI) is formed when (V) is heated (95°C, 2 h) in the absence of HCl.

spectra were recorded using a Bruker HX-90 spectrometer under pulsed conditions with noise suppression of spin — spin coupling with protons (85% H_3PO_4 as external standard).

The GLC analyses were performed using a glass column (2 m) packed with 2% silicone elastomer E-301 on Chromosorb W (80/100 mesh), with a flame-ionization detector, He carrier gas (30 ml/min), direct sample injection into the column, and a column temperature varying from 80 to 230°C at a rate of 6 deg/min for (II) and from 50 to 150°C at a rate of 3 deg/min for (VII). The TLC analyses were performed on Silufol UV-254 plates.

Catalytic Phosphorylation of p-Methyl-α-trifluoromethylbenzyl Alcohol (I) with $POCl_3$. A mixture of 4.0 g (0.021 mole) of (I), 32.1 g (0.21 mole) of $POCl_3$, and 50 mg (0.45 mmole) of anhydrous $CaCl_2$ was heated at 95°C for 8 h. The excess $POCl_3$ was distilled off and the residue fractionated in vacuo to give low-boiling (bp 58-104°C/3 mm) and high-boiling (bp 104-140°C/3 mm) fractions. The low-boiling fraction was chromatographed on Al_2O_3 (ether eluant) and the solvent removed. The residue was fractionated in vacuo to give 1.0 g (23%) of (VI), bp 90-91°C/29 mm, $n_D^{20} = 1.4647$, $d_4^{20} = 1.2665$ (cf. [9]). Found: C 51.8; H 4.0; Cl 16.8; F 27.7%. $C_9H_8ClF_3$. Calculated: C 51.8; H 3.9; Cl 17.0; F 27.3%. PMR spectrum (δ, ppm): 2.27 s (CH_3), 4.99 q (CH, $J_{H-F} = 6.9$ Hz), 7.04-7.52 m (C_6H_4). ^{19}F NMR spectrum (ppm): −5.00 d (CF_3, $J_{H-F} = 6.8$ Hz). The high-boiling fraction was treated analogously to give 0.4 g (11%) of (II), bp 113-115°C/1 mm, mp 24-29°C (cf. [2]).

p-Methyl-α-trifluoromethylbenzyl Dichlorophosphate (V). A solution of 3.8 g (0.02 mole) of (I) and 2.2 g (0.022 mole) of triethylamine in 5 ml of dry CH_2Cl_2 was added dropwise to a cooled (0°C) solution of 6.2 g (0.04 mole) of $POCl_3$ in 20 ml of dry CH_2Cl_2. The mixture was stirred at 0°C for 1 h and left overnight. The precipitate was filtered off, the solvent and excess $POCl_3$ removed, and the residue extracted with pentane. The extract was passed through a column of 2 g Al_2O_3 in an Ar atmosphere, the pentane was distilled off, and the residue was distilled in vacuo to give 3.7 g (60%) of (V), bp 89-90°C/1 mm, $n_D^{20} = 1.4755$, $d_4^{20} = 1.4294$. Found: C 35.3; H 2.8; Cl 23.1; F 18.3; P 9.8%. $C_9H_8Cl_2F_3O_2P$. Calculated: C 35.2; H 2.6; Cl 23.1; F 18.6; P 10.1%. PMR spectrum (δ, ppm): 2.34 s (CH_3), 5.93 (CH, $J_{H-F} = 6.0$, $J_{H-P} = 13.8$ Hz), 7.10-7.57 m (C_6H_4). ^{19}F NMR spectrum (ppm): −1.96 d (CF_3, $J_{H-F} = 6.0$ Hz). ^{31}P NMR spectrum (ppm): −6.90 s.

Alkylation of α-Polyfluoroalkylbenzyl Alcohols with α-Polyfluoroalkylbenzyl Dichlorophosphates. a) A mixture of 0.6 g (3.4 mmole) of (III) and 1.0 g (3.4 mmole) of (IV) was heated at 160°C for 2 h, extracted with CCl_4, and the extract chromatographed on Al_2O_3 (CCl_4 eluent). The solvent was removed and the residue distilled in vacuo to give 0.5 g (44%) of (VII), bp 94-96°C/2.5 mm, $n_D^{20} = 1.4680$ (cf. [3]).

b) A mixture of 0.6 g (3.2 mmole) of (I) and 1.0 g (3.2 mmole) of (V) was heated at 95°C for 2 h. The reaction mixture was worked up as above to give 0.55 g (48%) of (II), bp 113-115°C/1 mm, mp 24-29°C (cf. [2]).

α-Trifluoromethylbenzyl Chloride (VIII). Phosphorus pentachloride (3.8 g, 0.022 mole) was added portionwise to 3.5 g (0.02 mole) of (III). When HCl evolution ceased, the excess PCl_5 was filtered off and the filtrate distilled in vacuo to give 3.0 g (79%) of (VIII), bp 63-64°C/22 mm, $n_D^{20} = 1.4588$, $d_4^{20} = 1.3151$ (cf. [9]). Found: C 49.2; H 3.2; Cl 18.1; F 29.3%. $C_8H_6ClF_3$. Calculated: C 49.4; H 3.1; Cl 18.2; F 29.3%. PMR spectrum (δ, ppm): 5.01 q (CH, $J_{H-F} = 6.8$ Hz), 7.13-7.63 m (C_6H_5). ^{19}F NMR spectrum (ppm) −5.30 d (CF_3, $J_{H-F} = 6.8$ Hz).

p-Methyl-α-trifluoromethylbenzyl Dimethyl Phosphate (IX). A solution of 0.96 g (0.03 mole) of abs. CH_3OH and 3.0 g (0.03 mole) of triethylamine in 5 ml of dry CH_2Cl_2 was added dropwise to a cooled (0°C) solution of 4.2 g (0.014 mole) of (V) in 15 ml of dry CH_2Cl_2. The mixture was stirred at 0°C for 3 h and left overnight. Water was added until the precipitate completely dissolved, and the solution was extracted with ether. The extract was washed with water, dried with $MgSO_4$, the solvent removed, and the residue distilled in vacuo to give 2.2 g (55%) of (IX), bp 104-106°C/0.5 mm, $n_D^{20} = 1.4520$, $d_4^{20} = 1.2844$. Found: C 44.5; H 4.7; F 19.2; P 10.0%. $C_{11}H_{14}F_3O_4P$. Calculated: C 44.3; H 4.7; F 19.1; P 10.4%. PMR spectrum (δ, ppm): 2.29 s ($CH_3C_6H_4$), 3.45 d (CH_3OP, $J_{H-P} = 11.6$ Hz), 3.69 d (CH_3OP, $J_{H-P} = 11.6$ Hz), 5.72 m (CH, $J_{H-F} = 6.6$, $J_{H-P} = 10.2$ Hz), 7.08-7.59 m (C_6H_4). ^{19}F NMR spectrum (ppm): −1.10 d (CF_3, $J_{H-F} = 6.6$ Hz). ^{31}P NMR spectrum (CCl_4, ppm): −0.60 s.

CONCLUSIONS

1. The formation of α-polyfluoroalkylbenzyl ethers during the catalytic phosphorylation of α-polyfluoroalkylbenzyl alcohols is due to alkylation of these alcohols by α-polyfluoroalkylbenzyl dichlorophosphates formed as intermediates in the course of the reaction.

2. α-Polyfluoroalkylbenzyl dichlorophosphates containing a p-methyl group in the aromatic nucleus can be used as phosphorylating agents only in the presence of a hydrogen chloride acceptor at low temperatures.

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CARBOXYLATION OF DIALKYLALUMINUM HALIDES

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The carboxylation of organoaluminum compounds is a promising method for preparing fatty acids [1-3]. Trialkyl derivatives of aluminum react with CO_2 at normal pressure and room temperature to give either trialkylcarbinols or carboxylic acids, depending on the reaction conditions.

According to [4-6], dialkylaluminum chlorides R_2AlCl and alkylaluminum dichlorides $RAlCl_2$ (R = Me or Et) do not react with CO_2. At the same time, the carboxylation of dialkylaluminum chlorides R_2AlCl is also of interest from the point of view of preparing synthetic higher fatty acids, since higher R_2AlCl can be obtained by a chain-growth reaction from diethylaluminum chloride and ethylene in the presence of $TiCl_4$ [7].

Contrary to the data in [4-6], we have found that R_2AlCl do undergo carboxylation. In the present work, we have studied certain kinetic features of the carboxylation of $(C_2H_5)_2AlCl$ and $(n\text{-}C_{10}H_{21})_2AlCl$, and the effect of temperature, pressure, alkyl chain length, and halogen type on the carboxylation of higher R_2AlHal ($R = C_4$-C_{22}; Hal = Cl or Br).

The main products of the carboxylation of R_2AlCl are the corresponding acid and paraffin (Table 1)

$$R_2AlCl + xCO_2 \rightarrow (RCOO)_xR_yAlCl \xrightarrow{H_2O} xRCOOH + yRH + Al(OH)_3 + HCl\ ,$$

where $x + y = 2$.

The formation of 0.9-2.7 mole% olefins is observed at >150°C due to thermal decomposition. The degree of conversion of the Al—C bonds depends primarily on the temperature: Practically no reaction is observed at 100°C, but 29-32% conversion is observed in 5 h at 145-160°C. The acid yield is low (12.8-16%) and increases only slightly when the temperature is increased from 120 to 160°C, whereas the carboxylation selectivity decreases from 81 to 50% (see Table 1). The IR spectra of the reaction products indicate the absence of any oxygen-containing functional groups other than the carboxyl group. At the same time, unidentified neutral products were obtained in all experiments in the form of an undistillable residue.

Increasing the CO_2 pressure from 0 to 100-120 atm increased the acid yield to 42-48%, while the carboxylation selectivity was 90-96% (Table 2) and no unsaturated compounds were formed. Increasing the pressure to

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