mp 124–125 °C; mass spectrum, m/e 452 (M^+·), 200, 199; IR ν_{max} 2030 cm^{-1}. Calcd for $C_{24}H_{16}N_6S_2$: C, 63.7; H, 3.56; N, 18.57; S, 14.17. Found: C, 63.2; H, 3.50; N, 18.6; S, 14.2. Carbazole (18): 8%; mp 246–247 °C.

Acknowledgment. We acknowledge support from the Consiglio Nazionale Ricerche, Rome.

Registry No. 1a, 59328-04-0; 1b, 59327-96-7; 1c, 62284-29-1; 7, 54467-95-7; 8, 78715-74-9; 9, 149-30-4; 10, 23385-34-4; 12, 67173-64-2; 13, 78715-75-0; 14, 78715-76-1; 16, 67173-62-0; 17, 67173-63-1; 18, 86-74-8; 19, 1914-12-1; CS_2, 75-15-0; NaI, 7681-82-5.

Fluorination of Methanediphosphonate Esters by Perchloryl Fluoride. Synthesis of Fluoromethanediphosphonic Acid and Difluoromethanediphosphonic Acid[1]

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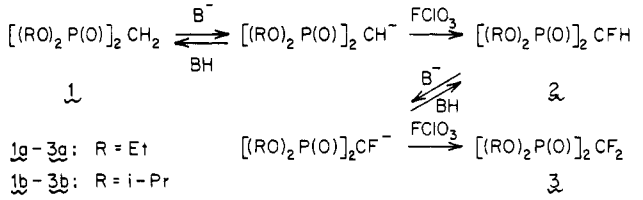
Although α-halogenated chloro, bromo, and iodo derivatives of tetraalkyl methanediphosphonates **1** have been known for some time,[3] the corresponding fluoro derivatives (**2, 3**) have not been available. Very recently, tetraethyl difluoromethanediphosphonate (**3a**) was prepared in 12% overall yield from dibromodifluoromethane and sodium diethyl phosphonate via diethyl bromodifluoromethanephosphonate.[4] Our interest in devising a *direct* route to both mono- and difluoromethanediphosphonates has led us to investigate the reaction of alkyl methanediphosphonates with perchloryl fluoride.[5,6] This reagent has been shown to α-fluorinate diethyl sodiomalonate,[7] giving a mixture of the mono- (29%) and difluoromalonate (42%) esters in toluene;[8] in ethanol, alkylation of the carbanion also occurs,[8] resulting in unwanted side product. The same method has been used to prepare other α-fluoro carboxylate derivatives, e.g., a series of 2-fluoro fatty acids with antifungal activity[9] and 2-alkyl 2-fluorocyanoacetates.[10]

In general, analogy between the methanedicarboxylate and methanediphosphonate groups in terms of methylene reactivity must be applied with caution. However, we find that perchloryl fluoride reacts smoothly with tetraisopropyl or tetraethyl methanediphosphonate carbanion in dry toluene to form both the corresponding fluorophosphonate and difluorophosphonate esters (**2a,b, 3a,b**) in total yields of up to 85%, if potassium *tert*-butoxide rather than Na or NaOEt is used as base (see Scheme I). The fluorination

Scheme I



Scheme II

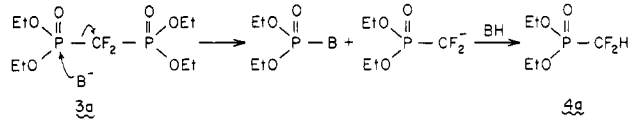


Table I. Fluorination of Methanediphosphonate Esters[a]

base	ester	base/ester ratio	% yield[b] 2	3	4
Na	1a	1.25:1	24[d]	17[d]	
t-BuOK	1a	2:1	34	21	7
t-BuOK	1a	1:1	47	16	trace
t-BuOK	1a	1:1[c]	22	45	18
Na	1b	1.30:1	28[d]	18[d]	
t-BuOK	1b	2:1	42	43	trace
t-BuOK	1b	3:1	32	33	trace
t-Bu-OK	1b	1:1	48	13	trace
t-BuOK	1b	0.60:1[c]	8	73	11

[a] As described in the Experimental Section. [b] By ^{19}F NMR analysis. [c] Retreatment of preceding reaction mixture. [d] Isolated yields.

reaction proceeds virtually as a titration of base with perchloryl fluoride and shows a readily recognizable end point marked by a characteristic color change from dark to pale yellow. Termination of the reaction is also indicated by the end of a temperature rise accompanying the reaction and cessation of perchloryl fluoride uptake.

Results illustrating the effects of some of the reaction parameters are summarized in Table I. By suitable adjustment of the proportion of starting materials, either product can be made to predominate; for example, with 1 equiv of potassium *tert*-butoxide as base, the monofluoromethane derivative of tetraisopropyl methanediphosphonate (**2b**) was prepared in 48% yield. With 2 equiv of this base, the difluoro (**3b**) derivative could be prepared directly in 43% yield, with an increase to 73% being possible on further reaction of the monofluoro product. The choice of base is important in this respect, since only a single equivalent of Na could be used, while NaOEt would be expected to give some alkylation side product, as discussed above. In addition to being a stronger base (the α-proton of **1** is less acidic than the α-proton in ethyl malonate), potassium *tert*-butoxide offers the advantages of allowing addition of more than 1 equiv of base if desired while avoiding unwanted alkylation of the carbanion and, in fact, gives the best yields. Exposure of the sodium salt[11] of tetraethyl methanediphosphonate (**1a**) in toluene solution to a stream of perchloryl fluoride results in the formation of resinous material, with reduced amounts of the desired mono- (**2a**) and difluorinated (**3a**) products. The yields are also lower when Na/toluene is used in place of potassium *tert*-butoxide with the isopropyl ester **1b**. With potassium *tert*-butoxide as the base, yields appear to be somewhat higher with the isopropyl ester than with the ethyl ester **1a**; addition of more than 1 equiv of base to the latter is accompanied by formation of a monophosphoryl side product, identified as **4a**. This com-

(1) Presented as part of a paper given at the International Conference on Phosphorous Chemistry, Duke University, Durham, N.C., June 1-6, 1981.
(2) Chinese Visiting Scholar, on leave from the Shenyang Research Institute of Chemical Industry, Shenyang, Liaoning, China.
(3) O. T. Quimby, J. D. Curry, D. A. Nicholson, J. B. Prentice, and C. H. Roy, *J. Organomet. Chem.*, **13**, 199 (1968).
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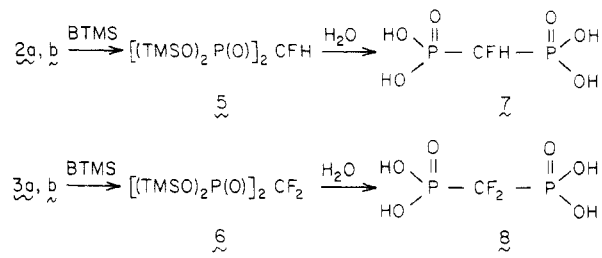
Scheme III



pound evidently arises from cleavage of a C–P bond in **3a** (Scheme II).

Treatment[12,13] of the alkyl esters **2** and **3** with bromotrimethylsilane gives the expected trimethylsilyl esters **5** and **6**. In agreement with a similar finding in the dealkylation of diethyl trichloromethanephosphonate,[12] the electron-deficient **2** and (particularly) **3** display somewhat attenuated reactivity in silyldealkylation by bromotrimethylsilane (BTMS), consistent with a phosphonium-like transition state in this reaction.[12] The ethyl esters **2a** and **3a** react under significantly milder conditions than the isopropyl esters **2b** and **3b**, again confirming earlier observations.[13]

Conversion of the ethyl or isopropyl esters (**2**, **3**) to the corresponding trimethylsilyl esters (**5**, **6**) has little effect on the ^{19}F NMR chemical shifts, but the ^{31}P NMR resonances are shifted upfield by 19 and 18 ppm, respectively (Experimental Section). An upfield shift of about 20 ppm per pair of alkyl → silyl substitutions appears to be characteristic for silyldealkylation of phosphonate and diphosphonate esters and as such provides a useful means of monitoring the progress of the reaction.[12]

Hydrolysis[12,13] of **5** and **6** affords respectively fluoromethanediphosphonic acid (**7**) and difluoromethanediphosphonic acid (**8**) (Scheme III). Taken together with the parent methanediphosphonic acid (MDPA), these new compounds show a smooth trend of decreasing melting point (MDPA, 203 °C;[14] **7**, 162 °C; **8**, 87 °C) and increased nuclear magnetic shielding at phosphorous as the α-hydrogen atoms of MDPA are replaced by fluorine atoms (*chemical shifts (δ) relative to* H_3PO_4: MDPA, 17.6;[14] **7**, 10.5; **8**, 3.7; Experimental Section).

The effect of fluorine substitution on the acidity of MDPA is of interest. In determining neutralization equivalents for **7** and **8**, we obtained approximate pK°_3 values of 6.5 (**7**) and 6.0 (**8**), corrected for a statistical factor of log (3/2). The error in these values is at least ±0.4 pK units. Grabenstetter and co-workers[15] have made careful determinations of pK values for a series of *gem*-diphosphonic acids. The data were found to correlate linearly with ^{31}P chemical shifts and also with Taft σ^* substitutent constants. We have used these empirical equations to estimate pK° values for **7** and **8**, which are compared with experimental pK° data[15] for MDPA (Table II). It should be noted that Grabenstetter[15] developed two alternative Taft equations for pK°_4, one giving an optimal fit with bulkier substitution (e.g., CH_3, CH_3 or Cl, Cl) and one to fit data for less sterically hindering substituents (e.g., H, H or H, Br). The second equation gives superior agreement with pK°_4 values calculated from ^{31}P chemical shift data for both **7** and **8**, presumably reflecting the small size of the fluoro group.

Table II. pK° Values[a] of Methanediphosphonic Acids, $XYC[P(O)(OH)_2]_2$

	XY				
	HF[b]		FF[b]		
	^{31}P	σ^*	^{31}P	σ^*	HH
pK°_4	10.1[c]	10.2[d]	9.07[c]	9.12[d]	11.0[e]
pK°_3	6.62[f]	6.82[g]	6.08[f]	5.89[g]	7.4[e]
pK°_2	2.78[h]	2.33[i]	2.57[h]	1.34[i]	3.1[e]

[a] For $\mu = 0$, uncorrected. [b] Calculated from empirical equations[15] based on ^{31}P δ values or Taft σ^* coefficients, as indicated below. A $\sigma^*(F)$ of 3.1 was used.[16] An uncertainty[17] of ~0.5 pK units is introduced by our uniform use of acid ^{31}P δ values.[15] [c] $pK^\circ = 8.51 + 0.15\delta$. [d] $pK^\circ = 11.29 - 0.35\sigma^*$. [e] Experimental data.[14] [f] $pK^\circ = 5.78 + 0.08\delta$. [g] $pK^\circ = 7.75 - 0.30\Sigma\sigma^*$. [h] $pK^\circ = 2.46 + 0.03\delta$. [i] $pK^\circ = 3.32 - 0.32\ \Sigma\ \sigma^*$.

The data presented in Table II indicate that the NMR and Taft approaches give similar pK°_4 and pK°_3 values, and the calculated pK°_3 values are consistent with our experimental estimate given above, but the pK°_2 values are divergent. Because the correlation coefficient for pK°_2 values calculated by the ^{31}P chemical shift method was significantly smaller for pK°_2 values than for pK°_3 and pK°_4 values (0.77 vs. 0.96 and 0.99, respectively),[15] we believe that the pK°_2 results derived from application of the Taft equation are probably more accurate. This choice is supported by a published estimate of 2.20 for the pK°_2 of bromomethanediphosphonic acid.[15] Since the latter acid has $pK^\circ_4 = 10.2$ and $pK^\circ_3 = 6.6$[15] (cf. corresponding values calculated for **7** and **8** in Table II), a pK°_2 greater than 2.5 for **7** or particularly **8**, predicted by the ^{31}P method, appears unreasonable.

The monofluoro acid **7** is predicted to have a pK°_4 of ~10.1, or 1 order of magnitude below that of MDPA, while the fourth proton of the difluoro acid **8** is calculated to be 100-fold more acidic than in the unfluorinated acid. The acidity of **7** is about comparable to that of dichloromethanediphosphonic acid (pK°_4 (expt) = 9.8, pK°_3 (expt) = 6.1[15]), which in turn is weaker than **8**, expected to be the strongest halomethanediphosphonic acid.

The enhanced acidity due to the presence of one or two α-fluoro groups was also apparent in the derivative chemistry of **7** and **8**. MDPA forms a bis(dicyclohexylamine) salt, but treatment of **7** and **8** with a small excess of the base led to formation of the tris(dicyclohexylamine) derivatives **9** and **10** (Experimental Section).

In conclusion, perchloryl fluorination of methanediphosphonate esters **1** has evident promise as a general method for entry into the fluoromethanediphosphonates **2** and **3**, which are easily converted into the corresponding fluoromethanediphosphonic acids **7** and **8**. These substances have possible biochemical applications as F-labeled, hydrolysis-inert analogues of pyrophosphate, both per se and as synthates for new fluorine-containing oligophosphonate analogues of compounds such as ATP.[1,18]

Experimental Section

Melting points were determined by using a Thomas-Hoover capillary apparatus except in the case of **7** and **8**, for which a

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(17) A detailed experimental study of pK values for **7** and **8** will be reported elsewhere.
(18) C. E. McKenna, N. D. Leswara, and P.-d. Shen, in preparation.

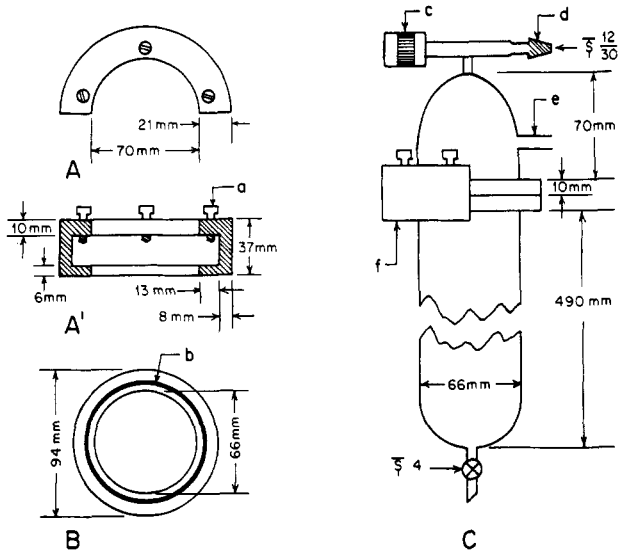

Figure 1. Modified column for flash chromatography (cf. ref 19). A and A′ are machined aluminum clamps secured with brass screws (a). B is an O-ring joint with an 85 mm × 2 mm O-ring (b). C is an assembled column, with a Teflon N_2 inlet valve (c, d) and a pressure release vent (e). One (f) of two clamps is shown mounted.

Fisher-Johns hot-stage apparatus was used. All melting points are uncorrected. IR spectra were measured with a Beckman AccuLab 2 spectrometer. Proton (^{1}H) and fluorine (^{19}F) magnetic resonance spectra were obtained with a Varian T-60 or (proton) XLFT-100 spectrometer. Phosphorous (^{31}P) NMR spectra were recorded on a Varian XLFT-100 (^{1}H coupled) or FT-80A (^{1}H decoupled) spectrometer. Chemical shifts are reported relative to internal Me_4Si (^{1}H), external $CFCl_3$ (^{19}F), or external H_3PO_4 (^{31}P). In product analyses by ^{19}F NMR, C_6F_6 was employed as an internal standard. Microanalyses were performed by Canadian Microanalytical Service and Galbraith Laboratories, Inc. Apparatus in contact with perchloryl fluoride was connected with Tygon tubing. Ground-glass joints were greased with 2S-25 halocarbon grease, and KF-3 halocarbon oil was used in gas bubblers (both available from Halocarbon Products Corp.). For general safety precautions with perchloryl fluoride, see ref 5. For preparative flash chromatography, the column design in ref 19 was modified by replacement of the ground-glass joints with O-ring joints secured by a metal yoke clamp (Figure 1) to provide a more secure pressure seal with large columns. Separations were repeated if necessary on mixed fractions to give essentially complete recovery of isolated products.

Tetraethyl Fluoromethanediphosphonate (2a). A solution of tetraethyl methanediphosphonate[20] (12.3 g, 0.043 mol) in dry toluene (10 mL) was added dropwise under N_2 to a well-stirred partial solution of potassium *tert*-butoxide (9.60 g, 0.086 mol) in the same solvent (80 mL) cooled externally with ice to 5 °C. Perchloryl fluoride[5] was passed rapidly into the vigorously stirred mixture via a subsurface addition tube, producing a noticeably exothermic reaction. The temperature was maintained below 22 °C. When neutralization was evident (50 min, vide supra), the turbid reaction mixture was suction filtered through Celite. The precipitate was washed with several portions of ether and the combined filtrate evaporated (10 mm, 50 °C) to leave a mixture (11.6 g) of **2a** (34%), **3a** (21%), and **4** (7%). Compounds **2a** and **3a** could not be easily separated by fractional distillation due to their similar boiling points. However, they were readily separated by conventional or (preferably) flash[19] column chromatography. Thus, the above reaction mixture (3.04 g) was eluted by flash chromatography on a 41 mm × 460 mm column of 40–63-nm silica gel 60 (E. Merck No. 9385) with ethyl acetate/ethanol (9:1) to yield four fractions, I–IV. Fraction IV (6%) was recovered starting material, and fraction II was a mixture which on further chromatography was resolved into I and III. Fraction III, identified as **2a**, was vacuum distilled to give an analytical sample: colorless oil; bp 112–115 °C (0.02 mm); TLC (EtOAc) R_f 0.31; IR (neat) 1255 cm^{-1} (s, phosphoryl); ^{1}H NMR ($CDCl_3$) δ 1.38 (t, J = 7 Hz, $4CH_3$), 4.30 (m, $4OCH_2$), 5.00 (dt, J_{HF} = 44 Hz, J_{HP} = 14 Hz, CHF); ^{19}F NMR (neat) δ 222.9 (dt, J_{FP} = 61 Hz, J_{FH} = 44 Hz); ^{31}P NMR (neat) δ 12.3 (ddp, J_{PF} = 62 Hz, J_{PH} = 14 Hz, J_{PH} = 4 Hz).

Anal. Calcd for $C_9H_{21}O_6FP_2$: C, 35.30; H, 6.91. Found: C, 34.93, H, 7.32.

Tetraethyl Difluoromethanediphosphonate (3a). Fraction I from the above procedure, identified as **3a** containing a little **4**, was vacuum distilled to give an analytical sample: colorless oil; bp 98–99 °C (0.01 mm) [lit.[4] bp 115–118 °C (0.4 mm)]; TLC (EtOAc) R_f 0.53; IR (neat) 1270 cm^{-1} (s, phosphoryl); ^{1}H NMR ($CDCl_3$) δ 1.40 (t, J = 7 Hz, $4CH_3$), 4.35 (m, $4OCH_2$) (lit.[4] δ 1.40, 4.39); ^{19}F NMR ($CDCl_3$) δ 120.6 (t, J_{FP} = 86 Hz) (lit.[4], δ 122); ^{31}P NMR ($CDCl_3$) δ 4.3 (tp, J_{PF} = 86 Hz, J_{PH} = 4 Hz) (lit.[4], δ 3.4).

Diethyl difluoromethanephosphonate (4a, from fraction I above): ^{1}H NMR δ 1.38 (t, J = 7 Hz, $2CH_3$), 4.3 (m, $2OCH_2$), 5.97 (dt, J_{HP} = 26 Hz, J_{HF} = 48 Hz, F_2CH); ^{19}F NMR δ 133.8 (dd, J_{FP} = 90 Hz, J_{FH} = 46 Hz) (lit.[4], δ 136); ^{31}P NMR δ 4.1 (t, J_{PF} = 91 Hz).

Tetraisopropyl Fluoromethanediphosphonate (2b). By use of the same procedure, tetraisopropyl methanediphosphonate[21] (11.8 g, 0.0342 mol) was reacted with potassium *tert*-butoxide (7.67 g, 0.0684 mol) in toluene (70 mL) followed by perchloryl fluoride to yield 4.56 g (42%) of **2b** and 5.56 g (43%) of **3b**. Only a trace of diisopropyl difluoromethanephosphonate (**4b**) was detectable by ^{19}F NMR. Further treatment of the isolated product mixture (3.71 g, 0.01 mol) with potassium *tert*-butoxide (0.75 g, 0.0067 mol) and perchloryl fluoride gave 2.78 g (73%) of **3b** and 0.29 g (8%) of recovered **2b**. When equimolar amounts of tetraisopropyl methanediphosphonate (8.59 g, 0.025 mol) and potassium *tert*-butoxide (2.80 g, 0.025 mol) were combined similarly and treated with 1 equiv of perchloryl fluoride, 4.45 g (48%) of **2b** was obtained with 1.3 g (13%) of **3b**. The ester **2b** was a colorless oil: bp 101–103 °C (0.02 mm); TLC (EtOAc/benzene, 2:1) R_f 0.33; IR (neat) 1258 cm^{-1} (s, phosphoryl); ^{1}H NMR δ 1.26 (d, J = 6 Hz, $8CH_3$), 4.77 (m, OCH), 4.82 (dt, J_{HP} = 14 Hz, J_{HF} = 44 Hz, CFH); ^{19}F NMR (neat) δ 221 (dt, J_{FP} = 63 Hz, J_{FH} = 44 Hz); ^{31}P NMR (neat) δ 10.7 (ddt, J_{PF} = 63 Hz, J_{PH} = 12 Hz, J_{PH} = 3 Hz).

Anal. Calcd for $C_{13}H_{29}O_6FP_2$: C, 43.09; H, 8.07. Found: C, 42.96; H, 8.37.

Tetraisopropyl Difluoromethanediphosphonate (3b). The compound was isolated as a colorless oil: bp 97–100 °C (0.01 mm); TLC (EtOAc/benzene, 2:1) R_f 0.55; IR (neat) 1270 cm^{-1} (s, phosphoryl); ^{1}H NMR ($CDCl_3$) δ 1.40 (d, J = 6 Hz, $8CH_3$), 4.93 (m, 4OCH); ^{19}F NMR (neat) δ 121 (t, J_{FP} = 85 Hz); ^{31}P NMR (neat) δ 2.80 (tt, J_{PF} = 84 Hz, J_{PH} = 3 Hz).

Anal. Calcd for $C_{13}H_{28}O_6F_2P_2$: C, 41.05; H, 7.42. Found: C, 40.82; H, 7.67.

Tetrakis(trimethylsilyl) Fluoromethanediphosphonate (5). Bromotrimethylsilane[22] (15.3 g, 0.100 mol) was added dropwise with stirring to 6.15 g (0.0200 mol) of **2a**. After 3 h at room temperature and an additional 3 h at 50 °C, ethyl bromide and excess silylating reagent were removed by rotary evaporation at reduced pressure to leave 9.65 g (100%) of the crude product, which was distilled to give 6.95 g (72%) pure **5**: colorless oil; bp 99–100 °C (0.01 mm); ^{1}H NMR δ 0.35 (s, $12CH_3$), 4.74 (dt, J_{HF} = 47 Hz, J_{HP} = 14 Hz, FCH); ^{19}F NMR δ 218 (dt, J_{FH} = 46 Hz, J_{FP} = 68 Hz); ^{31}P NMR δ −7.3 (d, J_{PF} = 67 Hz). The same product was obtained on similar treatment of **2b** with longer heating.

Tetrakis(trimethylsilyl) Difluoromethanediphosphonate (6). Bromotrimethylsilane (7.7 g, 0.050 mol) was stirred with **3a** (3.00 g, 0.0092 mol) at room temperature overnight. Evaporation as above gave 4.52 g (98%) of **6**; vacuum distillation provided an analytical sample: 3.30 g (72%); bp 93–95 °C (0.02 mm); ^{1}H NMR δ 0.37 (s, $12CH_3$); ^{19}F NMR δ 121 (t, J_{FP} = 90 Hz); ^{31}P NMR δ −15.0 (t, J_{PF} = 90 Hz). The same product was obtained on reaction of bromotrimethylsilane with **3b** under more vigorous conditions (10 h at 70 °C).

Anal. Calcd for $C_{13}H_{36}O_6F_2P_2Si_4$: C, 31.18; H, 7.25. Found: C, 30.93; H, 7.51.

(19) W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, **43**, 2923 (1978).

(20) J. A. Cade, *J. Chem. Soc.*, 2266 (1959).

(21) C. H. Roy, U.S. Patent 3 251 907 (1966).

(22) W. F. Gilliam, R. N. Meals, and R. O. Sauer, *J. Am. Chem. Soc.*, **68**, 1161 (1946). This is also available from Aldrich Chemical Co.

Fluoromethanediphosphonic Acid (7). To 5.5 g (0.011 mol) of **5** in a 50-mL round-bottomed flask flushed with N_2 was added, with stirring, 20 mL of H_2O. After 30 min, the organic phase was separated, and the aqueous phase was extracted twice with 15-mL portions of Et_2O and then evaporated to dryness. Further drying over P_2O_5 at 0.001 mm gave 2.04 g (96%) of the pure acid as a deliquescent, waxy, white solid: mp 162–163 °C; ^{19}F NMR δ 225 (dt, J_{FH} = 46 Hz, J_{FP} = 63 Hz); ^{31}P NMR δ 10.5 (d, J_{PF} = 64 Hz); neutralization equivalent 195 (calcd for $CH_5O_6FP_2$ 194). It was further characterized as the dicyclohexylamine salt **9**: a solution of 0.194 g (0.001 mol) of **7** in 0.8 mL of MeOH was added to a solution of dicyclohexylamine (0.73 g, 0.004 mol) in a mixture of 0.5 mL of acetone and 0.8 mL of benzene. The resulting precipitate was collected by filtration, washed with cold benzene, and dried, giving 0.57 g (77%) of the derivative. Analysis was performed on a twice-recrystallized sample dried in vacuo at 120 °C; mp 223–224 °C dec.

Anal. Calcd for $C_{37}H_{74}O_6FN_3P_2$: C, 60.22; H, 10.11; N, 5.69. Found: C, 60.09; H, 10.06; N, 5.66.

Difluoromethanediphosphonic Acid (8). By use of the above procedure, 2.85 g (0.0057 mol) of **6** was hydrolyzed with 15 mL of H_2O to yield 1.20 g (99%) of **8** as a viscous liquid which solidified on prolonged drying (0.01 mm, over P_2O_5): mp 87–90 °C; ^1H NMR (no resonances in D_2O); ^{19}F NMR δ 121 (t, J_{FP} = 86 Hz); ^{31}P NMR δ 3.7 (t, J_{PF} = 86 Hz); neutralization equivalent 214 (calcd for $CH_4O_6F_2P_2$ 212). The dicyclohexylamine salt **10** had a melting point of 259–260 °C.

Anal. Calcd for $C_{37}H_{73}O_6F_2N_3P_2$: C, 58.79; H, 9.73; N, 5.56. Found: C, 58.55; H, 9.52; N, 5.47.

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Registry No. **1a**, 1660-94-2; **1b**, 1660-95-3; **2a**, 78715-56-7; **2b**, 78715-57-8; **3a**, 78715-58-9; **3b**, 78715-59-0; **4a**, 1478-53-1; **4b**, 681-80-1; **5**, 78715-60-3; **6**, 78715-61-4; **7**, 10595-93-4; **8**, 10596-32-4; **9**, 78715-62-5; **10**, 78715-63-6; perchloryl fluoride, 7616-94-6.

Papyriferic Acid: a Triterpenoid from Alaskan Paper Birch

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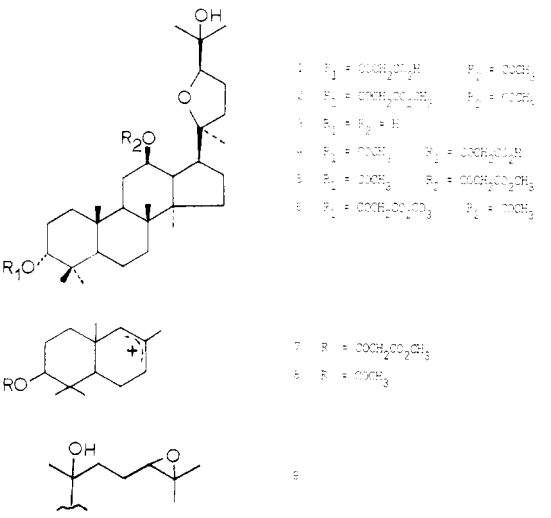
Chemical investigation of the herbivore-deterrent extract of Alaskan paper birch[1] (*Betula papyrifera* ssp. *humilis*) has led to the isolation and structure determination of papyriferic acid (**1**; see Chart I), a major triterpenoid of the juvenile stage of this species. Examination of the crude ether extract of juvenile twigs of *B. papyrifera* ssp. *humilis* by thin-layer chromatography (TLC) revealed a major component which could be eluted from silica gel with 20% methanol in diethyl ether. Trituration of the concentrated eluate with diethyl ether followed by recrystallization from acetone/cyclohexane afforded crystalline **1** ($C_{35}H_{56}O_8$). Infrared spectroscopy indicated the presence of ester (ν = 1752 cm^{-1}) and carboxylic acid (ν = 3570–2500, 1689 cm^{-1}) groups. The ^1H NMR spectrum (360 MHz) indicated a triterpene structure (eight methyl groups as 3H singlets in the δ 0.86–1.2 region), two acylated secondary alcohols [δ 4.72 (1 H, t, J = 2.2 Hz), 4.83 (1 H, dt, J = 5.2, 10.4 Hz)], one of which apparently occurred as an acetate [δ 2.02 (3 H, s)], and a secondary alcohol or ether [δ 3.67 (1 H, t, J = 7.0 Hz)]. An unusual 2H singlet at δ 3.48 was also evident. The ^{13}C NMR spectrum of **1** confirmed the presence of 35 carbons and indicated the presence of three secondary (75.6, 80.5, 83.3 ppm) and two tertiary (71.2, 85.8 ppm) carbons singly bonded to oxygen as well as three carbonyl groups (167.3, 169.1, 170.1 ppm).

Chart I



Treatment of **1** with diazomethane produced a methyl ester (**2**) which displayed an infrared spectrum in which hydroxyl (ν = 3580, 3400 cm^{-1}) and ester (ν = 1760, 1740 cm^{-1}) groups were evident.

The major structural features of **1** were elucidated by saponification to a triol having physical and spectral properties identical with those of betulafolientriol oxide I (**3**),[2] a constituent of two Japanese species of birch. The identity of **3** was confirmed by comparison of its infrared spectrum and chromatographic properties with those of an authentic sample of betulafolientriol oxide I.[3]

Consideration of the molecular compositions and ^1H NMR spectra of **1–3** led to assignments of the acylating groups in **1** as acetyl [δ 2.02 (3 H, s)] and malonyl [δ 3.48 (2 H, s)]. While the ^1H NMR spectrum of **1** required that it be a diacylated form of **3** in which the secondary hydroxyl groups of **3** (C-3 and C-12) were derivatized, the exact placement of acetate and malonate (i.e., **1** vs. **4**) was less straightforward. The tentative structural assignment of **1** was based upon the mass spectral data from methyl ester **2**. A low-intensity ion (ca. 3% of the base peak) was observed at m/e 307.194 392 ($C_{18}H_{27}O_4$) and was assignable to ion **7** from the well-known AB ring fragment of dammaranes.[4] No such ion was seen at m/e 249, corresponding to the ion **8** expected from fragmentation of the alternative ester **5**.[5] This assignment was confirmed by

(1) Bryant, J. P. In "Proceedings of the 1st International Logomorph Conference"; Meyeur, K., Ed.; Guelph University: Guelph, Ontario, Canada, in press.

(2) (a) Nagai, M.; Tanaka, N.; Tanaka, O.; Ichikawa, S. *Chem. Pharm. Bull.* **1973**, *21*, 2061. (b) Ohmoto, T.; Nikaido, T.; Ikuse, M. *Ibid.* **1978**, *26*, 1437.

(3) Both a sample and infrared spectrum of betulafolientriol oxide I were provided by Dr. T. Ohmoto of Toho University.

(4) Enzel, C. R.; Appleton, R. A.; Wahlberg, I. In "Biochemical Applications of Mass Spectrometry"; Waller, G. R., Ed.; Wiley: New York, 1979; p 370.

(5) This analysis was carried out with **2** instead of **1** because in the mass spectrum of **1** the only discernible oxygenated AB fragment was observed at m/e 249.187 252 ($C_{16}H_{25}O_2$). This ion can, in retrospect, be assigned to the AB fragment in which decarboxylation of the malonic acid has already taken place but is equally consistent with placement of acetate at C-3 (i.e., **4**). The intensities of oxygenated AB fragment ions in these spectra are low due to facile ester pyrolysis leading to $C_{14}H_{21}$ (m/e 189).

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