Direct Esterification of Phosphates with Various Halides and its Application to Synthesis of cAMP Alkyl Triesters

Toshiaki Furuta, Hiromi Torigai, Tomoko Osawa and Michiko Iwamura*
Department of Biomolecular Science, Faculty of Science, Toho University, 2-2-1 Miyama, Funabashi, Chiba 274, Japan

Esterification of phosphates with various halides, including acid chlorides, phosphoryl trichloride and tin chloride, was achieved in 57–99% isolated yield using silver(I) oxide. The reaction was successfully applied to the preparation of phosphate triesters sensitive to acids and bases. cAMP benzyl esters were also prepared by this method.

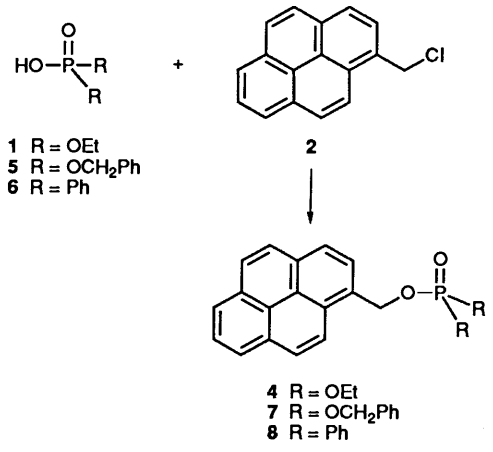
Alkyl esters of various phosphates, especially biologically important substances, are attractive synthetic targets both from biological and from chemical points of view.[1] Methods of synthesis employ one of the following two routes: (i) reaction of phosphoric acid halides or analogues with alcohols,[1b] (ii) alkylation of phosphates by diazo compounds.[2] Although each of these methods has a number of advantages over the other, the former is not applicable to molecules which are sensitive to acid or base, and the latter has inherent limitations in that it depends on the successful preparation of appropriate diazo compounds. Reactions of metal phosphates with alkyl halides were also reported and in some cases proved to be very useful.[3] However, the necessity of isolating metal phosphates makes this route difficult to apply more widely. In the course of our study on the development of photolabile and highly fluorescent protecting groups for biologically important molecules,[4] it was necessary to prepare new photolabile phosphate triesters. However, we could not synthesize such molecules by previously reported methods.†

We report herein a mild and practical method for the direct derivation of phosphates, including cAMP, with various halides promoted by silver(I) oxide. After completion of the reaction, the product can be isolated simply by removal of insoluble silver halide and the starting material which remains.

Results and Discussion

We first examined the reaction conditions for the esterification of diethyl hydrogen phosphate **1** with pyren-1-ylmethyl chloride **2** in the presence of silver(I) oxide **3** (Scheme 1). The results are summarized in Table 1. The use of acetonitrile as a solvent gave a better yield than that with tetrahydrofuran (THF) (entries 1 *vs.* 2). The yield of diethyl pyren-1-ylmethyl phosphate **4** decreased at longer reaction times; product **4** was obtained in only 37% yield after 20 h (entries 2 *vs.* 3). Finally, we found that the reaction of substrates **1** and **2** with silver(I) oxide **3** (in molar proportions 2 : 1 : 1) in MeCN for 3.5 h gave compound **4** in 92% isolated yield (entry 4).

These reaction conditions were successfully applied to the synthesis of various phosphate derivatives. The results are summarized in Table 2. The reaction of diethyl hydrogen phosphate **1** and arylmethyl halides proceeded smoothly at room temperature (entries 1 and 2). The introduction of



Scheme 1 *Reagents:* Ag_2O (**3**), MeCN

Table 1 The reaction of diethyl hydrogen phosphate **1** and pyren-1-ylmethyl chloride **2** in the presence of silver(I) oxide **3**

Entry	Solvent	Proportions (**1**:**2**:**3**)	Time (*t*/h)	Product yield (%)[a]
1	THF	1.8:1:1	6	66
2	MeCN	1.8:1:1	6	84
3	MeCN	1.8:1:1	20	37
4	MeCN	2.0:1:1	3.5	92

[a] Isolated yield based on halide used.

the highly fluorescent 7-methoxycoumarin group was accomplished in good yield (entry 3). It was necessary to use a slightly higher temperature for non-activated halides **12** and **13** in order to obtain better results (entries 4 and 5). The glycosyl phosphate **23** could also be synthesized successfully by using tetra-*O*-acetyl-α-D-galactosyl bromide **14** (entry 6). In this case, only the β-isomer **23** was formed at the anomeric centre. The use of benzoyl chloride **15** and diethylphosphoryl chloride **16** as the halides gave acyl phosphate **24** and pyrophosphate **25**, respectively, in good yield (entries 7 and 8). The synthesis of a tributylstannyl phosphate **26**, which decomposes in water, was also achieved by this method (entry 9). Other phosphates, dibenzyl hydrogen phosphate **5** and diphenylphosphinic acid **6**, could be alkylated in the same way (entries 10 and 11).

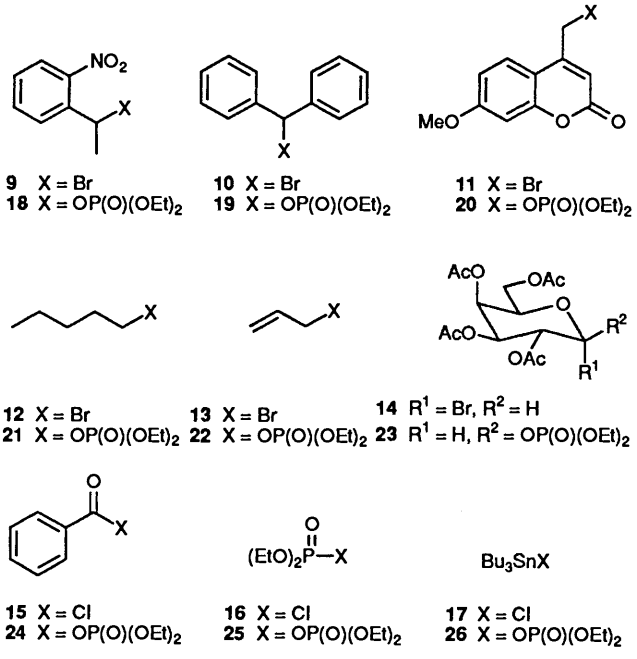
An attempt to alkylate unprotected adenosine 3′,5′-cyclic monophosphate (cAMP) **27** by the present *in situ* method did not give any alkylated product in acetonitrile. However, addition of a small amount of dimethyl sulfoxide (DMSO) to acetonitrile gave successful results (Scheme 2). The isolated

† For example, we attempted to prepare diethyl pyren-1-ylmethyl phosphate by the reaction of diethylphosphoryl chloride [$(EtO)_2$-P(O)Cl] and pyren-1-ylmethanol in the presence of various bases (pyridine, triethylamine and sodium hydride). Only the crude product was obtained, in low yield, because of its lability toward acids and bases.

Table 2 The esterification of phosphates with various halides[a]

Entry	Phosphate (phosphinate)	Halide	Temperature (T/°C)	Time (t/h)	Product yield (%)[b]
1	**1**	**9**	20	45	**18** (80)
2	**1**	**10**	20	3	**19** (57)
3	**1**	**11**	20	48	**20** (89)
4	**1**	**12**	60	25	**21** (84)
5	**1**	**13**	50	24	**22** (76)
6	**1**	**14**	20	0.5	**23** (71)
7	**1**	**15**	20	5	**24** (91)
8	**1**	**16**	20	49	**25** (92)
9	**1**	**17**	20	1.5	**26** (89)
10	**5**	**2**	20	6	**7** (99)
11	**6**	**2**	20	47	**8** (72)

[a] All reactions were carried out according to the general procedure (see Experimental section) except for the reaction temperature. [b] Isolated yield based on halide used.

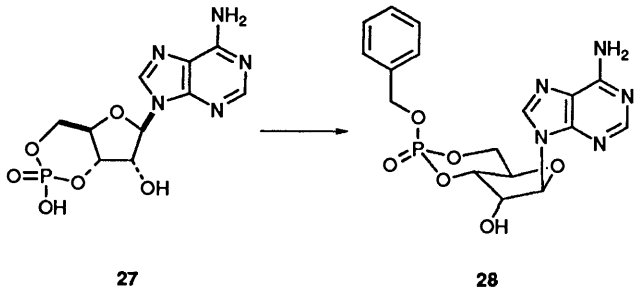


9 X = Br; **18** X = OP(O)(OEt)$_2$ — **10** X = Br; **19** X = OP(O)(OEt)$_2$ — **11** X = Br; **20** X = OP(O)(OEt)$_2$

12 X = Br; **21** X = OP(O)(OEt)$_2$ — **13** X = Br; **22** X = OP(O)(OEt)$_2$ — **14** R^1 = Br, R^2 = H; **23** R^1 = H, R^2 = OP(O)(OEt)$_2$

15 X = Cl; **24** X = OP(O)(OEt)$_2$ — **16** X = Cl; **25** X = OP(O)(OEt)$_2$ — **17** X = Cl; **26** X = OP(O)(OEt)$_2$

yield of cAMP benzyl ester **28** was 52% (ax:eq = 1.5:1) when the reaction was performed in a 10 to 1 mixture of acetonitrile and DMSO for 18 h at 65°C. Since cAMP **27** hardly dissolves in acetonitrile, the observed solvent effect can be accounted for by the increased solubility of substrate **27** in a mixed solvent containing DMSO. It is also clear that acetonitrile plays an essential role in the reaction because use of DMSO as the sole solvent led only to recovery of starting material. The yield and axial–equatorial ratio of product **28** were dependent on the reaction time and temperature. Use of higher temperatures and longer reaction times decreased the product yield and increased the axial–equatorial ratio. For example, we obtained only the axial isomer of compound **28** in 9% yield together with 83% of recovered cAMP **27** after 43 h at 70 °C. When the alkylation reaction proceeds, an equimolar amount of water might be formed. Therefore, hydrolysis of product **28** back to the initial cAMP **27** may have occurred at higher temperatures (> 70 °C) and longer reaction times. It was reported that the equatorial isomer of compound **28** was hydrolysed approximately four times as fast as the axial isomer in water at 50 °C,[2b] and therefore it is conceivable that we would obtain only the axial isomer in low yield after long reaction times.



27 **28**

Scheme 2 *Reagents:* $PhCH_2Br$, **3**, MeCN–DMSO (10:1)

The reaction may proceed *via* a silver phosphate intermediate because the silver salt of diethyl hydrogen phosphate could be isolated quantitatively in the absence of halides. Whereas it is known that silver phosphates prepared from phosphates and $AgNO_3$ can react with alkyl halides to give corresponding esters,[3a–f] the advantage of our *in situ* method was demonstrated by direct esterification of unprotected cAMP **27** because only trace amounts of compound **28** were detected by the reaction of the silver salt of cAMP and benzyl bromide. The superiority of our method can be accounted for by the double-activation mechanism; both phosphate and halide can be activated by silver oxide.

In conclusion, a mild and practical method for the direct alkylation of phosphates has been developed by the use of silver(I) oxide. The advantages of the method are as follows; (i) preparation of metal phosphates is not necessary, (ii) the reaction proceeds under neutral conditions, (iii) acid or base treatment is not necessary in the purification step, and (iv) choice of incorporated substituents depends only on availability of the corresponding halides. Thus, highly fluorescent diethyl pyren-1-ylmethyl phosphate, which is sensitive to acid and base, has been prepared for the first time by the present method. Finally, cAMP benzyl ester **28** was prepared.

Experimental

M.p.s. were determined on a Mitamura Riken Kogyo MEL TEMP instrument. ^{1}H NMR spectra were measured with a JEOL JNM-GSX270 FTNMR spectrometer. ^{31}P NMR spectra were measured with a JEOL JNM-EX270 FTNMR spectrometer. J values are given in Hz. IR spectra were obtained from a JASCO FT IR-5000 spectrometer. Mass spectra were obtained from a HITACHI M-80 mass spectrometer with EI mode (80 eV).

Synthesis of Diethyl Pyren-1-ylmethyl Phosphate **4** (*General Procedure*).—To a stirred solution of diethyl hydrogen phosphate **1** (0.340 g, 2.2 mmol) and pyren-1-ylmethyl chloride **2** (0.260 g, 1.00 mmol) in acetonitrile (3 cm^3) was added silver(I) oxide **3** (0.241 g, 1.00 mmol) and the resulting black suspension was vigorously stirred for 3.5 h at room temperature. The reaction was quenched by filtration of excess of silver oxide and insoluble precipitate [probably silver(I) chloride]. The filtrate was evaporated and the residual oil was dissolved in methylene dichloride. Washing with water, drying over $MgSO_4$ and concentration under reduced pressure gave compound **4** (0.35 g, 92%) as an oil (Found: M^+, 368.1153. $C_{21}H_{21}O_4P$ requires M, 368.1177); δ_H(270 MHz; $CDCl_3$; Me_4Si) 8.37 (1 H, d, J 9.0, pyrene 10-H), 8.22–8.0 (8 H, m, pyrene), 5.79 (2 H, d, J 8.0, CH_2O), 4.06 (4 H, dq, J 7.0 and 8.0, $MeCH_2O$) and 1.24 (6 H, dt, J 1.0 and 8.0, $MeCH_2O$); ν_{max}(film)/cm^{-1} 3042, 2986, 1265 (P=O), 1007 (P–O) and 980 (P–O); m/z (EI) 368 (M^+, 54%), 230 (14), 216 (31), 215 (55), 214 (81), 127 (99), 125 (14), 111 (33), 99 (100), 82 (35), 81 (15) and 28 (40).

Diethyl 1-(2-*Nitrophenyl*)*ethyl Phosphate* **18**.—δ_H(270 MHz; $CDCl_3$; Me_4Si) 7.98 (1 H, dd, *J* 8.0 and 1.5), 7.83 (1 H, dd, *J* 8.0 and 1.5), 7.68 (1 H, ddd, *J* 8.0, 8.0 and 1.5), 7.47 (1 H, ddd, *J* 8.0, 8.0 and 1.5), 6.04 (1 H, dq, *J* 5.0 and 5.0, 1-H), 4.08–4.00 (4 H, m, $MeCH_2O$), 1.71 (3 H, d, *J* 6.0, Me), 1.27 (3 H, dt, *J* 1.0 and 7.0, $MeCH_2O$), 1.23 (3 H, dt, *J* 1.0 and 7.0, $MeCH_2O$); ν_{max}(film)/cm^{-1} 2990, 1531 (NO_2), 1350 (NO_2), 1270 (P=O), 1033 (P–O) and 980 (P–O); *m*/*z* (EI) 304 (M^+ + 1, 3%), 257 (20), 229 (2), 201 (7), 155 (3), 150 (100) and 134 (3).

Diphenylmethyl Diethyl Phosphate **19**.—(Found: M^+, 320.1115. $C_{17}H_{21}O_4P$ requires M, 320.1177); δ_H(270 MHz; $CDCl_3$; Me_4Si) 7.41–7.22 (10 H, m, Ph), 6.41 (1 H, d, *J* 8, Ph_2CHO), 3.93 (4 H, dq, *J* 7.0 and 7.0, $MeCH_2O$) and 1.17 (6 H, dt, *J* 1.0 and 7.0, $MeCH_2O$); ν_{max}(film)/cm^{-1} 3066, 3032, 2986, 2934, 1495 (ArC–C), 1456 (ArC–C), 1263 (P=O), 1031 (P–O), 743 and 700; *m*/*z* (EI) 320 (M^+, 4%), 319 (25), 184 (100), 183 (25), 168 (4), 167 (38), 166 (31) and 105 (79).

Diethyl (7′-*Methoxy*-2′-*oxobenzo*[b]*pyran*-4′-*yl*)*methyl Phosphate* **20**.—M.p. 39–41 °C; δ_H (270 MHz; $CDCl_3$; Me_4Si) 7.40 (1 H, d, *J* 9.5, 5′-H), 6.87 (1 H, dd, *J* 9.5 and 2.5, 6′-H), 6.86 (1 H, d, *J* 2.5, 8′-H), 6.43 (1 H, t, *J* 1.5, 3′-H), 5.22 (2 H, dd, *J* 7.0 and 1.5, CH_2O), 4.20 (4 H, dq, *J* 7.0 and 7.0, $MeCH_2O$), 3.88 (3 H, s, MeO) and 1.37 (6 H, dt, *J* 1.1 and 7.0, $MeCH_2O$); ν_{max}(film)/cm^{-1} 2988, 2922, 1727 (CO), 1618 (C=C), 1267 (P=O), 1019 (P–O), 1060 (P–O) and 855; *m*/*z* (EI) 343 (M^+ + 1, 25%), 342 (M^+, 100), 314 (7), 216 (19), 206 (17), 190 (18) and 188 (15).

Diethyl Pentyl Phosphate **21**.—δ_H(270 MHz; $CDCl_3$; Me_4Si) 4.11 (4 H, dq, *J* 7.3 and 7.3, $MeCH_2O$), 4.03 (2 H, dt, *J* 6.7 and 6.7, CH_2O), 1.74–1.65 (2 H, m), 1.42–1.32 (4 H, m), 1.34 (6 H, dt, *J* 1.0 and 7.0, $MeCH_2O$) and 0.91 (3 H, t, *J* 7.0); ν_{max}(film)/cm^{-1} 2964, 2938, 1265 (P=O) and 1035 (P–O).

Allyl Diethyl Phosphate **22**.—(Found: C, 43.0; H, 7.75. $C_7H_{15}O_4P$ requires C, 43.32; H, 7.79%); δ_H(270 MHz; $CDCl_3$; Me_4Si) 5.95 (1 H, ddt, *J* 10, 17 and 5.6, 2-H), 5.37 (1 H, dd, *J* 17 and 1.0, 3-H), 5.25 (1 H, dd, *J* 10 and 1.0, 3-H), 4.45 (2 H, dt, *J* 1.0 and 5.5, CH_2O), 4.12 (4 H, ddq, *J* 1.0, 7.3 and 7.3, $MeCH_2O$) and 1.34 (6 H, dt, *J* 0.5 and 7.0, $MeCH_2O$); ν_{max}(film)/cm^{-1} 2988, 1653 (C=C), 1270 (P=O), 1029 (P–O) and 980 (P–O).

Diethyl 2,3,4,6-*Tetra*-O-*acetyl*-β-D-*galactopyranosyl Phosphate* **23**.—δ_H(270 MHz; $CDCl_3$; Me_4Si) 5.43 (1 H, dd, *J* 3.5 and 1.0, 4-H), 5.32–5.26 (2 H, m, 1- and 2-H), 5.04 (1 H, m, 3-H), 4.18–4.04 (7 H, m), 2.17 (3 H, s, Ac), 2.08 (3 H, s, Ac), 2.05 (3 H, s, Ac), 2.00 (3 H, s, Ac), 1.34 (3 H, dt, *J* 1.0 and 7.0, $MeCH_2O$) and 1.32 (3 H, dt, *J* 1.0 and 7.0, $MeCH_2O$); ν_{max}(film)/cm^{-1} 2988, 1756 (C=O), 1375 (C–O), 1224 (P=O) and 1033 (P–O); *m*/*z* (EI) 485 (M^+), 331, 288, 271 and 197.

Benzoyl Diethyl Phosphate **24**.—(Found: C, 51.0; H, 5.7. $C_7H_{15}O_4P$ requires C, 51.17; H, 5.86%); δ_H(270 MHz; $CDCl_3$; Me_4Si) 7.69–7.45 (5 H, m, Ph), 4.37 (4 H, dq, *J* 7.0 and 7.0, $MeCH_2O$) and 1.42 (6 H, dt, *J* 1.0 and 7.0, $MeCH_2O$); ν_{max}(film)/cm^{-1} 1748 (C=O), 1454, 1249 (P=O), 1017 (P–O) and 961 (P–O); *m*/*z* (EI) 259 (M^+ + 1, 39%), 258 (M^+, 16), 230 (16), 132 (45), 129 (16), 106, (24), 105 (100) and 104 (27).

Tetraethyl Pyrophosphate **25**.—δ_H(270 MHz; $CDCl_3$; Me_4Si) 4.26 (8 H, dq, *J* 7.0 and 7.0, $MeCH_2O$) and 1.39 (12 H, dt, *J* 1.0 and 7.0, $MeCH_2O$); δ_P(109 MHz; $CDCl_3$; 85% H_3PO_4) −12.7 (heteronuclear decoupled); ν_{max}(film/cm^{-1}) 1299 (P=O), 1036 (P–O), 982 (P–O) and 944 (P–O); *m*/*z* (EI) 290 (M^+, 75%), 263 (97) and 32 (100).

Diethyl Tributyl Phosphate **26**.—δ_H(270 MHz; $CDCl_3$; Me_4Si) 3.88 (4 H, dq, *J* 7.0 and 7.0, OCH_2Me), 1.67–1.60 (6 H, m, OCH_2Me), 1.37–1.17 (18 H, m, $Sn[CH_2]_3Me$) and 0.90 (9 H, t, *J* 7.0, $Sn[CH_2]_3Me$); δ_P(109 MHz; $CDCl_3$; 85% H_3PO_4) − 6.6 (heteronuclear decoupled).

Dibenzyl Pyren-1-*ylmethyl Phosphate* **7**.—δ_H(270 MHz; $CDCl_3$; Me_4Si) 8.29–7.96 (9 H, m, pyrene), 7.25–7.17 (10 H, m, Ph), 5.73 (2 H, d, *J* 8, pyrenylCH_2O) and 4.97 (4 H, d, *J* 8, PhCH_2O); ν_{max}(KBr)/cm^{-1} 1276 (P=O), 1002 (P–O), 737 and 698.

Pyren-1-*ylmethyl Diphenylphosphinate* **8**.—M.p. 81–84 °C (Found: M^+, 432.1267. $C_{29}H_{21}O_2P$ requires M, 432.1279); δ_H(270 MHz; $CDCl_3$; Me_4Si) 8.3–7.0 (19 H, m) and 5.72 (2 H, d, *J* 7.2, CH_2O); ν_{max}(KBr)/cm^{-1} 1183 (P=O), 1131, 961 (P–O), 845, 729 and 694; *m*/*z* (EI) 432 (M^+, 32%), 273 (56), 218 (97), 217 (100) and 216 (25).

Synthesis of cAMP Benzyl Ester **28**.—In an oven-dried, 20 cm^3, two-necked, round-bottom flask equipped with a magnetic stirring bar and a rubber septum was placed cAMP·H_2O (63.8 mg, 0.1837 mmol). The flask was evacuated under vacuum, then was flushed with argon. Dry MeCN (10 cm^3), DMSO (1 cm^3), and benzyl bromide (0.10 cm^3, 0.8 mmol) were added *via* syringe. After the addition of solid silver(I) oxide (88 mg, 0.38 mmol), the resulting black suspension was stirred at 65 °C for 18 h under argon. The reaction mixture was filtered through filter paper and the residue was washed with chloroform. The combined filtrate was evaporated under reduced pressure. Purification by column chromatography [SiO_2, E. Merck No. 7774 (15 g); 4.7% MeOH–CH_2Cl_2, then 6.2% MeOH–CH_2Cl_2] gave compound **28** (40 mg, 52%) as a mixture of two stereoisomers (ax/eq = 1.5/1). The residual black solid was washed with distilled water and the aqueous filtrate was evaporated under reduced pressue to give cAMP·H_2O (19 mg, 30% recovery) as a solid.

Compound **28**-axial, δ_H(270 MHz; $CDCl_3$; Me_4Si) 8.18 (1 H, s, 8-H), 7.82 (1 H, s, 2-H), 7.51–7.48 (2 H, m, Ph), 7.43–7.35 (3 H, m, Ph), 5.94 (1 H, s, 1′-H), 5.64 (2 H, br, NH_2), 5.49 (1 H, ddd, *J* 9.5, 5.0 and 1.5, 3′-H), 5.24 (2-H, d, *J* 8.5, PhCH_2), 4.83 (1 H, d, *J* 5.0, 2′-H), 4.55 (1 H, ddd, *J* 22, 8.5 and 4.0, 5′-H), 4.42–4.30 (2 H, m, 4′- and 5′-H) and 3.7 (1 H, br s, OH); δ_P(109 MHz; $CDCl_3$; 85% H_3PO_4) − 5.56 (heteronuclear decoupled); ν_{max}(KBr)/cm^{-1} 3500–3300, 1644, 1603, 1292 (P=O), 1133, 1002, 915 and 837.

Compound **28**-equatorial, δ_H(270 MHz; $CDCl_3$; Me_4Si) 8.31 (1 H, s, 8-H, 7.82 (1 H, s, 2-H), 7.43–7.37 (5 H, m, Ph), 5.95 (1 H, s, 1′-H), 5.67 (2 H, br, NH_2), 5.56 (1 H, m), 5.22 (1 H, m), 5.20 (2 H, d, *J* 10.0, PhCH_2), 4.90 (1 H, d, *J* 5.0, 2′-H) and 4.55–4.45 (3 H, m).

Acknowledgements

We thank Professor T. Kawashima and Mr. H. Takami of the University of Tokyo for performing the ^{31}P NMR measurements. We thank Dr. G. Yamamoto of the University of Tokyo for measurement of high resolution mass spectra.

References

1 For reviews see (*a*) J. F. Wootton and D. R. Trentham, in *Photochemical Probes in Biochemistry*, ed. P. E. Nielsen, Kluwer Academic, Dordrecht, 1988, pp. 277–296; (*b*) Y. Hayakawa, *Inorganic Acid Derivatives*, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 6, pp. 601–630.

2 For example (*a*) J. Engels and W. Pfleiderer, *Nucleic Acids Res., Special Publ.*, 1975, **1**, s113; (*b*) J. Engels and E. J. Schlaeger, *J. Med. Chem.*, 1977, **20**, 907; (*c*) J. W. Walker, G. P. Reid, J. A. McCray and D. R. Trentham, *J. Am. Chem. Soc.*, 1988, **110**, 7170.

3 For example Ag: (*a*) J. Baddiley, V. M. Clark, J. J. Michalski and A. R. Todd, *J. Chem. Soc.*, 1949, 815; (*b*) F. Cramer and H. Hettler, *Chem. Ber.*, 1958, **91**, 1181; (*c*) V. I. Shvets, A. I. Lyutik, M. A. Kabanova, L. D. Alekseeva, A. S. Tkachenko and R. P. Evstigneeva, *Bioorg. Khim.*, 1975, **1**, 758; (*d*) Y. G. Molotkovskii, L. F. Nikulina and L. D. Bergel'son, *Chem. Phys. Lipids*, 1976, **17**, 108; (*e*) M. Kates and A. J. Hancock, *Chem. Phys. Lipids*, 1976, **17**, 155; (*f*) G. P. Sokolov, M. Gavars and J. Freimanis, *Zh. Org. Khim.*, 1988, **24**, 2553; (*g*) J. E. Baldwin, A. W. McConnaughie, M. G. Maloney, A. J. Pratt and S. B. Shim, *Tetrahedron*, 1990, **46**, 6879; for R_3Sn: (*h*) K. Yamaguchi, T. Kamimura and T. Hata, *J. Am. Chem. Soc.*, 1980, **102**, 4534; for NR_4: S. Kataoka, J. Isono, N. Yamaji and K. Kato, *Chem. Lett.*, 1986, 1221; (*j*) S. Kataoka, R. Uchida and N. Yamaji, *Heterocycles*, 1991, **32**, 1351.

4 M. Iwamura, T. Ishikawa, Y. Koyama, K. Sakuma and H. Iwamura, *Tetrahedron Lett.*, 1987, **28**, 679; M. Iwamura, K. Tokuda, N. Koga and H. Iwamura, *Chem. Lett.*, 1987, 1729; M. Iwamura, C. Hodota and M. Ishibashi, *Synlett*, 1991, 35; T. Furuta, H. Torigai, T. Osawa and M. Iwamura, *Chem. Lett.*, 1993, 1179.

Paper 3/03505K
Received 17*th June* 1993
Accepted 7*th September* 1993