room temperature by an external channel ratio method. Dioxane containing the usual scintillators was used as solvent. A counting efficiency of about 85% with a background of about 50 cpm was obtained.

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A New Phosphorylating Reagent. I. The Preparation of Alkyl Dihydrogen Phosphates by Means of 2-Chloromethyl-4-nitrophenyl Phosphorodichloridate

Tsujiaki Hata, Yoshitaka Mushika, and Teruaki Mukaiyama

Contribution from the Laboratory of Organic Chemistry, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo, Japan.
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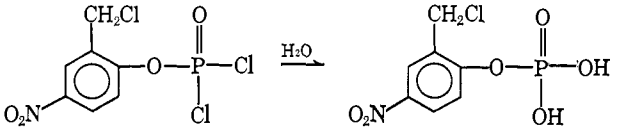
Abstract: A convenient method for the preparation of alkyl dihydrogen phosphates was investigated. 2-Chloromethyl-4-nitrophenyl phosphorodichloridate (**2**), a phosphorylating agent having a new protecting group, was prepared from 2-chloromethyl-4-nitrophenol (**1**) and phosphoryl chloride. It reacts smoothly with alcohols in the presence of tertiary amines to give the corresponding alkyl 2-chloromethyl-4-nitrophenyl phosphorochloridates (**3**), which were in turn converted by hydrolysis into alkyl 2-chloromethyl-4-nitrophenyl hydrogen phosphates (**4**). When the phosphates **4** are treated with pyridine, they change to inner salts of 1-(2′-alkyl hydrogen phosphoroxy-5′-nitrobenzyl)pyridinium hydroxide (**7**). The inner salts **7** readily underwent hydrolysis to yield the corresponding alkyl dihydrogen phosphates (**8**) and inner salt of 1-(2′-hydroxy-5′-nitrobenzyl)pyridinium hydroxide (**9**) in good yields.

A considerable number of phosphorylation methods have been investigated and successfully applied to the syntheses of various phosphates and pyrophosphates. However, there are few reports dealing with general methods of the preparation of alkyl dihydrogen phosphates except those concerned with phosphorylation of alcohols by means of β-cyanoethyl phosphate and dicyclohexylcarbodiimide (DCC),[1] trichloroacetonitrile and inorganic phosphoric acid,[2] or dibenzyl phosphorochloridate.[3] Recently it has been demonstrated in this laboratory that inorganic phosphorous acid reacts with mercuric chloride to give an intermediate complex, from which alkyl dihydrogen phosphates can be obtained by further reaction with alcohols.[4]

In the present study, a convenient method for the syntheses of alkyl dihydrogen phosphates by the use of 2-chloromethyl-4-nitrophenyl phosphorodichloridate (**2**), a phosphorylating reagent having a new protecting group, was investigated. The phosphorodichloridate **2** was chosen on the following assumptions; first, one of the two chlorine atoms of **2** would exclusively react with 1 equiv of alcohol to give alkyl 2-chloromethyl-4-nitrophenyl phosphorochloridate (**3**). Second, alkyl 2-chloromethyl-4-nitrophenyl phosphate (**4**) derived from **2** would yield, when treated with a tertiary amine, the inner salt of 1-(2′-alkyl hydrogen phosphoroxy-5′-nitrobenzyl)trialkylammonium hydroxide (**6**), an active phosphorylating reagent. This reasoning is based on the facile generation of a phosphoryl cation by the elimination of a phenoxy group when activated by two electron-withdrawing groups, $-NO_2$ and $-CH_2N^+<$.

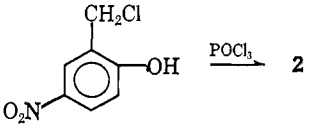
Thus the 2-chloromethyl-4-nitrophenyl group acts as a protecting group in the first stage of this process and, in the next stage, it functions as a strongly electron-withdrawing group, activating the phosphate to generate an active phosphoryl cation. Therefore, this group may be called an "activatable protecting group."

The phosphorylating reagent **2**[5,6] was readily prepared in 71% yield by refluxing 2-chloromethyl-4-nitrophenol (**1**) and 2.5 mol of phosphoryl chloride for 6 hr. In this



2 **12**

reaction, the yield of **2** decreased considerably when a large excess of phosphoryl chloride was used. This is probably due to the lower reaction temperature.



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Alcohols were selectively phosphorylated with **2** to give the corresponding alkyl 2-chloromethyl-4-nitrophenyl phosphorochloridates (**3**) by the reaction of 1 mol of **2** and 1 mol of an alcohol in the presence of

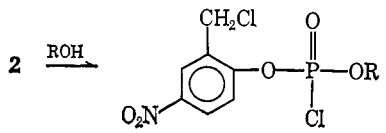
(1) G. M. Tenner, *J. Am. Chem. Soc.*, 83, 159 (1961).
(2) F. Cramer and G. Weimann, *Chem. Ind.* (London), 46 (1960).
(3) F. R. Atherton, H. T. Openshaw, and A. R. Todd, *J. Chem. Soc.*, 382 (1945).
(4) T. Obata and T. Mukaiyama, *J. Org. Chem.*, 32, 1063 (1967).
(5) The preparation of compound **2** was first carried out in the laboratory of Professor F. Cramer, Max-Planck-Institut für experimentelle Medizin in Göttingen.
(6) The structure of **2** was supported by the elemental analysis and was further confirmed by derivating to 2-chloromethyl-4-nitrophenyl dihydrogen phosphate (**12**) by hydrolysis.

Table I. Alkyl 2-Chloromethyl-4-nitrophenyl Hydrogen Phosphates (4)

No.	R	Yield,[a] %	Mp, °C	Appearance	R_f[d]	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
4a	Ethyl	89	112–114	White leaflets[b]	0.84	$C_9H_{11}ClNO_6P$	36.57	3.75	4.74	36.27	4.08	4.82
4b	*n*-Amyl	94		Viscous oil[c]	0.86	$C_{12}H_{17}ClNO_6P$	42.67	5.04	4.15	42.32	5.18	4.20
4c	*n*-Hexadecyl	83	76–77	White powder[b]	0.85	$C_{28}H_{39}ClNO_6P$	56.15	7.99	2.85	56.68	8.06	2.96
4d	Cyclohexyl	93		Viscous oil[c]	0.86	$C_{13}H_{17}ClNO_6P$	44.64	4.91	4.01	43.02	4.96	4.22
4e	Bornyl	85		Viscous oil[c]	0.92	$C_{17}H_{23}ClNO_6P$	50.54	5.74	3.43	48.01	5.76	3.52
4f	Benzyl	93		Viscous oil[c]	0.85	$C_{14}H_{13}ClNO_6P$	47.01	3.67	3.92	47.82	4.87	4.09
4g	Phenyl	90		Viscous oil[c]	0.89	$C_{13}H_{11}ClNO_6P$	45.42	3.21	4.07	42.85	3.82	3.77

[a] Yields were based on 2-chloromethyl-4-nitrophenyl phosphorodichloridate (**2**). [b] It was recrystallized from a mixture of ether, petroleum ether (bp 35–50°), and a trace of acetone. [c] It was extracted with benzene and then washed with a mixture of petroleum ether and chloroform (10:1 v/v). [d] Paper chromatography was carried out by the ascending technique using Toyo Roshi No. 50 paper. Solvent system used was: isopropyl alcohol–concentrated ammonium hydroxide–water (7:1:2, v/v).

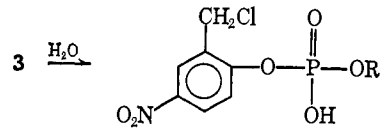
tertiary amines. In general, the reactions were carried out in anhydrous tetrahydrofuran in the range about −20 to −10°. In the cases of higher alcohols and phenols, a higher temperature was required because of



3

their lower solubility or reactivity. An equimolar amount of tertiary amine was used in order to avoid further reaction with the chloromethyl group of the starting material **2** and of the product **3**. Of three tertiary amines examined, it was found that pyridine was more effective as a hydrogen chloride acceptor than triethylamine and diethylaniline.

Alkyl 2-chloromethyl-4-nitrophenyl hydrogen phosphates (**4**) were prepared by treating **3** with water containing an equimolar amount of pyridine at a temperature below 15°. The phosphates **4** were successfully



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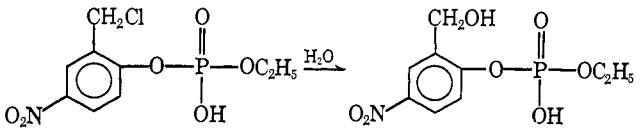
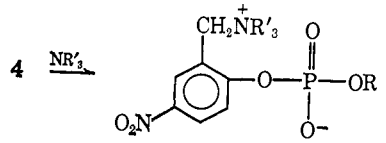
separated from the reaction mixtures by the use of benzene. The results are summarized in Table I.

On hydrolysis with hot water, **4** gave alkyl 2-hydroxymethyl-4-nitrophenyl hydrogen phosphates (**5**); for example, when ethyl derivative **4a** was treated with a large excess of hot water (90°) for 2 hr, ethyl 2-hydroxymethyl-4-nitrophenyl hydrogen phosphate (**5a**) was obtained in 54% yield. It was confirmed that the chloro-



4a **5a**

methyl group of the compounds **4** was not hydrolyzed



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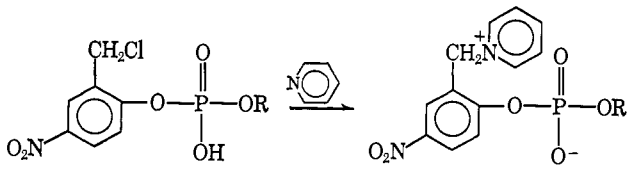
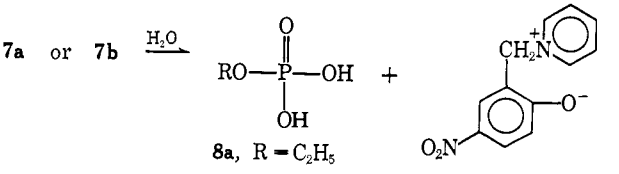
with water at temperatures below 50°. When aqueous pyridine solutions of the chloromethyl derivatives **4** were kept standing for 2 days, **4** was completely converted into inner salts of 1-(2′-alkyl hydrogen phosphoroxy-5′-nitrobenzyl)pyridinium hydroxide (**7**); for example, ethyl (**7a**) and *n*-amyl (**7b**) derivatives were isolated in 69 and 41% yields from **4a** and **4b**. Their struc-



4a, R = C_2H_5
b, R = *n*-C_5H_{11}

7a, R = C_2H_5
b, R = *n*-C_5H_{11}

tures were confirmed by elemental analysis and ir and uv spectra. In the above reactions, small amounts of alkyl dihydrogen phosphates (**8a** and **8b**) and 1-(2′-hydroxymethyl-5′-nitrobenzyl)pyridinium chloride (hydrogen chloride of **9**) were detected by paper chromatography. They are assumed to have been formed by the decompositions of the active inner salts **7a** and **7b** with water. This shows that **7** would be



8a, R = C_2H_5
b, R = *n*-C_5H_{11}

9

readily hydrolyzed with water to yield compounds **8** and **9**. Indeed, alkyl dihydrogen phosphates (**8**) were successfully prepared from **4**, without isolating the intermediate **7**, by treating **4** with aqueous pyridine at 90°. The phosphates **8** were obtained as their monoanilinium salts in good yields either by means of method A or method B described in the Experimental Section. The compound **9** was easily separated from the reaction mixture by the addition of ethanol. The results are listed in Table II.

In addition to the pyridine inner salt, **7**, the triethylammonium salt (**10**) was isolated in good yield as white

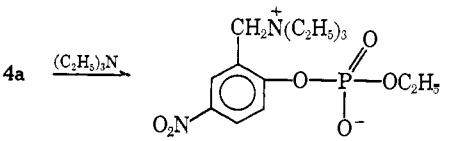


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Table II. Monoanilinium Salts of Alkyl Dihydrogen Phosphates (8)

No.	R	Yield,[a] %	Mp, °C	Recryst from	R_f[b]	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
8a	Ethyl	71	164–165	95% ethanol	0.24	$C_8H_{14}NO_4P$	43.84	6.44	6.39	43.97	6.50	6.19
8b	*n*-Amyl	66	139–141	Acetone	0.49	$C_{11}H_{20}NO_4P$	50.57	7.72	5.36	50.70	7.96	5.34
8c	*n*-Hexadecyl	90	122–124	95% ethanol		$C_{22}H_{42}NO_4P$	63.59	10.19	3.37	63.97	10.15	3.43
8d	Cyclohexyl	66	170–171	95% ethanol	0.40	$C_{12}H_{20}NO_4P$	52.74	7.38	5.13	53.38	7.43	5.43
8e	Bornyl	56	189–190	95% ethanol	0.54	$C_{16}H_{26}NO_4P$	58.70	8.01	4.28	58.35	8.24	4.41
8f	Benzyl	69	168–169	95% ethanol	0.35	$C_{13}H_{16}NO_4P$	55.52	5.73	4.98	55.51	6.11	5.34
8g	Phenyl	68	179	95% ethanol	0.32	$C_{12}H_{14}NO_4P$	53.93	5.28	5.24	53.40	5.22	5.47

[a] Yields were based on alkyl 2-chloromethyl-4-nitrophenyl hydrogen phosphates (4). [b] Paper chromatography was carried out by ascending technique using Toyo Roshi No. 50 paper. Solvent system used was: isopropyl alcohol–concentrated ammonium hydroxide–water (7:1:2, v/v).

prisms by the reaction of ethyl derivative **4a** with triethylamine. It was observed that the hydrolysis of **10** proceeded more sluggishly than that of pyridinium derivative **7a**.

In conclusion, it is to be noted that the 2-chloromethyl-4-nitrophenyl group can be successfully used as a protecting group, and alkyl dihydrogen phosphates (**8**) are obtainable in good yields starting from the phosphorodichloridate **2** *via* four steps. This method is superior to the other methods cited above for the phosphorylation of valuable alcohols, because it can be successfully carried out by the use of just 1 equiv of alcohol.

Since the hydrolysis of **4** proceeds through the pyridinium derivatives **7**, it can be expected that unsymmetrical dialkyl hydrogen phosphates will be produced *via* the same intermediates **7**, if **4** is treated with various alcohols in place of water in the above reaction.

Experimental Section

Reagents. Alcohols, amines, and solvents were purified and dried by ordinary procedures. 2-Chloromethyl-4-nitrophenol (**1**) was prepared by a known procedure[7] and dried over phosphorus pentoxide. Phosphoryl chloride was freshly distilled before use.

2-Chloromethyl-4-nitrophenyl Phosphorodichloridate (2). A mixture of 18.7 g (0.1 mol) of 2-chloromethyl-4-nitrophenol (**1**) and 23 ml (0.25 mol) of phosphoryl chloride was refluxed for 6 hr in the presence of a catalytic amount of potassium chloride (1 g) until the evolution of hydrogen chloride ceased. After removal of excess phosphoryl chloride by evaporation, the viscous oily residue was distilled under reduced pressure to give 21.3 g (71%) of the phosphorodichloridate **2**, bp 165–167° (0.2 mm), as a pale yellow viscous liquid. It was solidified when chilled: mp 43–44°.

Anal. Calcd for $C_7H_5Cl_3NO_4P$: C, 27.61; H, 1.66; N, 4.60. Found: C, 26.96; H, 1.63; N, 4.81.

***n*-Amyl 2-Chloromethyl-4-nitrophenyl Hydrogen Phosphate (4b).** To a solution of 3.04 g (0.01 mol) of 2-chloromethyl-4-nitrophenyl phosphorodichloridate (**2**) in 15 ml of tetrahydrofuran (THF) was added, dropwise, a solution of *n*-amyl alcohol (1.08 ml, 0.01 mol) and pyridine (0.8 ml, 0.01 mol) in 10 ml of THF with stirring at $-20 \sim -10°$ over a period of about 1 hr. A white precipitate soon appeared. The stirring was continued for 5 hr under cooling. Then, the reaction mixture was poured with stirring into 50 ml of water containing 0.8 ml (0.01 mol) of pyridine at a temperature below 15°. After removal of THF by evaporation, the residue was extracted with three 30-ml portions of benzene. The combined extracts were washed with water and dried over anhydrous sodium sulfate. The solvent was removed by evaporation to give 3.15 g (94%) of the phosphate **4d**, a pale yellow oil, which was finally dried under high vacuum at 40–50° for 1 hr. The viscous oily product was chromatographically pure: λ_{max}^{MeOH} 290 mμ (log ε 3.94); ν_{max} 3080, 2954, 2930, 2860, 2590 (broad), 2210 (broad), 1670 (broad), 1615, 1585, 1520, 1478, 1375, 1345, 1235 (vs), 1195, 1030 (vs), 945, 810, 755, and 680 cm^{-1} (film).

Anal. Calcd for $C_{12}H_{17}ClNO_6P$: C, 42.68; H, 5.07; N, 4.15. Found: C, 43.15; H, 5.73; N, 4.49.

(7) C. A. Buchler, F. K. Kirchner, and G. F. Deebel, *Org. Syn.*, **20**, 59 (1940).

Ethyl (**4a**), *n*-hexadecyl (**4c**), cyclohexyl (**4d**), bornyl (**4e**), and benzyl (**4f**) derivatives were prepared in the same way (see Table I).

Phenyl 2-Chloromethyl-4-nitrophenyl Hydrogen Phosphate (4g). To a solution of 3.04 g (0.01 mol) of 2-chloromethyl-4-nitrophenyl phosphorodichloridate (**2**) in 15 ml of THF was added a solution of phenol (0.94 g, 0.01 mol) and pyridine (0.8 ml, 0.01 mol) in THF. The reaction mixture was continuously stirred at room temperature for 15 hr. Work-up of the reaction mixture as described above gave 3.08 g (90%) of the phosphate **4g** as a pale yellow viscous oil.

2-Chloromethyl-4-nitrophenyl Dihydrogen Phosphate (12). A solution of 20 g (0.066 mol) of 2-chloromethyl-4-nitrophenylphosphorodichloridate (**2**) in a mixture of concentrated hydrochloric acid (150 ml) and acetone (50 ml) was kept at 30° for 30 min. Acetone was removed by evaporation and the resulting solution was washed with three 100-ml portions of chloroform. Then the aqueous layer was concentrated under reduced pressure at a temperature below 40° until some white crystals appeared, and the solution was allowed to stand in a refrigerator overnight to afford 7.5 g (48%) of the product **12** as a white powder: mp 137–139°; $\lambda_{max}^{H_2O}$ 293 mμ (log ε 3.93).

Anal. Calcd for $C_7H_7ClNO_6P$: C, 31.42; H, 2.64; N, 5.24. Found: C, 31.39; H, 2.52; N, 5.34.

Ethyl 2-Hydroxymethyl-4-nitrophenyl Hydrogen Phosphate (5). A solution of 3.0 g (0.01 mol) of ethyl 2-chloromethyl-4-nitrophenyl hydrogen phosphate (**4a**) in 50 ml of water was heated on a steam bath for 2 hr. After cooling to room temperature, the reaction mixture was neutralized to pH 7 with ammonium carbonate and concentrated to dryness under reduced pressure. To the residue, 30 ml of dry acetone was added and then the mixture was warmed on a steam bath for several minutes. White crystals of ammonium chloride (0.45 g) were removed by filtration. The filtrate was again evaporated to dryness under reduced pressure and the resulting syrup was dissolved in 20 ml of benzene. The benzene solution was allowed to stand overnight in a refrigerator to afford 1.7 g (54%) of ammonium salt of the phosphate **5**. Recrystallization from a mixture of acetone and ethanol afforded white needles: mp 137–138°; R_f 0.73 (isopropyl alcohol–concentrated ammonium hydroxide–water, 7:1:2, v/v), 0.46 (1-butanol–water–acetic acid, 5:4:1, v/v); $\lambda_{max}^{H_2O}$ 292 mμ (log ε 3.93).

Anal. Calcd for $C_9H_{15}N_2O_7P$: C, 36.74; H, 5.14; N, 9.52. Found: C, 36.70; H, 5.42; N, 9.82.

Inner Salt of 1-(2′-Ethyl hydrogen phosphoroxy-5′-nitrobenzyl)-pyridinium Hydroxide (7a). A solution of 3.0 g (0.01 mol) of ethyl 2-chloromethyl-4-nitrophenyl hydrogen phosphate (**4a**) in a mixture of pyridine (4.0 ml, 0.05 mol) and water (1.8 ml, 0.10 mol) was kept at room temperature for 2 days. To the reaction mixture, 100 ml of dry acetone was added and the mixture was stirred at room temperature for several minutes. A pale yellow precipitate was collected by filtration and washed with two 50-ml portions of dry acetone to afford 2.34 g (62%) of the crude **7a**: mp 164–166° dec. The aqueous solution of the crude product was passed through a column (12 × 300 mm) of Amberlite IRC 50 resin (H^+ form) and the column was washed with water until the washings were neutral to litmus. The combined original eluent and washings were evaporated to dryness under reduced pressure. The syrupy residue was dissolved in 50 ml of dry acetone and the solution was kept at room temperature for several hours. A white precipitate was collected by filtration and recrystallized from a mixture of ethanol and acetone to afford the pure product **7a** as white powder: mp 172–173° dec; R_f 0.61 (isopropyl alcohol–concentrated ammonium hydroxide–water, 7:1:2, v/v); $\lambda_{max}^{H_2O}$ 261 mμ (log ε 3.91), 267.5 (3.90), and 293 (0.92); ν_{max}^{KBr} 3430 (OH), 1628 (pyridine), 1518, 1350 (NO_2), 1250 (P=O), and 1040 (POC) cm^{-1}.

Anal. Calcd for $C_{14}H_{15}N_2O_6P \cdot H_2O$: C, 47.20; H, 4.81; N, 7.86. Found: C, 46.79; H, 4.40; N, 7.82.

Inner Salt of 1-(2′-*n*-Amyl hydrogen phosphoxy-5′-nitrobenzyl)-pyridinium Hydroxide (7b). In a similar manner, **7b** was obtained from *n*-amyl 2-chloromethyl-4-nitrophenyl hydrogen phosphate (**4b**) and aqueous pyridine in 41% yield as white prisms: mp 139–140° (acetone–ethanol); R_f 0.78 (isopropyl alcohol–concentrated ammonium hydroxide–water, 7:1:2, v/v); $\lambda_{max}^{H_2O}$ 261 mμ (log ε 3.95), 267.5 (3.95), and 292 (3.96).

Anal. Calcd for $C_{17}H_{21}N_2O_6P \cdot H_2O$: C, 51.26; H, 5.82; N, 7.03. Found: C, 51.73; H, 5.90; N, 7.13.

Alkyl Dihydrogen Phosphate (8). General Procedure. A solution of 0.01 mol of alkyl 2-chloromethyl-4-nitrophenyl hydrogen phosphate (**4**) in a mixture of pyridine (4.0 ml, 0.05 mol) and water (5.4 ml, 0.3 mol) was kept at room temperature for 2 days and then heated at 80° for 8 hr. To the reaction mixture, 20 ml of absolute ethanol was added, and the mixture was stirred at room temperature for several minutes. A yellow precipitate, 1-(2′-hydroxy-5′-nitrobenzyl)pyridinium chloride (hydrogen chloride salt of **9**), was filtered and washed with two 20-ml portions of absolute ethanol. From the combined alcoholic filtrate and washings, the corresponding alkyl dihydrogen phosphates (**8**) were isolated as monoanilinium salts by means of either method A or method B. *n*-Hexadecyl **8c**, benzyl **8f**, and phenyl dihydrogen phosphate **8g** were obtained according to method A and the other derivatives listed in Table II were isolated by method B.

Method A. The combined alcoholic filtrate and washings were evaporated to dryness under reduced pressure and the residue was dissolved in 50 ml of dry acetone. A small amount of insoluble yellow crystals was removed by filtration and then 2 ml of aniline was added to the filtrate. The mixture was stored in a refrigerator overnight to give monoanilinium alkyl dihydrogen phosphate (**8**) as white crystals.

Method B. To the combined alcoholic filtrate and washings was added 40 ml of water and the resulting solution was passed through a column (12 × 200 mm) of Amberlite IR 120 resin (H^+ form). The column was washed with 50% ethanol until the washings were no longer acid to litmus. The combined eluent and washings were evaporated to dryness under reduced pressure. The pale yellow syrupy residue was dissolved in 10 ml of 95% ethanol (in the case of R = *n*-amyl, 10 ml of dry ether was used) and then 2 ml of aniline was added to the solution. The mixture was allowed to stand in a refrigerator overnight to give the monoanilinium salt of **8** as white crystals.

1-(2′-Hydroxy-5′-nitrobenzyl)pyridinium Chloride (Hydrogen Chloride Salt of 9). Two grams (0.0107 mol) of 2-chloromethyl-4-nitrophenol (**1**) was dissolved in 20 ml of dry pyridine. An exothermic reaction occurred and a yellow precipitate soon appeared. The reaction mixture was stirred at room temperature for 2 hr. Then the precipitate was collected by filtration and washed with ethanol to give 2.7 g (95%) of the HCl salt of **9**. Repeated recrystallization by means of hot water afforded pale yellow prisms for an analytical sample: mp >250°; R_f 0.71 (isopropyl alcohol–concentrated ammonium hydroxide–water, 7:1:2, v/v); $\lambda_{max}^{H_2O}$ 260 mμ (log ε 3.85), 266.5 (shoulder), and 3.16 (3.93).

Anal. Calcd for $C_{12}H_{11}ClN_2O_3$: C, 54.04; H, 4.16; N, 10.51. Found: C, 54.16; H, 4.45; N, 10.62.

Inner Salt of 1-(2′-Ethyl hydrogen phosphoxy-5′-nitrobenzyl)-triethylammonium Hydroxide (10). A solution of 3.0 g (0.01 mol) of ethyl 2-chloromethyl-4-nitrophenyl hydrogen phosphate (**4a**) in 20 ml of triethylamine was warmed at 50–55° for 6 hr. After removal of excess triethylamine by evaporation, the resulting oily residue was dissolved in 50 ml of dry acetone and the solution was allowed to stand at room temperature about for 2 hr. The triethylammonium chloride which separated was removed by filtration. The filtrate was kept standing in a refrigerator overnight to afford 2.6 g (72%) of the crude **10**: mp 177–178° dec. It was purified by passing through a column of Amberlite IRC 50 (H^+ form) as mentioned in the above experiment (preparation of **7a**). Repeated recrystallization by means of acetone containing a trace of water afforded white cubes for an analytical sample: mp 175–176° dec; R_f 0.67 (isopropyl alcohol–concentrated ammonium hydroxide–water, 7:1:2); $\lambda_{max}^{H_2O}$ 288 mμ (log ε 3.95).

Anal. Calcd for $C_{15}H_{25}N_2O_6P$: C, 50.00; H, 6.99; N, 7.77. Found: C, 49.77; H, 7.04; N, 7.75.

Acknowledgment. This work was supported by a grant from the Kawakami Foundation. We also wish to thank Mr. M. Koezuka for his help with elemental analysis.

Metal–Ammonia Reduction. IV.[1] Single-Stage Reduction of Polycyclic Aromatic Hydrocarbons

Ronald G. Harvey, Leonida Arzadon, John Grant, and Kathryn Urberg

Contribution from the Ben May Laboratory, University of Chicago, Chicago, Illinois 60637. *Received January 9, 1969*

Abstract: Reduction by lithium dissolved in liquid ammonia of a series of representative polycyclic aromatic hydrocarbons (naphthacene, dibenz[*a*,*h*]anthracene, 9-alkyl- and 9,10-dialkylanthracene, 7-methyl- and 7,12-dimethylbenz[*a*]anthracene, 3-methylcholanthrene, phenanthrene, and pyrene) was selectively directed to the dihydro stage. Product structure accorded, in general, with predictions based upon molecular orbital calculations of the positions of highest electron density in the corresponding anionic intermediates. Reduction of 9,10-dialkylanthracene proceeded stereospecifically when the alkyl function was ethyl, benzyl, or *n*-butyl to furnish *trans*-9,10-dialkyl-9,10-dihydroanthracene; when the alkyl group was methyl, *cis* and *trans* diastereomers were formed in equal proportion. The *cis*-diethyl, dibenzyl, and di-*n*-butyl isomers were independently synthesized, and differences in the chemical reactivity of the *cis* and *trans* diastereomers were related to the conformational properties of the hydrocarbons and their anionic derivatives; preferential axial attack during alkylation or protonation is proposed.

Reduction of polycyclic aromatic hydrocarbons, despite a long history of investigation,[2] remains one of the least predictable and controllable reactions of the polynuclear hydrocarbons. Not only do chemical reduction and catalytic hydrogenation frequently lead to different products, but variations of either method often influence both the extent of reduction and the distribution of isomeric hydroaromatic products. Much of this complexity is a consequence of secondary processes which include isomerization of double bonds, dispro-

(1) Part III: R. G. Harvey and K. Urberg, *J. Org. Chem.*, 33, 2206 (1968).

(2) E. Clar, "Polycyclic Hydrocarbons," Vol. I and II, Academic Press, New York, N. Y., 1964.