

Total Resolution of the Hexakis(2-aminoethanethiolo)tricobalt(III) Cation by Ion-Exchange Chromatography¹

Sir:

Numerous attempts to resolve optically active transition metal complexes into their antipodes by relatively rapid and simple chromatographic techniques have been reported.^{2,3} In general, these procedures have resulted in partial resolution, with the notable exception of the resolution of mixed $[\text{Co}(\text{en})_n(\text{l-pn})_{3-n}]^{3+}$ complexes on cellulose by Dwyer and co-workers.⁴ We report the total resolution of the hexakis(2-aminoethanethiolo)tricobalt(III) cation (Figure 1) using cation-exchange cellulose.

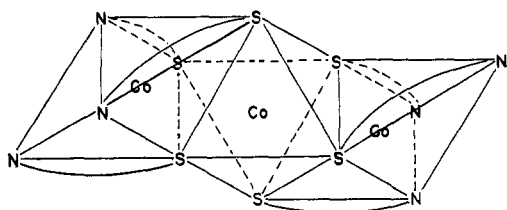


Figure 1. The hexakis(2-aminoethanethiolo)tricobalt(III) cation.

Hexakis(2-aminoethanethiolo)tricobalt(III) bromide was prepared by the method of Busch and Jicha.⁵ Bio-Rad Cellex CM cation-exchange cellulose (26 g) was poured into a column 22 mm in diameter, according to the instructions of the supplier,⁶ to give a bed about 38 cm in length. A saturated aqueous solution containing 0.5 g (0.57 mequiv) of $\text{Co}_3\text{L}_6\text{Br}_3$ was poured onto the column and equilibrated with water flowing about 3.5 ml/min. The complex was eluted with 0.1 *N* NaCl at approximately the same rate. The effluent was collected in 22-ml fractions, and the optical density and circular dichroism were determined at 540 $m\mu$. The molecular rotation of $\text{Co}_3\text{L}_6\text{Br}_3$ was determined at 589 $m\mu$.

Within experimental uncertainties, the first 110 ml of effluent displayed a constant $\Delta\epsilon$ at 540 $m\mu$ of -23.4 ; M_D (at 589 $m\mu$) -4020° . This value corresponds closely with the $\Delta\epsilon$ (540 $m\mu$) of $+23.7$, M_D (589 $m\mu$) of $+3980^\circ$, obtained from a sample of $[\text{Co}_3\text{L}_6]^{3+}$ resolved by fractional crystallization of the $(+)\text{_{589}}\text{[Co}_3\text{L}_6\text{]}(-)\text{_{546}}\text{[Co(EDTA)]}_3$ diastereoisomer from water. In addition to the optical antipodes, the trinuclear $[\text{Co}_3\text{L}_6]^{3+}$ cation exists in an inactive *meso* form. This isomer dominates the later fractions of the effluent and has not been successfully separated from the more strongly adsorbed optical antipode, though the latter comprised some 75% of the last fractions collected. The electronic properties of the hexakis(2-aminoethanethiolo)tricobalt(III) cation and related species will be discussed in detail elsewhere.

(1) This work was supported by a research grant (GM10829-08) from the Division of General Medical Studies, Public Health Service; work performed at the University of Pittsburgh.

(2) H. Krebs and R. Rasche, *Z. Anorg. Allgem. Chem.*, **276**, 236 (1954), and references cited therein.

(3) J. P. Collman, R. P. Blair, A. L. Slade, and R. L. Marshall, *Chem. Ind.*, (London), 141 (1962).

(4) F. P. Dwyer, T. E. MacDermott, and A. M. Sargeson, *J. Am. Chem. Soc.*, **85**, 2913 (1963).

(5) D. H. Busch and D. C. Jicha, *Inorg. Chem.*, **1**, 884 (1962).

(6) Bio-Rad Laboratories, Richmond, Calif., Price List Q, 1965.

The remarkable success of our method may be due, in part, to the high charge density and high formula weight (634.6) of the $[\text{Co}_3\text{L}_6]^{3+}$ entity. We have, however, achieved some success in the resolution of *N*-alkyl-substituted *N,N'*-ethylenediaminediacetato-(ethylenediamine)cobalt(III) complexes related to $[\text{Co}(\text{EDDA})(\text{en})]^{+}$.⁷ These results will be reported elsewhere.

(7) J. I. Legg and D. W. Cooke, *Inorg. Chem.*, **4**, 1576 (1965).

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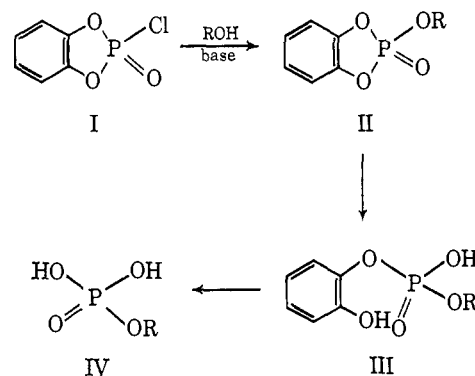
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o-Phenylene Phosphorochloridate. A Convenient Phosphorylating Agent

Sir:

Reich's surprising claim¹ that phosphotriesters of type II undergo hydrolysis to give catechol and the corresponding monoesters IV has not been substantiated. Lora Tomayo and Calderón² treated a number of primary aliphatic alcohols with *o*-phenylene phosphorochloridate (I) in the presence of base and showed that the products (II) were readily hydrolyzed to the corresponding *o*-hydroxyphenyl phosphate esters (III). Calderón later reported³ that hydrogenolysis of the latter diesters (III) in the presence of platinum oxide gave the required monoesters (IV) and cyclohexanol. However, Nagasawa⁴ subsequently found no evidence for such platinum-catalyzed hydrogenolysis.



We now wish to report that when these *o*-hydroxyphenyl derivatives (III) are treated, in neutral aqueous buffer solution, with an excess of bromine water at room temperature they are rapidly converted into the corresponding monoesters (IV) in good yield. The possibility, which was suggested by the oxidative

(1) W. S. Reich, *Nature*, **157**, 133 (1946).

(2) M. Lora Tomayo and J. Calderón, *Anales Real Soc. Espan. Fis. Quim.* (Madrid), **46B**, 475 (1950); *Chem. Abstr.*, **45**, 7046e (1951).

(3) J. Calderón, *Anales Real Soc. Espan. Fis. Quim.* (Madrid), **53B**, 69 (1957); *Chem. Abstr.*, **51**, 11273f (1957).

(4) K. Nagasawa, *Chem. Pharm. Bull. Japan*, **7**, 397 (1959).

Table I. Preparation of *o*-Hydroxyphenyl Phosphate Esters

Alcohol (ROH)	Solvent	Base	Moles of I ^a	% yield of III ^b
<i>t</i> -Butyl alcohol	Tetrahydrofuran	Triethylamine	1.0	83 ^c
2',3'-O-Isopropylidene-adenosine	Acetonitrile	2,6-Lutidine ^d	1.1	70 ^d
2',3'-O-Isopropylidene-uridine	Acetonitrile	2,6-Lutidine	1.0	91 ^e
3'-O-Acetylthymidine	Acetonitrile	2,6-Lutidine	1.1	70 ^f

^a *I.e.*, number of molecular equivalents of I with respect to alcohol. ^b Satisfactory analytical data were obtained for all new compounds described. ^c Isolated as a crystalline triethylammonium salt, mp 116–118°. ^d Isolated as the free acid. In another preparation, the isopropylidene group was removed and the crystalline *o*-hydroxyphenyl ester of adenosine 5'-phosphate (mp 207–208°) was obtained in 75% over-all yield. ^e Isolated as the barium salt. In another preparation, the barium salt of uridine 5'-*o*-hydroxyphenyl phosphate was obtained in 75% over-all yield. ^f Isolated as crystalline ammonium thymidine 5'-*o*-hydroxyphenyl phosphate. ^g Practical 2,6-lutidine (purchased from Hopkin and Williams, Ltd.) was heated under reflux with calcium hydride and then distilled.

phosphorylation studies of Clark, *et al.*,⁵ of converting the diesters (III) into monoesters (IV), under the conditions described, considerably increases the usefulness of *o*-phenylene phosphorochloridate (I) as a phosphorylating agent.

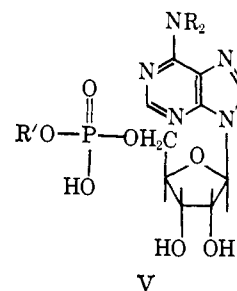
The latter is a colorless crystalline compound, which may easily be prepared in molar or larger quantities.⁶ It reacts rapidly and apparently quantitatively with a wide range of alcohols and, as was suggested by earlier work,^{2,3} *o*-hydroxyphenyl phosphate esters (III) may often be isolated from the hydrolysate of the initial products in a pure crystalline state. Some of our results are listed in Table I.

The phosphorylation of *t*-butyl alcohol was complete in 10 min at 20°, thus establishing the high reactivity of the phosphorylating agent (I). The nucleoside derivatives were allowed to react with the latter at 20° for 3 hr. The *o*-hydroxyphenyl esters, formed after the addition of water, were sufficiently stable to acidic and basic conditions to allow isopropylidene and acetyl protecting groups to be removed without concomitant dephosphorylation.

The oxidative removal of the *o*-hydroxyphenyl group was initially demonstrated with *o*-hydroxyphenyl phosphate (III, R = H) and its methyl ester (III, R = Me). When solutions of these compounds in pH 7.5 aqueous buffer⁸ were treated at 20° with *ca.* 6 molar equiv of bromine,⁹ rapid darkening was observed. After 5 min, examination of the respective products by paper electrophoresis and chromatography revealed that orthophosphate and methyl phosphate (IV, R = Me) were the sole phosphorus-containing components.

In a preparative-scale experiment, a solution of the triethylammonium salt of *t*-butyl *o*-hydroxyphenyl phosphate (III, R = *t*-Bu) in aqueous barium acetate was treated with 7 molar equiv of bromine. After a suitable work-up, colorless crystals of the barium salt of *t*-butyl phosphate (IV, R = *t*-Bu) were isolated in

70% yield. Similarly, oxidation of adenosine 5'-*o*-hydroxyphenyl phosphate (V, R = H; R' = *o*-



HOC₆H₄) and its N⁶,N⁶-dimethyl derivative (V, R = Me; R' = *o*-HOC₆H₄) in pH 7.5 aqueous buffer solution with 6 molar equiv of bromine led to adenosine 5'-phosphate (V, R = R' = H) and its dimethyl derivative (V, R = Me; R' = H). The respective products were obtained crystalline in 78 and 43% over-all yields, based on the 2',3'-O-isopropylidene nucleosides¹⁰ as starting materials. The preparations of *t*-butyl phosphate¹¹ and N⁶,N⁶-dimethyladenosine 5'-phosphate (V, R = Me; R' = H)¹² appear to be the most convenient so far reported.

Except for unsaturated alcohols, as complications may then arise in the oxidation step, *o*-phenylene phosphorochloridate appears to be one of the most convenient and powerful phosphorylating agents available.

(10) We thank Dr. Beverly Griffin for a gift of N⁶,N⁶-dimethyl-2',3'-O-isopropylideneadenosine, and Mr. A. Wilcox for assistance with its phosphorylation.

(11) F. Cramer, W. Rittersdorf, and W. Bohm, *Ann.*, **654**, 180 (1962); A. Lapidot, D. Samuel, and M. Weiss-Brodsky, *J. Chem. Soc.*, 637 (1964).

(12) M. Ikehara, E. Ohtsuka, and F. Ishikawa, *Chem. Pharm. Bull. Japan*, **9**, 173 (1961).

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Electrolytic Method of Converting an Aliphatic Trichloromethyl Group into a Dichloromethyl or Monochloromethyl Group

Sir:

Few investigations have so far been made on the reduction of *gem*-chlorinated aliphatic compounds.

(5) V. M. Clark, D. W. Hutchinson, G. W. Kirby, and A. Todd, *J. Chem. Soc.*, 715 (1961).

(6) Reaction between catechol and phosphorus pentachloride gives 2,2-dihydro-2,2,2-trichloro-1,3,2-benzodioxaphosphole⁷ in 80% yield. When the latter is heated on a steam bath with acetic anhydride (1.1 molar equiv), a nearly quantitative yield of acetyl chloride may be collected within 20 min, by distillation (at atmospheric pressure). Distillation (under reduced pressure) of the residue gives *o*-phenylene phosphorochloridate (I) [bp 91° (0.9 mm)] in 88% yield. Thus 100–200-g quantities of I may be prepared in a few hours, starting from catechol.

(7) L. Anschütz, *Ann.*, **454**, 71 (1927).

(8) Triethylammonium bicarbonate (0.2 M) was found to be a suitable buffer.

(9) A 2% aqueous solution of bromine was used in all experiments.