Discussion

The experiments described here show that liquid ammonia solutions of potassium and potassium tetracyanopalladate(II) react in the ratio of 2:1 to form moderately soluble potassium tetracyanopalladate(0) which is more soluble and less stable than the corresponding compound of nickel. Both cyanopalladate(0) and the cyanonickelate(0) reduce azobenzene to hydrazobenzene and silver and mercuric ions to the metals. Ammonium cyanopalladate(0) exists in ammonia solution but has not been isolated. In contrast to nickel, palladium appears to form no compound of the type of $K_2Pd(CN)_3$. At least the composition of the precipitate is the same throughout the precipitation. It seems likely that Manchot and Schmid actually prepared a solution of $K_4Pd(CN)_4$ and not $K_2Pd(CN)_3$ as they supposed.

Experience in this Laboratory has not confirmed the experience of Eastes and Burgess in their inability to prepare $K_4Ni(CN)_4$ by the action of potassium on solutions of $K_2Ni(CN)_4$. Only occasionally did the reduction stop at the $K_2Ni(CN)_3$ stage. A possible cause of these apparent inconsistencies may lie in the physical character of the initial precipitate. Since the reaction $K_2Ni(CN)_3 + K + KCN \rightarrow K_4Ni(CN)_4$ requires the reaction of two soluble materials with a precipitate, a firm coating of more insoluble material over the surface may well block further action.

It is interesting to note that in the compounds $K_4Ni(CN)_4$ and $K_4Pd(CN)_4$ the central atom of the complex ion exhibits an *effective atomic number* (E. A. N.) equal to that of the rare gas at the end of the period in which the element is placed in the periodic classification: *i. e.*, E. A. N. of Ni in $Ni(CN)_4^{==}$ = 36 (Kr); E. A. N. of Pd in $Pd(CN)_4^{==}$ = 54 (Xe). Hence, these complex ions are to be compared to the known carbonyl of nickel, $Ni(CO)_4$, and the expected carbonyl of palladium, $Pd(CO)_4$. The difference lies in the fact that the CN^- ion, although isoelectronic with the CO molecule, carries with it a negative charge which must be balanced by a corresponding charge on a positive ion. Hence, the same pattern of combination leads to a neutral molecule in the one case, $Ni(CO)_4$, and to a complex ion in the other, $Ni(CN)_4^{==}$ (or $Pd(CN)_4^{==}$).[13]

Summary

1. Potassium tetracyanopalladate(0), $K_4Pd(CN)_4$, has been prepared by the reaction between potassium and potassium cyanopalladate(II) in liquid ammonia solution.

2. Some of the properties of $K_4Pd(CN)_4$ have been determined and compared with those of $K_4Ni(CN)_4$.

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[13] For a discussion of the relation between E. A. N. and stability of complex ions see A. A. Blanchard, *Chem. Rev.*, **26**, 409–422 (1940), *Science*, **94**, 311–317 (1941).

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Methods for Resolution of Enantiomorphs. III. Chromatographic Adsorption[1a,b]

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The separation of diastereoisomers by rectification by Bailey and Hass[1] suggested that other counter-current processes might be attempted. A partial separation by counter-current liquid-liquid extraction has been accomplished by Shapiro and Newton.[1b] That diastereoisomers differ in their adsorbability was demonstrated by Fischgold and Ammon[3] without the use of Tswett columns. Stoll and Hofman[4] were able to resolve isolysergic acid by chromatographic adsorption of the *d*-isopropanolamide on columns of alumina. Jamison and Turner[5] have recently reported a small separation of the *l*-menthyl *dl*-mandelates by selective adsorption on alumina.

The methods of chromatographic adsorption have also been used to resolve stereoisomers. The first separation of that kind was claimed by Winterstein and Stein.[6] Cook and others[7] were able to separate *cis*- and *trans*-azobenzene on

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(1) (a) Original manuscript received August 22, 1942. (b) Abstracted from the M.S. thesis of H. H. Jaffé. Previous papers of this series were by M. E. Bailey and H. B. Hass, THIS JOURNAL, **63**, 1969 (1941), and by E. Shapiro and R. F. Newton, *ibid.*, **65**, 777 (1943).

(2) McCoy Research Fellow, 1941–1942.

(3) A. Fischgold and R. Ammon, *Biochem. Z.*, **234**, 39 (1931).

(4) A. Stoll and A. Hofman, *Z. physiol. Chem.*, **251**, 155 (1938).

(5) M. M. Jamison and E. E. Turner, *J. Chem. Soc.*, 611 (1942).

(6) A. Winterstein and G. Stein, *Z. physiol. Chem.*, **220**, 247 (1933).

(7) (a) A. H. Cook, *J. Chem. Soc.*, 876 (1938); (b) L. Zechmeister, O. Frehden and P. Fischer-Jörgensen, *Naturwissenschaften*, **26**, 496 (1938).

TABLE I

SUMMARY OF RESOLUTION EXPERIMENTS

Adsorbent	Solvent	Size of column, cm.	Amount used, g. and ml.	Typical results[a] α_D	$[\alpha]_D$
	A. *dl*-α-Phenylethylammonium bi-*d*-tartrate				
Aluminum oxide	60% ethanol	1 × 13	1.7/50	−0.03	−0.3
Calcium sulfate	60% ethanol	1 × 13	1.7/50	+ .02	+0.2
Carbon	Water	1 × 13	20/100	+ .04	+0.3
Carbon	60% acetone	1 × 13	20/100	+ .16	+1.4
Carbon	60% ethanol	1 × 13	1.7/50	+ .29	+1.7
Carbon	60% ethanol	2.2 × 50	20/100	+ .07	+1.2
Carbon	60% ethanol	5.2 × 120	50/250	+ .05	+7.2
Fuller's earth	60% ethanol	1 × 13	1.7/50	− .02	−0.4[b]
Magnesium oxide	Water	1 × 10	20/100	− .05	−0.4[b]
Magnesium oxide	60% ethanol	1 × 13	5.6/100	− .02	−0.2
	B. Brucine *dl*-mandelate				
Calcium sulfate	Benzene	2.8 × 55	35/350	+0.05	+4.4
Carbon	Benzene	2.2 × 50	35/200	+ .16	+2.7
Cotton	Benzene	2.2 × 50	40/350	− .02	0.0
Dextrose	Benzene	5.2 × 120	105/1000	+ .18	+4.1[c]
Dextrose	Chloroform	5.2 × 120	39/200	− .05	−0.3
Dextrose	Carbon tetrachloride	2.2 × 50	35/350	− .02	0.0
Dextrose	2-butanol	2.2 × 50	35/300	− .23	−0.7
Fuller's earth	Benzene	2.2 × 50	35/350	− .03	−1.7
Magnesium oxide	Benzene	2.2 × 50	35/300	.0	0.0

[a] Maximum observed rotation of α-phenylethylamine in ether and mandelic acid in water recovered from the best of four to nine liquid chromatograms. [b] See Table II for further details. [c] See Table III.

alumina. Coleman and his co-workers[8] separated sugar azoates using "magnesol" and silicic acid as adsorbents.

In this investigation a study was made of the separation of diastereoisomers by the well-known methods of chromatographic adsorption.

Materials. *dl*-α-Phenylethylammonium Bi-*d*-tartrate.—*dl*-α-Phenylethylamine was prepared according to the method of Ingersoll[9] from ammonium formate and acetophenone. The final product was analyzed and found to be sufficiently pure for this investigation. The amine was added to an equivalent amount of nearly saturated *d*-tartaric acid solution. The mixture solidified nearly completely within a few hours. The salt was collected on a filter and dried at room temperature; m. p. 159–162°.

Anal. Calcd. for $C_{12}H_{17}O_6N$: C, 53.13; H, 6.32. Found: C, 52.3; H, 6.3.

Brucine *dl*-Mandelate.—One-twentieth mole of brucine was dissolved in 300 ml. of hot benzene and an equivalent amount of *dl*-mandelic acid (U. S. P. grade, Merck & Co.) was added. Solutions of brucine *dl*-mandelate in 2-butanol and in carbon tetrachloride were prepared in the same manner. Chloroform solutions were prepared by dissolving the constituents in cold solvent. Solutions with hexane could not be prepared. Attempts to prepare *l*-nicotine *dl*-mandelate and *l*-nicotine *dl*-α-bromopropionate were unsuccessful. Only pasty tars resulted.

Adsorbents.—A variety of adsorbents were used. For example, one part of "Micron magnesium oxide, 2641" (California Chemical Co.) was mixed with two parts of hyflo-supercel (Johns–Manville Co.) to increase the rate of filtration. Similarly, fuller's earth (Lloyd's Reagent, Eli Lilly and Co.) was used, mixed with an equal weight of hyflo-supercel. Carbon (Norit A) when used was first extracted with hydrochloric acid and washed with water. The addition of hyflo-supercel did not appreciably increase an impractically slow filtration rate. Hydrated calcium sulfate and anhydrous aluminum oxide (Brockmann) were used for several experiments. Finally, cotton and dextrose were also used. With most of the columns it was necessary to apply nitrogen pressures up to three atmospheres to obtain a practical rate of flow.

Analysis.—To determine the efficiency of resolution, the desired compound was recovered from the solution and its rotation measured for the sodium D line in 1-dm. tubes with a Schmidt and Haensch, model 52B, polarimeter, with monochromator attached. The α-phenylethylamine was extracted with ether for the bi-tartrate solution after it had been concentrated and made alkaline with sodium hydroxide solution. The rotation of the ether solution was measured to ±0.01°. The concentration of the amine was determined by adding a standard hydrochloric acid and back-titrating with sodium hydroxide, with methyl red as indicator.

Mandelic acid was recovered by extracting the benzene, chloroform or carbon tetrachloride solutions of its brucine salt with one normal sulfuric acid (stronger acid decomposed the brucine). The aqueous layer would then contain brucine sulfate and mandelic acid. Three successive extractions with 50-ml. portions of ether removed the mandelic acid and possibly traces of brucine. The latter was removed by extraction with 10 ml. of water. The mandelic acid in the 150 ml. of ether was transferred to 10

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(8) G. H. Coleman, A. F. Farnham and A. Miller, THIS JOURNAL, **64**, 1501 (1942).

(9) A. W. Ingersoll, "Organic Syntheses," **17**, 76 (1937).

ml. of water by evaporation of the ether layer over a layer of water. The rotation of the aqueous solution was measured. The concentration of the mandelic acid was determined by titration with standard sodium hydroxide with phenolphthalein as indicator. The absence of brucine was checked with concentrated nitric acid, which gives a dark red color with even traces of brucine.

Procedure.—Columns of four different sizes were used. The smallest was 1 cm. in diameter and 15 cm. long and the largest was 5 by 120 cm. Various solvents were used such as benzene, 2-butanol, carbon tetrachloride, chloroform, water and aqueous solutions of acetone or ethanol (40% water). It was necessary to use moderately concentrated solutions of the diastereoisomers in order to obtain, even at best, some significant polarimeter readings for the successive liquid chromatograms. The concentrations varied from 4 to 20% and the volume from 50 to 1000 ml., depending on the size of the column. The chromatograms were developed with a sufficient volume of the solvent until the desired results were obtained.

Results.—In Table I are summarized the experimental details and results. The following are two typical experiments described in some detail.

dl-α-**Phenylethylamine.**—Twenty grams of *dl*-α-phenylethylammonium bi-*d*-tartrate dissolved in 100 ml. of water was filtered through a column (10 × 100 mm.) packed with magnesium oxide mixed with two parts of hyflosupercel. The chromatogram was developed with 600 ml. of water. Four successive liquid chromatograms were collected (their volumes are listed in the second column of Table II). The amine was recovered in ether solutions and the rotations measured to ±0.01° in a 1-dm. tube. The $[\alpha]_D$ of pure α-phenylethylamine is +39.9, hence the results show that practically no resolution was obtained. Similarly there was little resolution when other solvents and adsorbents were used. The results of 21 experiments have been summarized in Table I. The *ld* salt was adsorbed less than the *dd* salt on all adsorbents with the exception of carbon.

TABLE II

RESOLUTION OF *dl*-α-PHENYLETHYLAMINE

Filtrate	Ml.	Concn. of amine in ether, g./ml.	α_D	$[\alpha]_D$
1	40	0.118	−0.05	−0.4
2	100	.118	− .05	− .4
3	200	.0078	.0	.0
4	200	.0007	+ .03	(40)

dl-**Mandelic Acid.**—One hundred five grams of brucine-*dl*-mandelate in 1000 ml. of benzene was filtered through a column (5.2 × 120 cm.) packed with dextrose. The chromatogram was developed with benzene. The mandelic acid was recovered from five liquid chromatograms and its rotation was measured in aqueous solution. The $[\alpha]_D$ of pure *d*-mandelic acid in aqueous solution is 155.5. Hence the results tabulated in Table III show that the maximum resolution was about 3%. Some resolution was also obtained on fuller's earth, carbon and calcium sulfate. The *d* salt was adsorbed less than the *l* salt. No reproducible results could be obtained on magnesium oxide or on cotton with benzene as solvent, or on dextrose with chloroform or carbon tetrachloride as solvents. With 2-butanol as solvent and dextrose as adsorbent, the $[\alpha]_D$ of mandelic acid recovered from four 300-ml. filtrates were −0.71, 0.0, +7.1 and +16°, respectively. The results of 17 experiments are summarized in Table I.

TABLE III

RESOLUTION OF *dl*-MANDELIC ACID

Filtrate	Ml.	Concn. of acid in water, g./ml.	α_D	$[\alpha]_D$
1	320	0.0311	+0.10	+3.2
2	370	.0441	+ .18	+4.1
3	340	.0406	+ .18	+4.4
4	290	.0201	+ .02	+1.0
5	450	.0212	− .06	−2.8

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Summary

The techniques of chromatographic adsorption were applied to the resolution of racemic compounds after converting them to soluble diastereoisomers. *dl*-α-Phenylethylammonium bi-*d*-tartrate and brucine *dl*-mandelate were prepared and only partial resolutions were obtained on magnesium oxide, fuller's earth, carbon, calcium sulfate, cotton and dextrose.

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