Optically Active Co-ordination Compounds. Part XXXVI.[1] Convenient Resolution of the (Ethylenediaminetetra-acetato)cobaltate(III) Ion

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Experimental directions are given for convenient large-scale optical resolution of the ion $[Co(edta)]^-$ (edta = ethylenediaminetetra-acetato) using the L-histidinium cation. A typical application is described.

OPTICAL enantiomers of the ion (ethylenediaminetetra-acetato)cobaltate(III), which contains sexidentate edta, have been widely used. The resolution of the ion has been reported by several methods including the use of: (*a*) its diastereoisomeric salts with strychnine;[2] (*b*) preferential adsorption on active quartz,[2] although doubt has been cast[3] on this report (and, indeed, all other resolutions by this method); (*c*) its diastereoisomeric salts[4,5] with the ion $(+)[Co(en)_3]^{3+}$ (en = ethylenediamine); (*d*) stereoselective reaction with (−)1,2-diaminopropane;[5] (*e*) spontaneous resolution by crystallization[6] of the ammonium or rubidium salts; and (*f*) its diastereoisomeric salts[7] with the ion $(+)[Co(en)_2(NO_2)_2]^+$. Although this last method is suitable for the preparation of small quantities of $[Co(edta)]^-$, the necessity for prior resolution[8] of the cobaltate(III) cation precludes its use in the synthesis of larger quantities.

The present description gives experimental details of an extremely convenient method[9] whereby quantities up to 100 g or more are readily obtained. This method involves the differing solubilities[‡] of the diastereoisomers $[H_2(\text{L-histidine})]\{(+)_{546}[Co(edta)]\}_2,2H_2O$ and $[H_2(\text{L-histidine})]\{(-)_{546}[Co(edta)]\}_2,2H_2O$: 60 and 35 g l^{-1} respectively in water; 24 and 12 g l^{-1} respectively in water–ethanol (4 : 1 v/v); and 9 and 5 g l^{-1} respectively in water–ethanol (3 : 2 v/v) at 22 °C. L-Histidine is a cheap natural α-amino-acid, which exists as its dipositive cation in sufficiently acidic solution. With this convenient resolving relay $(+)[Co(edta)]^-$ to hand, it may be used to resolve singly charged cations, *e.g.* $[M(en)_2(C_2O_4)]^+$ (M = Co[10a] or Rh[10b]). Similarly, it becomes more logical to invert an earlier procedure,[7] and to use the ion $(+)[Co(edta)]^-$ to resolve $(\pm)[Co(en)_2(NO_2)_2]^+$; practical details are given in the Experimental section.

EXPERIMENTAL

Preparations.—*L-Histidinium* $(+)_{546}$*(ethylenediaminetetra-acetato)cobaltate*(III) *dihydrate*. Barium (ethylenediaminetetra-acetato)cobaltate(III) tetrahydrate[¶] (13·55 g, 0·030 mol anion) dissolved in warm water (40 cm³) was passed slowly through a column (15 cm × 1 cm) of cation-exchange resin (*e.g.* ' ZeoKarb 225 ' or an equivalent strongly acidic resin) in its hydrogen form. Elution of the solution of the salt $(H_3O)[(\pm)Co(edta)]$ was completed with water (60 cm³). L-Histidine (2·33 g, 0·015 mol) was then added to the eluate, and the solution warmed to 50 °C. When the L-histidine

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[‡] For all water–ethanol compositions from 100% water to 95% ethanol, solubilities of the diastereoisomers are in a fairly constant ratio of *ca.* 2 : 1.

[¶] Prepared from cobalt(II) carbonate, ethylenediaminetetra-acetic acid, and barium carbonate; the quantity of ethanol used in the recipe given[11] may be decreased from 1 700 to 500 cm³ with only a slightly lower yield (90%) than that reported.

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had dissolved, ethanol (30 cm^3) was added and the resulting solution allowed to cool at room temperature (20 °C) overnight. Crystals of $[H_2(\text{L-histidine})]\{(+)_{546}[Co(edta)]\}_2,2H_2O$ [4 g; 0·009 mol anion, *i.e.* 60% of the (+)enantiomer] were filtered off and washed with ethanol (Found: C, 35·2; H, 4·3; Co, 13·8; N, 11·2. Calc. for $C_{26}H_{39}Co_2N_7O_{20}$: C, 35·2; H, 4·4; Co, 13·3; N, 11·1%). Warming the mother liquor, followed by addition of more ethanol (30 cm^3), gave a further quantity of the salt which was much less optically pure (*ca.* 35%). Precipitation of all the complex remaining in the mother liquor by addition of ethanol (*ca.* 100 cm^3) gave $[H_2(\text{L-histidine})]\{(-)_{546}[Co(edta)]\}_2,2H_2O$ (6·0 g) (Found: C, 35·1; H, 4·6; N, 11·0. Calc. for $C_{26}H_{39}Co_2N_7O_{20}$: C, 35·2; H, 4·4; N, 11·1%). The optical purity of this sample was, however, only 60% [*i.e. ca.* 0·006 mol (−)-anion and 0·002 mol (+)-anion].

Potassium $(+)_{546}$*(ethylenediaminetetra-acetato)cobaltate*(III) *dihydrate*. A solution of the above histidinium salt in water was passed through a cation-exchange resin in the potassium form. The resulting eluate was evaporated to dryness *in vacuo* to give dark purple crystals of potassium $(+)_{546}$(ethylenediaminetetra-acetato)cobaltate(III) dihydrate in quantitative yield (Found: C, 28·3; H, 3·7; N, 6·6. Calc. for $C_{10}H_{16}CoKN_2O_{10}$: C, 28·4; H, 3·8; N, 6·6%).

Resolution of the cis-$[(\pm)Co(en)_2(NO_2)_2]^+$ *Ion using* $(+)_{546}[Co(edta)]^-$.—As a source of the *cis*-$[Co(en)_2(NO_2)_2]^+$ ion, we used the nitrate salt (which necessitates conversion to the chloride as described), because the commonly used nitrite salt could not be purified easily. The salt $[(\pm)Co(en)_2(NO_2)_2]NO_3$ (10 g, 0·030 mol) in water (*ca.* 750 cm^3) was converted to the chloride on Deacidite FF-IP SRA66 anion-exchange resin. The resin was rinsed with water until the eluate was colourless and the resulting solution concentrated to *ca.* 100 cm^3 under reduced pressure.

A solution of the salt $[H_2(\text{L-histidine})]\{(+)_{546}[Co(edta)]\}_2,2H_2O$ (13·3 g, 0·030 mol anion, in water (*ca.* 200 cm^3) was converted (ZeoKarb 225 SRC22 cation-exchange resin) to the potassium salt and the resin rinsed with water until a colourless eluate was obtained. The resulting solution of the salt $K[(+)_{546}Co(edta)]$ was concentrated to *ca.* 100 cm^3 under reduced pressure. {A similar solution, $2{\cdot}87 \times 10^{-4}$M-$K[(+)_{546}Co(edta)]$, made from the same batch of $[H_2(\text{L-histidine})]\{(+)_{546}[Co(edta)]\}_2,2H_2O$ gave $\alpha_{546} = +1\,180°$ and $\Delta\varepsilon_{588} = -1{\cdot}85$ l mol^{-1} cm^{-1} [*cf.* $\alpha_{546} = +1\,000°$ (ref. 7) and $\Delta\varepsilon_{588} = +1{\cdot}7$ l mol^{-1} cm^{-1} (ref. 12*a*)].}

These solutions were mixed and cooled in an ice-bath to <10 °C. The side of the vessel was scratched to induce crystallization. The solution was then maintained at 0—4 °C for an additional 10 min to ensure complete crystallization. The product was collected (preserving the filtrate) and washed with ice-cold aqueous ethanol, ethanol, and diethyl ether. The product (10 g) was suspended in water (*ca.* 100 cm^3), stirred at 50 °C for 15 min, and cooled to <10 °C in an ice-bath. Filtering and washing as above produced the salt $[(-)Co(en)_2(NO_2)_2][(+)_{546}Co(edta)],3H_2O$ (8·3 g) having $\alpha_{437} = +367°$ (Found: C, 24·7; H, 4·5; N, 16·4. Calc. for $C_{14}H_{34}Co_2N_8O_{15}$: C, 25·0; H, 5·1; N, 16·7%).

The filtrate from the initial crystallization of the diastereoisomer was concentrated to *ca.* 100 cm^3 under reduced pressure and, on addition of a solution of NH_4Br (1·6 g) in water (5 cm^3), the salt $[(+)Co(en)_2(NO_2)_2]Br$ crystallized out. The mixture was set aside in an ice-bath for 25 min, and the resulting product was filtered off and washed with iced water (5 cm^3). This impure product was transferred on a filter paper to a flask containing water (20 cm^3) at 55 °C and the flask then shaken. Freshly precipitated AgCl [prepared from $AgNO_3$ (4·25 g)] was added and the mixture shaken for 3—4 min. The resulting mixture was then filtered and the product washed with hot water (5 cm^3). A solution of NH_4Br (2·5 g) was added to the filtrate. The mixture was cooled to <10 °C, and after the side of the beaker had been scratched to induce crystallization, the mixture was set aside for 30 min, then filtered, and the product washed with ice-cold aqueous ethanol, ethanol, and diethyl ether (yield 2·29 g, 0·0065 mol; 43·5% based on half the racemic starting material) (Found: C, 13·4; H, 4·7; N, 23·6. Calc. for $C_4H_{16}BrCoN_6O_4$: C, 13·7; H, 4·6; N, 24·0%). A solution of this product gave $\Delta\varepsilon_{460} = +1{\cdot}6$ l mol^{-1} cm^{-1} (lit.,[12b] 1·4).

The diastereoisomer obtained above was ground in a mortar with water (25 cm^3). A solution of NaI (5·56 g) was added and the mixture triturated for *ca.* 3 min. The resulting impure salt $[(-)Co(en)_2(NO_2)_2]I$ was collected by filtration and washed with iced water. The product and filter paper were then transferred to a flask and shaken with water at 55 °C. Freshly precipitated AgCl prepared from $AgNO_3$ (4·25 g) was added and the mixture shaken for 3—4 min. The mixture was then treated as above for the (+)isomer (yield 3·68 g, 0·010 mol; 70% based on half the weight of the racemic starting material) (Found: C, 13·8; H, 4·6; N, 23·9. Calc. for $C_{14}H_{16}BrCoN_6O_4$: C, 13·7; H, 4·6; N, 24·0%). A solution of this product gave $\Delta\varepsilon_{460} = -1{\cdot}6$ l mol^{-1} cm^{-1} (lit.,[12b] 1·4).

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