

Title: Resolution of Racemic 2-Phenylbutanedioic Acid

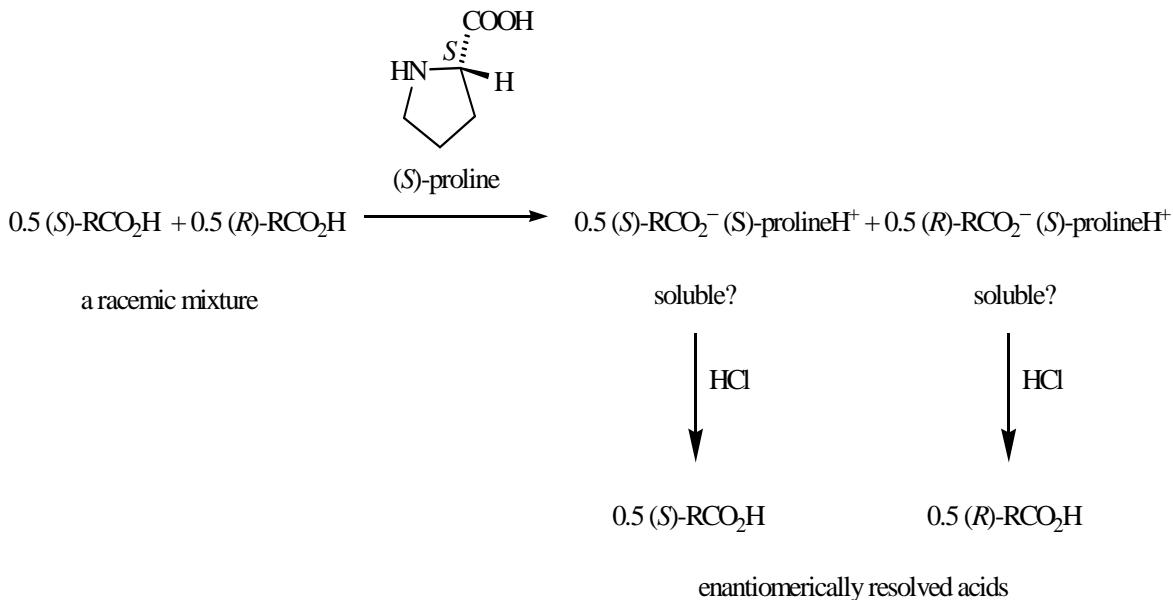
New tricks: F5

New principles: Optical activity

Instrument Operation: Digital polarimeter (see instructor for information on instrument operation)

Introduction:

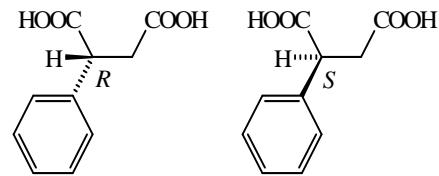
This experiment demonstrates the classic use of an optically pure chiral base to separate the two enantiomers of an organic acid that is a racemic mixture, as shown below.



The idea is very simple: The two enantiomeric acids, being mirror images of each other, have the same physical properties – same pKa, same melting point, same boiling point, same NMR spectrum, same IR spectrum, and same solubilities in common solvents. However, when the two enantiomeric acids react with a chiral optically pure base (that is, a base that is only one of two possible enantiomers), the two product salts are *diastereomeric* – that is, they have different physical and chemical properties, and, most importantly, different solubilities. If we're lucky, one of the two salts will precipitate out of solution, leaving the other behind. This effects separation of the two enantiomers of the acid. Decomposition of the salts by addition of HCl returns the acid in its neutral form, free of the base, and allows isolation of the pure enantiomer. This overall process is called *enantiomeric resolution*.

Note that it is never obvious *which* of the two diastereomeric salts will precipitate. *In this experiment, that is for you to figure out!* If you do your prelaboratory work, you will know which enantiomer, (R) or (S), has a positive optical rotation. Only by measuring the optical rotation of your product will you know *which* enantiomer formed the crystalline salt.

The acid we have chosen for you to use in this experiment is 2-phenylbutanedioic acid (pronounced two FEN-yl BYU-tain dye-OH-ic), shown on the right. Now, an interesting complication may occur to you: 2-phenylbutanedioic acid is a *dicarboxylic acid*. Could that be a problem? We'll just have to see!



Green aspects:

(S)-Proline is a member of a group of naturally-occurring compounds known as amino acids, which are the building blocks for making proteins. Since proline is produced in Nature as only the (S)-enantiomer, it serves as an environmentally benign, optically-pure resolving agent. Besides 2-propanol, solvents you will encounter in this experiment include methanol, ethanol, acetone, and water. In principle, (S)-proline may be recycled by adjusting the pH of the filtrate, obtained after HCl treatment, and collecting the resulting precipitate. However, in general, enantiomeric resolutions are NOT VERY GREEN, because typically half the material is wasted.

PRIOR TO LAB:

1. Prepare an introduction, including balanced equations for the *actual* reactions you will carry out, reactant table, and product table. You do not need to do a Green Chemistry Process Analysis. Make sure to copy this information into your notebook as well as having it in Word document form.
2. Find the following properties of (S)-2-phenylbutanedioic acid: registry number, melting point range, and specific rotation, $[\alpha]_D$. [Note: There's a good chance you won't be able to find this information on the web. Consider using a resource you haven't used yet, like the *Dictionary of Organic Compounds* in the reference section of the science library.] In reporting the optical rotation, be sure to indicate the solvent that was used, which should be listed after it.
2. Explain how you might isolate the *other* enantiomer of 2-phenylbutanedioic acid from the first filtrate if you wanted to do that.

Analysis and Discussion:

Report the melting points of both the salt and the resolved acid. How does the melting point of the resolved acid compare to what you found in the literature? Which enantiomer formed an insoluble salt with (S)-proline? How do you know? Using the optical rotation you measured, calculate the specific rotation of your sample. Assuming this material is pure, use that number to calculate the *enantiomeric excess* (or *optical purity*) of your sample. About that dicarboxylic acid: Does the NMR spectrum of the salt suggest a 1:1 or 1:2 complex of acid:base? Calculate your percent yield for both the salt and the final acid with this in mind.

Procedure (revised):

Combine 1.72 g of (S)-proline and 1 mL of water in a 250-mL Erlenmeyer flask. Heat this mixture on a hot plate just long enough to dissolve the proline. Add 75 mL of 2-propanol followed by 2.91 g of (\pm)-2-phenylbutanedioic acid. Swirl the flask vigorously to produce a clear solution. Continue swirling until crystals form. Set the mixture aside to crystallize for at least 20 minutes.

2-phenylbutanedioic acid is a potential skin irritant. Wear gloves while handling this material. 2-propanol is a flammable liquid and an irritant.

You should notice a VOLUMINOUS white precipitate forming. If you do not, consult your instructor. This is the insoluble salt.

Collect the resulting crystals by suction filtration. Wash the crystals with two 15-mL portions of acetone and allow them to air dry in the funnel with the vacuum on for at least 30 minutes. *Weigh this solid and record your percent yield.* Save several milligrams of these crystals for a melting point determination and an NMR spectrum.

Add the salt in portions with swirling to 15 mL of 6M HCl in an Erlenmeyer flask in an ice bath. Stir the mixture for 5 minutes in the ice bath. Collect the resulting solid by suction filtration, washing with two 15-mL portions of ice-cold water. Recrystallize the solid from a *minimum* amount of hot water, cool in an ice bath, and collect the crystals by suction filtration. Allow the crystals to dry and then determine the yield, melting point, and specific rotation of the product (dissolve 0.1 g of product in 25 mL of acetone).

HINT: Weigh the top part of the funnel, with filter paper BEFORE doing the filtration.

Acetone is a common organic solvent that dissolves most organic compounds and also is soluble in water. In this case it is being used to remove water and help dry the crystals. It is quite flammable and volatile. Do not use acetone near a hot plate!

Your instructor will discuss with you how to take this NMR spectrum.

Be sure to use a minimum amount of water!

Use a 25-mL volumetric flask to make up your solution for measuring optical rotation. Your instructor or lab assistant will demonstrate how to properly fill a 2-deciliter polarimeter tube.