ARGONAUT
TECHNOLOGIES

QUEST 205 USER MANUAL

Part Number 102965

Quest 205 User Manual.
Part Number 102965
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1 Introduction

This manual will assist with operating and maintaining the Quest 205 Synthesizer and is organized into the following sections.

- Section 1, Introduction: Contains general information on the Quest 205 Synthesizer, brief description of the instrument, warranties, and safety information.
- Section 2, Quest 205 Installation: Provides instructions on installing the Quest 205 Synthesizer.
- Section 3, Quest 205 Overview: Defines the Quest 205 hardware parts and provides an overview of how these parts work together.
- Section 4, Operating the Quest 205: Provides step-by-step instructions for performing solid phase or solution phase reactions.
- Section 5, Maintenance: Provides step-by-step instructions on maintenance procedures for optimum instrument performance.
- Section 6, Glossary: Defines terms specific to the Quest 205 Synthesizer.
- Section 7, Controller Unit Display Screens: Provides a list of the possible display screens and how to change parameters on the appropriate screens.
- Section 8, Reactor Unit Plumbing Schematic
- Section 9, Accessories: Describes accessories available for the Quest 205 Synthesizer. Includes installation and use instructions.
- Section 10, User Tutorial: Provides an introduction to the instrument by guiding the user through a parallel solution phase reaction, work-up and purification.

Quest 205 Product Description

WARNING: The Quest 205 Synthesizer is designed for use in chemical syntheses, including potentially hazardous chemical reactions and should be operated in a fume hood. Potential hazards of chemical synthesis include but are not limited to burns, explosions, and exposure to carcinogens and toxic chemicals. Always wear eye protection and suitable gloves.

The Quest 205 Synthesizer runs in parallel up to 10 liquid or solid phase organic chemistry reactions. The unique design of the Quest 205 incorporates heating/cooling, agitation, and the inert environment needed to run these reactions. The mechanical features of the Quest 205 also provide for simple operation of the instrument.

The Quest 205 consists of four main parts: the Reactor Unit, the Controller Unit, the Solvent Bottle Assembly, and the Reactor Interface Harness.

The **Reactor Unit** contains the manual solvent and gas control valves and components for heating, cooling, agitation, as well as holds the Teflon Reaction Vessels. Solvents may be added to the Reaction Vessels (RVs) in parallel using the manual rotary valves. Reagents are added via luer ports located at the top of each Reaction Vessel.

The **Controller Unit** contains the controls to set the reaction temperature, heating duration, and agitation conditions. The Controller Unit also contains connections for system power and gas, and interface connections for the Reactor Unit. A serial computer port is included on the Controller Unit to download firmware upgrades.

The **Solvent Bottle Assembly** consists of the solvent bottle, plastic bottle safety carrier, and a Bottle Cap Assembly. The Bottle Cap Assembly can either pressurize or vent the solvent bottle. The Solvent Bottle Assembly connects to the Quest Reactor Unit and provides the solvent for parallel delivery to the Reaction Vessels for resin washing and system cleaning.

The **Interface Harness** links the Control Unit to the Reactor Unit. Solvent, drain gas, metered gas, agitation pressure, and temperature control information are supplied and/or communicated through the harness. The solvent, drain gas, and metered gas movements are directed via the Reactor Unit's manual control valves. The agitation and heating parameters are set using the Controller Unit components.

See System Overview for a detailed description of the Quest 205 Synthesizer.

Quest 205 Specifications

REACTION VESSELS	1-10 disposable Reaction Vessels with frit 100 mL transparent Teflon
AGITATION	Proprietary vertical oscillation mechanism
TEMPERATURE RANGE	–40°C to 130°C ± 5% (requires recirculating chiller for temperature control below ambient)
COLLECTION RACK	Accommodates 14/20, 19/22, 24/40, 29/26, and 29/42 pear-shaped or round flasks
DIMENSIONS	
Reactor Assembly (w x d x h) Weight	 19" (48 cm) × 19" (48 cm) × 30" (76 cm) 75 lbs (34 kg)
Controller Unit (w x d x h) Weight	 10" (25 cm) × 16.5" (42 cm) × 12" (30 cm) 20 lbs (9 kg)
ELECTRICAL RATINGS	100-120V/200-240VAC 50/60Hz 8.3A
ENVIRONMENTAL CONDITIONS	15°C to 35°C Ambient Temperature 30-70% Relative Humidity
FUSE RATING	T10AH/250V

Quest 205 Limited Warranty Agreement

Warranty Term

The standard Warranty Agreement begins on the ship date of the Quest 205 Synthesizer and terminates 1 year from that date, unless other contractual agreements have been made.

Who Is Protected?

This warranty may be enforced by the original purchaser only.

What Is Covered?

Argonaut Technologies warrants the Quest 205 Synthesizer and Options against defects in materials and workmanship for the term of the Warranty Agreement. Argonaut Technologies will use reasonable efforts to repair or replace the product, at its sole discretion, at no charge provided that Argonaut Technologies is notified in a timely manner of defects within the warranty period.

Additional expenses covered by the Warranty are:

1. Labor and materials for covered items.

2. Shipping of repaired systems and accessories back to the Customer after service.

3. Shipment costs for repair parts sent to the Customer for Customer repair.

Consumable products or the like are only warranted to conform to the quantity and content stated on the label at the time of delivery.

What Is Not Covered?

Argonaut Technologies makes, and the Customer receives, no other warranty expressed or implied and all warranties of merchantability and fitness for a particular purpose are expressly excluded. Neither party shall have any liability with respect to its obligations under this agreement for consequential, exemplary, or incidental damages even if it has been advised of the possibility of such damages.

Argonaut Technologies does not warrant and will not be held responsible for loss or damages resulting from a cause other than defects in material or workmanship, including:

1. Damage caused by servicing or modification by the Customer other than what is recommended in the customer servicing and maintenance documentation or which has not been recommended by a qualified Argonaut Technologies technical support representative.

2. Damage caused by neglect, accident, or any natural disaster, including earthquake, lightning, flood, or fire; electrical surges or use of improper power sources.

3. Damage caused by failure to perform routine preventative maintenance as specified in the Quest 205 User Manual.

4. Damage caused by non-conformance to recommended instrument operation procedures.

5. Any product on which the serial number has been defaced, modified, or removed.

6. Damage caused by shipment of the product. (Claims must be presented to the carrier.)

7. Any accessories used in connection with the product, which are not covered under warranty.

Additional expenses not covered by the Warranty are:

1. Removal or installation of the system or accessories.

2. Costs associated with installation, including adjustment of user controls.

3. Shipment costs to return systems or accessories to the factory for repair.

4. Shipping boxes or packaging used to return systems and accessories to the factory for repair.

Preparation and Installation

Unless other contractual agreements have been arranged, it is the responsibility of the Customer to unpack the equipment, move the equipment to its location, and perform the installation as described in the provided manual. Contact the local Argonaut Technologies Representative for pricing of installation services by a qualified Argonaut Technologies Representative.

NOTE: It is the Customer's responsibility to retain the original system packaging.

How to Get Warranty Service

Argonaut Technologies has a fully staffed technical support hot line to help the Customer repair minor problems over the phone, or by FAX or e-mail. Major repairs that cannot be handled over the phone are repaired at the nearest Quest 205 repair center. Argonaut Technologies does not perform on-site repair of the Quest 205 Synthesizer unless other contractual agreements have been pre-arranged.

To establish the Quest 205 warranty, the warranty return card, provided in the shipping box, must be filled out and mailed after installation is complete.

To qualify for warranty repair, first contact the appropriate repair center detailed in this chapter, Contact Information.

Interference Information

This equipment generates and uses radio frequency energy and, if not installed and used in strict accordance with the manufacturer's instructions, may cause interference to radio and television reception. The equipment has been type tested and found to comply with the limits for a Class B computing device in accordance with the requirements set forth in the European Standard EN 55011:1997. Class B equipment is equipment suitable for use in domestic establishments and in establishments directly connected to a low voltage power supply network which supplies buildings used for domestic purposes. However, there is no guarantee that interference will not occur in a particular installation. If this equipment does cause interference to radio or television reception, determined by turning the equipment off and on, the user is encouraged to try to correct the interference by one or more of the following measures:

- Reorient the receiving antenna
- Relocate the equipment with respect to the receiver
- Move the equipment away from the receiver
- Plug the equipment into a different outlet so that the Controller Unit and the Reactor Unit are on different branch circuits

Immunity Information

This equipment has been type tested and found to comply with the Requirements of the Generic Immunity Standard: EN50082-1/1997.

If the equipment is used in a manner not specified by the manufacturer, the protection provided by the equipment may be impaired.

Safety

This equipment has been tested and found to comply with the requirements as set forth in the European Immunity Standard: EN50082-1/1997.

The following hazard symbols are found on the Quest 205 Synthesizer:

	This symbol indicates a hot surface. Use caution when working near or on the Reactor Assembly. When heating, the Reactor Unit becomes hot. Allow it to cool before attempting to access Reaction Vessels.
	This symbol indicates a shock hazard. Use care when working around an area with this symbol.

Laboratory Safety

Every laboratory has specific practices and policies designed to protect personnel from potential hazards, both obvious and hidden. When working with a Quest 205 Synthesizer, the manufacturer recommends that the following safety equipment be readily available: fire extinguisher, eye wash station, safety shower, eye protection, lab coat, and hand protection. Adherence to these recommendations, as well as the other requirements presented in this manual, will help to ensure both the successful installation and safe use of the Quest 205.

WARNING: If the equipment is used in a manner not specified by the manufacturer, the protection provided by the equipment may be impaired.

This equipment has been type tested and found to be in accordance with the requirements for Laboratory Instruments set forth in the European Standard EN 61010-1:1993/A2:1995. Copies of the TUV certificates are available upon request from Argonaut Technologies Inc.

Material Safety Data Sheets (MSDS)

The MSDS associated with each chemical used with the Quest 205 Synthesizer must be kept at the user's facility for easy reference by employees.

Contact Information

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NOTE: If you have any questions or comments regarding the content of this manual or instrument installation requirements, please contact Argonaut Technologies at the phone numbers or e-mail addresses provided on the previous page.

2 Quest 205 Installation

Installation Procedure

Installation of the Quest 205 Synthesizer involves connecting the system to a gas source and making some simple tubing connections. The process typically takes less than 1 hour.

Parts

- Quest 205 Reactor Unit
- Quest 205 Controller Unit
- Accessory Kit
- Voltage Kit (power cord)
- Solvent Bottle Safety Carrier (4L capacity for Domestic Instruments or 2.5L capacity for International Instruments)

User-Supplied Items

- If using a single gas source:
  55-60 psi house nitrogen supply or other high-purity (>99.98%) inert gas
- If using dual gas source:
  40-60 psi house nitrogen supply or other high purity (>99.98%) insert gas
  55-60 psi clean, dry compressed air
- One 100-120 or 200-240 VAC, 50-60 Hz grounded outlet capable of supplying 10 amps.
- Recirculating chiller (optional, required for temperatures below ambient)
- Solvents and reagents

Installation Glossary

Bulkhead fitting: The female threaded ports found on the front of the Controller Unit and on various places of the Reactor Unit.

Ferrule: The yellow, conical-shaped piece which mates to the PPS fitting. Used for Teflon tube connections.

Interface Harness: The bundle of tubing and electrical wires that connects the Controller Unit to the Reactor Unit.

PPS fitting: The tan colored threaded fittings made from PPS and used for Teflon®* tubing connections.

*Teflon is a registered trademark of DuPont

Teflon tubing: The semi-transparent, semi-rigid tubing (0.125 inch [3.175 mm] O.D.) used for gas and liquid connections.

Tygon tubing: The flexible tubing with a slight yellow color to it. Used for gas connections within the Quest 205 Controller Unit.

Setting up the Quest 205 Synthesizer

1. Clear a space about 2-1/4 feet (70 cm) wide by 2 feet (60 cm) deep in a fume hood for the Quest 205 Reactor Unit.
2. Clear a space on the lab bench adjacent to the fume hood for the Quest 205 Controller Unit.
3. Carefully unpack the instrument and place the Reactor Unit in the hood and the Controller Unit on the lab bench next to the hood. Remove any packaging material from the units.
4. The Interface Harness is already connected to the Reactor Unit. Free the harness from any packing material and lay it out so the free end is placed in front of the Controller Unit.

NOTE: It is recommended that the following safety equipment be readily available: fire extinguisher, eye wash station, safety shower, eye protection, lab coat, and hand protection.

Connecting the Interface Harness to the Controller Unit

1. Press the round male electrical connector labeled "Heaters" (connector with large pins) on the Interface Harness into the round female connector on the Controller Unit labeled "Heaters". Twist the housing of the connector to lock the cable into place.

WARNING: 100-120 or 200-240 VAC is present within this connection during heater operation. Do not disconnect the "Heaters" connection with power applied to the controller.

2. Press the round male electrical connector labeled "Signal" on the Interface Harness into the Controller Unit receptacle labeled "Signal." Twist the housing of the connector to lock the cable into place.

3. Remove the tape from the Controller Unit female ports labeled 1, 2, 3, 4, 5, and 6.

NOTE: Ensure the bushing is loose on the Teflon tube prior to screwing in the fittings. The bushing should not be "bound" to the yellow ferrule, as this can cause twisting of the Teflon tube during installation. To release a bound bushing from a ferrule, grasp the ferrule between the thumb and index finger and gently rock the bushing back to free it.

4. Six loose Teflon tubes with fittings protrude from the "Controller" side of the Interface Harness. These tubes are labeled 1, 2, 3, 4, 5, and MEM.

   Screw in the tan PPS fittings at the end of tubes 1, 2, 3, 4, 5, and MEM into the matching female threaded port until the connection is finger tight.

NOTE: Be careful to not cross-thread the fittings.

NOTE: Ensure that the flat surface of the ferrule (perpendicular to the end of the Teflon tube) is free of dust or fibers. This is the surface that creates the seal for the tubing connection.

Connecting the Bottle Cap Assembly

There are two tubes protruding from the middle of the Interface Harness. These tubes are labeled BTL PRESS and SOLVENT and connect to the Bottle Cap Assembly.

The Bottle Cap Assembly has three female ports oriented in a triangle (see Figure 2-1).

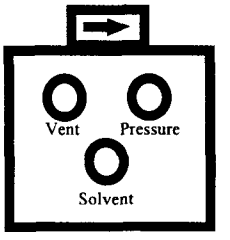

Figure 2-1 Solvent Bottle Cap Female Ports

1. Connect the Interface Harness tubes labeled BTL PRESS and SOLVENT to the corresponding ports on the Bottle Cap Assembly.
2. Find the Vent tube (in Accessory Kit). This tube can be identified by the ferrule and PPS fitting on one end and no fitting on the other end. Connect this tube to the VENT port of the Bottle Cap Assembly.

   Use the dial on the top of the Bottle Cap Assembly to select between PRESSURE and VENT for a solvent bottle.

NOTE: When the dial is turned to VENT, gas and solvent fumes will escape through the tube connected to the Vent port of the Bottle Cap Assembly. Point the tube towards the rear of the fume hood or tape it down to a convenient spot in the fume hood.

Connecting the Reactor Unit Manifold Tubes

Six tubes (three on each side of the Quest 205) must be connected to bulkhead fittings on the upper area of the Reactor Unit and to female ports on the Upper Manifold.

The tubes are located in the Accessory Kit. Each tube has a PPS fitting and ferrule on each end. Two tubes are labeled MAN DELIVERY, two are labeled MAN VENT, and two are labeled MEM PRESSURE.

The three female bulk head fittings for these tube connections are located near the manual valves towards the edge of the front face of the Upper Reactor Unit. The tubes will lead from these upper bulkhead fittings to a set of three female fittings located on the Upper Manifold. These latter fittings form a canted triangle configuration (see Figures 2-2 and 2-3).

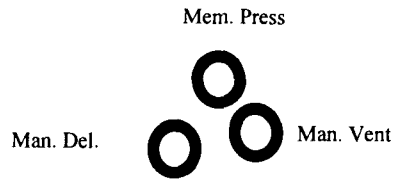

Figure 2-2 Upper Manifold Port Connections – Side A (Reaction Vessels 1-5)

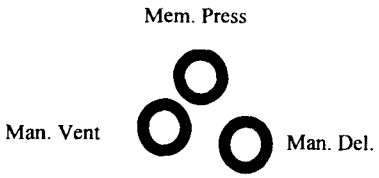

Figure 2-3 Upper Manifold Port Connections - Side B (Reaction Vessels 6-10)

1. Screw in the PPS fitting from one end of the tube labeled MEM PRESSURE into the red bulkhead fitting on the upper Reactor Unit labeled MANIFOLD.
2. Screw the other end of the MEM PRESSURE tube into the female threaded port on the Upper Manifold located at the top of the triangle of ports (see Figures 2-2 and 2-3).
3. Screw in the PPS fitting from one end of the tube labeled MAN VENT into the red bulkhead fitting on the upper Reactor Unit labeled VENT.
4. Screw the other end of the MAN VENT tube into the female threaded port on the Upper Manifold in the middle of the triangle of ports (see Figures 2-2 and 2-3).
5. Screw in the PPS fitting from one end of the tube labeled MAN DELIVERY into the remaining red bulkhead fitting labeled DLVRY located on the front face of the upper Reactor Unit.
6. Screw the other end of the MANUAL DELIVERY tube into the female threaded port on the Upper Manifold at the bottom of the triangle of ports (see Figures 2-2 and 2-3).
7. Repeat the tubing installation (steps #1-#6) for the other side of the Reactor Unit.

Installing the Waste Tank

1. Unpack the rectangular plastic waste tank from the box.
2. Locate the waste tray below the Lower Manifolds on the Reactor Unit.
3. Grasp the waste tray handles, press the buttons on the handles, and move the tray to its lowest position.
4. Place the waste tank on the waste tray.
5. Grasp the waste tray handles, press the buttons, and raise the tray and tank.
6. Attach the supplied Teflon tubing to the drain valve located on the waste tank. Place the other end of the tubing into an appropriate waste container.

Setting the Manifold Control Valves

Check the orientation of the Manifold Control Valves. The two valves on both sides of the Reactor Unit should be set to CLOSED.

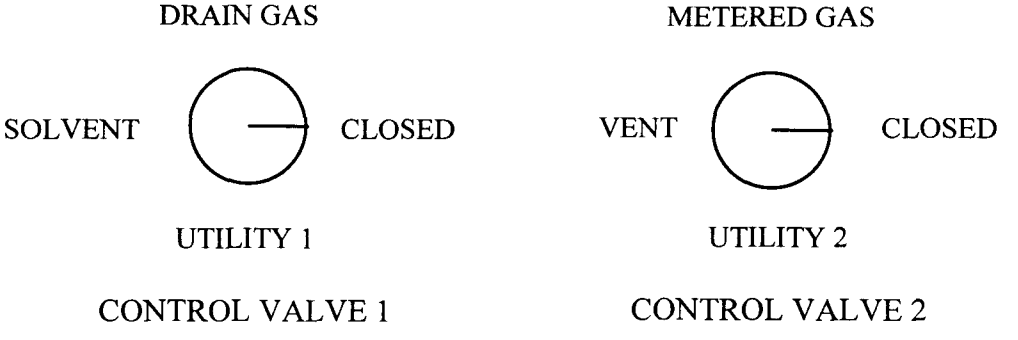

Figure 2-4 Manifold Control Valves

Connecting Gas to the Controller Unit

The dual gas feature on the Quest 205 synthesizer allows the user to use either one or two gas sources with the instrument.

Connecting a Single Gas Source

1. Ensure that the inert gas source is of high purity (>99.98%), has a regulated output of 55-60 psi, and is capable of mating with 0.25 inch (0.64 cm) O.D. by 0.17" inch (0.43 cm) I.D. polyethylene tubing.
2. Attach the end of the Gas Supply Assembly without the quick disconnect fittings to the inert gas source.
3. The other end of the Gas Supply Assembly has a "T" with two quick disconnect fittings.
   a. Connect one of the quick disconnect fittings to the inert gas inlet on the rear panel of the Controller Unit.
   b. Connect the other quick disconnect fitting to the compressed air inlet on the rear panel of the Controller Unit.
   c. Push the fittings over the inlet ports until an audible click is heard from each fitting.

Connecting Two Gas Sources

If either gas source is more than 5 feet (1-1/2 m) from the Controller Unit, additional tubing is required.

1. Check the gas sources.
   a. Ensure that the inert gas source is of high purity (>99.98%), has a regulated output of 40-60 psi, and is capable of mating with 0.25 inch (0.64 cm) O.D. by 0.17" inch (0.43 cm) I.D. polyethylene tubing.
   b. Ensure that the compressed gas source is clean, dry compressed air with a regulated output of 55-60 psi and is capable of mating with 0.25 inch (0.64 cm) O.D. by 0.17" inch (0.43 cm) I.D. polyethylene tubing.
2. Remove the "T" and quick disconnect fittings from the end of the Gas Supply Assembly.

3. Cut the remaining 10 ft (3 m) polyethylene line in half.
4. Connect the first line to the inert gas source and the Controller Unit.
   a. Install a quick disconnect fitting onto one end of the newly cut polyethylene line.
   b. Attach the open end of the line to the inert gas source.
   c. Push the end of the line with the quick disconnect fitting onto the inert gas inlet on the rear panel of the Controller Unit until an audible click is heard.
5. Connect the second line to the compressed air source and the Controller Unit.
   a. Install a quick disconnect fitting onto one end of the second newly cut polyethylene line.
   b. Attach the open end of the line to the compressed air source.
   c. Push the end of the line with the "quick connect" fitting onto the compressed air inlet on the rear panel of the Controller Unit until an audible click is heard.

Connecting Power to the Quest 205

1. Plug the power cord into the female receptacle on the left rear of the instrument.
2. Plug the cord into a 100-120 or 200-240 VAC 50-60 Hz grounded wall outlet (10A minimum rating).
3. Turn on the power to the Quest 205 using the switch on the left rear of the Controller Unit.

Installing the Solvent Bottle

1. Ensure all four Manifold Control Valves are set to "Closed."
2. Place the solvent bottle in the safety carrier and set it on the lab bench.

WARNING: Always place the solvent bottle in the plastic safety carrier when working with the Quest 205.

3. Install a polyethylene end line filter on the end of the long "pickup" tube, which protrudes from the bottom of the Bottle Cap Assembly.

NOTE: Change the end line filter each time the solvent bottle is installed.

4. Place a Teflon bottle seal on the top of the solvent bottle.
5. Place the "pickup" tube in the solvent bottle and screw down the outside of the cap.
6. Turn the dial on the top of the Bottle Cap Assembly towards the tube marked "Pressure." Wait about a minute for the bottle to pressurize.

   In the "Pressure" position, 9 psi gas flows from the Controller Unit into the solvent bottle via the pressure line.

WARNING: Always vent the solvent bottle prior to unscrewing the cap. Vent the bottle by rotating the dial so the arrow points to the Teflon tube labeled "VENT."

WARNING: Always wear eye protection and appropriate clothing when operating the Quest 205.

3 Quest 205 Overview

The Quest 205 system consists of the Reactor Unit, Controller Unit, Interface Harness, and Solvent Bottle Assembly.

The Reactor Unit holds 10 Reaction Vessels for parallel synthesis along with components needed for heating, cooling, and agitation. The Reactor unit also contains the Upper Manifold Control and Metered Gas Valves. These valves provide control for solvent and gas flow in the Reactor Unit, which are used for such functions as solvent addition, vessel draining, and inert gas pressure.

The Controller Unit is used to set the reaction temperature, heating duration, and agitation conditions via the keypad and LCD screens. Parameters set on the display screens are executed by the firmware, which is resident on PC boards in the Controller Unit.

The Controller Unit has ports to connect lines from the Reactor Unit. These lines (from the Reactor Unit) make up the Interface Harness and include the electrical, metered gas (9 psi), drain gas (30 psi), solvent, and two agitation lines. The Interface Harness enables the Controller Unit and the Reactor Unit to interact.

The Solvent Bottle Assembly connects to the Quest Reactor Unit and provides the solvent for parallel delivery to the Reaction Vessels for resin washing and system cleaning.

Reactor Unit

The Reactor Unit performs the following functions:

- Runs up to 10 liquid or solid phase reactions in parallel
- Heats/cools the reaction solutions
- Mixes the reaction solutions
- Controls the solvent and gas flow required for manual solvent addition to the Reaction Vessels, draining of solution from the Reaction Vessels, isolating the Reaction Vessels and applying a metered gas flow over the reaction solution
- Collects reaction products

Reaction Vessel Bank and Reaction Vessels

Reaction Vessels

Reaction Vessels (RVs) are 100 mL disposable clear Teflon tubes, intended for one time use only. A frit is pre-installed in the bottom of each Reaction Vessel. A frit is a Teflon filter that allows for draining of solution from the Reaction Vessels while keeping the solid support resin within the RV.

Reaction Vessel Bank

Each side of the Reactor Unit contains a Reaction Vessel bank that holds up to five Reaction Vessels, for a total of 10 synthesis positions.

Above each Reaction Vessel bank is the Upper Manifold, which contains fluidic pathways to the Reaction Vessels. Below each Reaction Vessel Bank is the Lower Manifold, which controls Reaction Vessel draining. Both manifolds have male fittings that press into the Teflon Reaction Vessels. By lowering the Upper Manifold over the bank of RVs, the ends of the Reaction Vessels press over the male fittings of both Upper and Lower Manifolds. This along with the upper and lower RV clamp creates a leak-tight seal for the Reaction Vessels.

Heating and Cooling

NOTE: Reaction temperature parameters may be set using the Control Unit display and keypad. For instructions on setting the temperature parameters, see Operating the Quest 205, Temperature Control.

Heating and Cooling Blocks

The heating and cooling blocks are aluminum plates mounted behind the Reaction Vessel holders on each side of the instrument. A resistive heater mounted inside the heater block provides heat. A user-supplied recirculating chiller can be used to flow cold liquid (such as ethanol) through a channel mounted at the rear of the heater block to cool the RVs.

Reaction Vessels mounted on the instrument are in contact with the heater block. Each Reaction Vessel Bank on the Quest 205 (Side A and Side B) can be set to two independent temperatures.

Reaction Mixing

NOTE: Agitation parameters are set using the Controller Unit. For instructions, see Operating the Quest 205, Setting Agitation Parameters.

Agitation

The Quest 205 agitation system consists of a pneumatically actuated magnet bar which vertically oscillates between the two Reaction Vessel Banks. Teflon-encapsulated magnets are placed in the Reaction Vessels. Mixing occurs when the magnet bar oscillates, causing the magnets in the Reaction Vessels to vertically oscillate.

Magnet Bar

The magnet bar is an aluminum assembly with cylindrical magnets mounted along its length. It is positioned between the two Reaction Vessel Banks, perpendicular to the Reaction Vessels. The magnet bar is attached to a vertical rod that is controlled by a pneumatic cylinder. The rod oscillates vertically when gas is supplied to either end of the pneumatic cylinder. Valves in the Controller Unit alternately supply 30 psi gas to the bottom and top of the gas cylinder, moving the piston and magnet bar up and down.

The velocity of the oscillating vertical mixing strokes is controlled by regulating the gas flow rate to the pneumatic cylinder via a needle valve on the front panel of the Controller Unit

Fluidic System

The Quest 205 fluidic system allows parallel delivery of solvent to the Reaction Vessels and supplies gas for draining, isolating, and/or blanketing the Reaction Vessels. See Section 8: Quest 205 Plumbing Schematic.

NOTE: Solvent and gas flow are controlled by the Upper Manifold Control Valves and the Metered Gas Valve. For instructions on setting the solvent and gas flow controls, see Operating the Quest 205.

Manifold Control Valves

Each side of the Reactor Unit contains two Manifold Control Valves: Control Valve 1 (on the left) and Control Valve 2 (on the right).

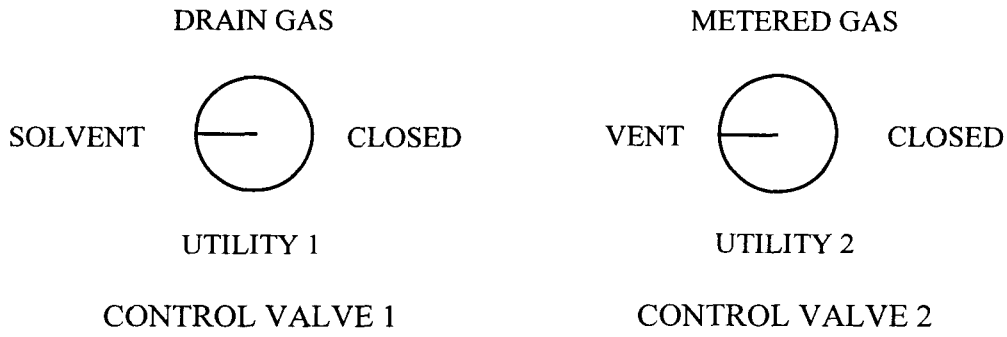

Figure 3-1 Quest Manifold Control Valves (Solvent Delivery Configuration)

Control Valve 1, set to "SOLVENT" or "DRAIN", allows either solvent or drain gas (30 psi) into the corresponding Upper Manifold common pathway. Setting Control Valve 1 to UTILITY 1 attaches the corresponding Upper Manifold common pathway to the utility 1 port located on the top of the Reactor Unit.

Control Valve 2 can be set to "Vent" or "Metered Gas. Set to " "Vent" connects the corresponding Upper Manifold common pathway to Teflon tubing which vents into the waste tank. Set to "Metered Gas" allows 9 psi gas into the corresponding Upper Manifold common pathway. Setting Control Valve 2 to UTILITY 2 attaches the corresponding Upper Manifold common pathway to the utility 2 port located on the top of the Reactor Unit.

The manifold control valves are set in conjunction with each other to create various fluidic pathways, listed below.

- Solvent Delivery: Creates a flow path to deliver solvent from the external bottle in parallel to the bank of five Reaction Vessels.
- Solvent Line Flush: Creates a path for 30 psi gas to flow through the manifold to blow the residual solvent into the Reaction Vessels after solvent delivery.
- Vessel Draining: Supplies 30 psi gas to the Upper Manifold common path and pressurizes the upper RV head space to drain waste liquid into the waste tank.

Lower Manifold Drain Valves

Each side of the Reactor Unit has five drain valves. The drain valves are located on the Lower Manifold and mechanically seal the lower exit paths from the Reaction Vessels. Each drain valve has a lever to toggle between the "Closed" and "Drain" positions. The drain lever toggles a piston that works against a Teflon membrane within the Lower Manifold.

When the lever is up ("Closed"), the plunger pushes against the membrane and seals the Reaction Vessel drain path.

When the drain valve is down ("Drain"), the plunger is moved back and the membrane opens. With gas pressure applied to the top head space, the solution in the Reaction Vessel drains to waste.

Drain valves can be opened individually or in groups.

Waste Tank

The Quest 205 is equipped with a rectangular plastic tank for waste collection. The Waste Tank is equipped with a plug valve to which Teflon tubing is attached to drain waste into an appropriate waste container.

The waste tank sits on the waste tray, which is below the lower manifold on the Reactor Unit. The tray is lowered, via buttons on its handles, for removal or installation of the waste tank. The waste tank is removed when collecting synthesis product.

Sample Collection

A flask rack for sample collection that accommodates up to five 14/20, 19/22, 24/40, 29/26, or 29/42 pear shaped or round flasks is included in the Accessory Kit

The flask rack is positioned on the waste tray when it is time to collect reaction products.

Upper Manifold

The Upper Manifold is an aluminum and Teflon block that contains two common pathways. One pathway is used for parallel solvent delivery, drain gas, and the Utility 1 port. The other pathway is used for venting, metered gas, and the Utility 2 port. The wetted portion of each pathway is Teflon.

Each pathway has a common channel and inlet paths to each Reaction Vessel. The common channels also connect to the Manifold Control Valves, so that the selected source liquid or gas can flow into the common channel. These pathways make possible solvent addition to the Reaction Vessels, waste or product draining from the Reaction Vessels, or a gas flow over reaction solutions.

The Upper Manifold also contains a Teflon membrane that seals against the common paths and Reaction Vessel inlet paths to protect against crossover of the fluid or gas contents of the RVs.. Supplying 30 psi gas to the outside of the membrane forces it to flatten against the flow paths of the Upper Manifold. The Manifold switch, located at the top of the Reactor Unit, controls gas flow to the membrane, switching the membrane from open to closed.

In Addition the Upper Manifold contains individual mechanically actuated plungers above each Reaction Vessel inlet path. This allows selected Reaction Vessels to be closed, while allowing solvent delivery to the remaining Reaction Vessel on that same bank.

Luer Ports

The luer ports are located at the top of each Upper Manifold. Each port is a beveled hole with a corresponding luer port adaptor and luer plug. Removal of the luer plug allows access to the Reaction Vessel to allow for the addition of reagents and also provides a connection point for accessories (for more information on accessories refer to Section 9). To facilitate addition of larger quantities of reagents or solids the luer port adapter may be removed to offer greater access to the Reaction Vessel

NOTE: that a low flow of metered gas can be applied to the Reaction Vessels during manual addition of chemicals through the luer ports or luer port adapter.

WARNING: Always vent the reactions vessels before removing a luer plug or a luer port adapter as contents may be under pressure.

- Product Collection: Supplies a metered flow of 9psi gas to the Upper Manifold common pathway, which pressurizes the upper RV head space so product liquid drains into collection flasks. Product collection is done at a lower pressure than draining to eliminate splashing during collection.
- Inert Gas Blanket: Provides a constant pressure of 9 psi to the Reaction Vessels.
- Inert Gas Sweep: Provides a metered flow of 9 psi gas across the RVs.
- Reaction Vessel Venting: Vents the Reaction Vessels through Teflon tubes routed to the waste tank.

Metered Gas Needle Valve

Metered gas is used primarily to provide an inert atmosphere to the Reaction Vessels and a lower pressure drain gas for product collection. The Metered Gas Needle Valve is a control knob that increases or decreases the flow rate of 9 psi gas into the Reaction Vessels. The one needle valve controls the flow for both Reactor Unit Sides A and B.

The Metered Gas Needle Valve is used to increase or decrease the gas flow rate once the Manifold Control Valves are set to deliver 9 psi gas to the Reaction Vessels.

To decrease the flow rate, turn the Metered Gas Needle Valve clockwise.

To increase the flow rate, turn the Metered Gas Needle Valve counter clockwise.

NOTE: A bubbler may be attached to the Quest 205 so that the gas flow rate can be seen. See Section 9: Accessories.

The metered gas input line is in a "T" configuration, with a single input line feeding both of the number 2 Manifold Control Valves.

Utility Ports

External accessories are attached to the Quest 205 via the utility ports. The two utility ports are labeled Utility Port 1 and Utility Port 2. The utility ports input lines are in a "T" configuration, with a single input line feeding both of the corresponding Manifold Control Valves on each side of the Quest 205. A common Accessory that would utilize a utility port would be a gas bubbler

Controller Unit

The Controller Unit contains an LCD screen, keypad, electronics, and firmware to operate the Quest 205 Synthesizer. The Controller Unit controls the following functions:

- Reaction temperature.
- Reaction temperature duration.
- Agitation parameters including agitation frequency and stroke duration.
- Connections for the system gas pressure and electrical power.

Other components of the Controller Unit include agitation control valves, agitation needle valve, gas pressure regulators, gas distribution manifolds, and electronics boards.

LCD Screen and Keypad

The Controller Unit LCD screen and keypad are used to set the reaction temperature, temperature duration, and agitation parameters.

LCD Screen

The LCD screen presents the various Quest 205 programming screens. The screens display the status of the agitation and temperature settings. Reaction temperature, temperature duration, and agitation parameters may be changed using the keypad in association with the appropriate screen.

The display screens include:

- Sign-on Screen: Identifies this instrument as the Argonaut Technologies Quest 205.
- Firmware Version Screen: Shows the Quest 205 firmware version number.

- Agitation Control Screen: Allows user to set the agitation parameters: MixEvery, UpStroke, and % Upward.

  The MixEvery parameter sets the agitation frequency expressed in seconds. The agitation frequency is defined as the time between consecutive up-strokes.

  The UpStroke parameter is the amount of time the agitation bar will be in the upper position. This number is necessarily less than the agitation frequency value. The time begins with the UpStroke initiation and ends with the downstroke initiation.

  The % Upward parameter controls the upstroke in the same manner as the "Upstroke" parameter, but is expressed in terms of a percentage of the agitation frequency rather than a time.

- Set Temperature Screen: Allows user to set the temperature for each of the two Reaction Vessel banks, turn on the heaters, designate how long each Reaction Vessel bank should remain at this temperature, and indicate the volume in the 100 mL Reaction Vessels.

- Monitor Temperature Screen: Displays the set-point temperature of the Reaction Vessel banks, the actual temperature, remaining heating time and heater status (on or off).

- Other Functions Screen: Allows access to functions not available on the main screens. The "other functions" are Proceed to main, , Show Firmware Version, Adjust LCD, Self Test, Show Agitation history, Show Heater History and Restore Defaults.

Keypad

The keypad buttons are used to move between screens, select a parameter on an active screen, and increase or decrease the chosen parameter value. The Mode, Forward, Back, Parameter, START/STOP, and Agitator ON buttons are described in the next five subsections of this chapter.

Mode Button

Pressing the Mode button allows the user to move from the current display screen to the subsequent screen.

For information on the function of the Mode button in a particular screen, see Section 7: Controller Unit Display Screens.

Forward and Back Buttons

The Forward and Back buttons (right and left arrow buttons) allows the user to select a parameter on the display screen.

Press the Forward button (right arrow) to move to the next parameter or digit on the display screen.

Press the Back button (left arrow) to move to the previous parameter on the display screen.

For information on the function of the Forward and Back buttons in a particular display screen, see Section 7: Controller Unit Display Screens.

Parameter Setting Buttons

The Parameter Setting buttons (up and down arrow buttons) allows the user to increase or decrease the display parameter selected with the Forward and Back buttons.

Press the Up Parameter button (up arrow) to increase the value of the selected parameter.

Press the Down Parameter button (down arrow) to decrease the value of the selected parameter.

For information on the function of the Parameter Setting buttons in a particular display screen, see Section 7: Controller Unit Display Screens.

START/STOP Button

Pressing the START/STOP button when the Set Temperature screen is displayed starts or stops the heaters, as specified.

Press the START/STOP button to turn on the heater for the first bank of Reaction Vessels after the reaction bank temperature and temperature duration on the Set Temperature screen have been set.

Set the reaction bank temperature and temperature duration for the second bank of Reaction Vessels and press START/STOP to turn on that heater.

The heaters remain at the specified temperature for the specified time, at which point the heaters turn off.

The START/STOP Heaters display screen appears when the START/STOP button is pressed while in any other display screen.

For more information, see Section 7: Controller Unit Display Screens.

Agitator Control Buttons

The three Agitator Control buttons are located on the keypad to the right of the LCD screen.

The uppermost button causes the agitator bar to move to, and stay in, the up position.

The lower button causes the agitator bar to move to, and stay in, the down position.

The middle button causes the agitator bar to oscillate continually. Press the middle agitation button to start mixing the reaction solution once the agitation parameters have been set on the Agitation Control screen.

For detailed information on setting the agitation, see Operating the Quest 205, Setting of Agitation Parameters.

Agitation Needle Valve

The Agitation Needle Valve controls the speed at which the agitator bar moves.

Turn the Agitation Needle Valve counter clockwise to increase the speed.

Turn the Agitation Needle Valve clockwise to decrease the speed.

For detailed information on setting the agitation frequency, see Operating the Quest 205, Mixing of the Reaction Vessel Solution. For a definition of the agitator bar, see Reactor Unit, Components for Mixing the Reaction Solution in this section.

Controller Unit Gas and Power Connections

System Gas

The Quest 205 can use either one or two sources of gas. With two gas sources, the inert gas is used for delivering solvents, draining Reaction Vessels, and creating an inert reaction environment. The compressed air drives the agitation system. If a single source of gas is used, the agitation system is driven by the inert gas. Using compressed air for agitation significantly reduces the quantity of inert gas consumed by the Quest 205.

If a single source of gas is connected to the Quest 205, the gas should be a regulated 55-60 psi high-purity (>99.98%) inert gas. If two gas sources are connected to the Quest 205, one should be a regulated 40-60 psi high-purity (>99.98%) inert gas and the second should be a regulated 55-60 psi source of clean, dry compressed air.

The gas ports are located on the rear of the Controller Unit adjacent to the power switch and the electrical socket. "Quick connect" fittings are used to interface the Controller Unit with the gas sources.

Electrical Outlet

The power cord connects to the rear of the Controller Unit. The instrument can operate on 110-120 0r 200-240 VAC, 50-60 Hz .

Power Switch

The power switch turns the power on and off after the Quest 205 power cord is plugged into the power outlet.

Interface Harness

The Controller Unit is connected to the Reactor Unit via the Interface Harness. The Controller Unit ports are as follows.

- Heater Power: Supplies power to the heaters within each Reaction Vessel bank.
- Signal: Carries thermocouple readings from the Reactor Unit to the Controller Unit.
- Agitation Gas: Ports 1 and 2 supply gas to the pneumatic gas cylinder.

- Solvent Gas Pressure: Port 5 supplies 9psi gas pressure to the Solvent Bottle Assembly.
- Drain Gas: Port 3 supplies 30 psi gas line to the Reactor Unit.
- Metered Gas: Port 4 supplies 10 psi gas line to the Reactor Unit and is flow regulated by a needle valve on the Reactor Unit.

Solvent Bottle Assembly

The Solvent Bottle Assembly consists of the solvent bottle, plastic bottle safety carrier, and the bottle cap assembly. The bottle cap assembly has three Teflon lines attached to it. One line supplies pressure to the bottle, the second line allows venting of the bottle, and the third line provides the path for solvent flow to the Reactor Unit. The pressure and delivery lines protrude from the middle of the Interface Harness. The vent line, found in the Accessory Kit, connects to the bottle cap assembly.

WARNING: Ensure the vent line is anchored within the fume hood and pointed away from the user.

A long Teflon line runs from the bottom of the Teflon cap. This line is the "pickup" tube for the solvent in the bottle and should reach the bottom of the bottle. Additionally, a polyethylene filter is placed on the end of the line to prevent particulates from entering the Quest's fluidic system.

When a flow path is created from the Solvent Bottle Assembly delivery line to a reactor manifold, the gas pressure forces the fluid through the tubing, via the Interface Harness, into the Reaction Vessels.

WARNING: Always wear eye protection when operating the Quest 205.

To install a solvent bottle, see Section 2: Installation. Before removing a solvent bottle, it must be vented. Rotate the dial so that the arrow is pointed to the Teflon tube labeled "VENT."

WARNING: Always vent the bottle prior to unscrewing the cap.

WARNING: Always place the solvent bottle in the plastic bottle safety carrier when working with the Quest 205.

4 Operating the Quest 205

This section provides step-by-step instructions for using the Quest 205 Manual Synthesizer to complete a liquid or solid phase chemistry reaction. These instructions include:

- Preparing the Quest 205 for a synthesis
- Installing the Reaction Vessels on the Quest 205
- Running reactions on the Quest 205

Preparing the Quest 205 for a Synthesis

1. Ensure the Reactor Unit is placed in a fume hood and that the Controller Unit is outside of the fume hood and away from chemical hazards (see Section 2, Installation).
2. Verify that there is sufficient system gas at the supply.
3. Install a solvent bottle (if necessary) and a filter (see Installing the Solvent Bottle in Section 2).
4. Install the rectangular waste tank underneath the Reactor Unit (see Installing the Waste Tank in Section 2).

Remove Used Reaction Vessels

NOTE: The Reaction Vessels installed on the Reactor when received were installed to protect the Upper and Lower Manifolds during shipment. These vessels must be removed and new vessels installed prior to use. Failure to replace the Reaction Vessels can result in gas and/or solvent leakage.

NOTE: Always wear gloves and eye protection when working with the Quest 205.

1. Drain the Reaction Vessels that are to be removed. For instructions, see Draining the Reaction Vessels in this section of the manual.

NOTE: Ensure Reaction Vessels are drained before removing them.

2. Vent the Reaction Vessels.
   a. Rotate the Manifold Control Valves as shown in figure 4-1.
   b. Slowly approach the VENT setting on the valve. The pressure must be vented slowly to avoid "bumping" the solution.

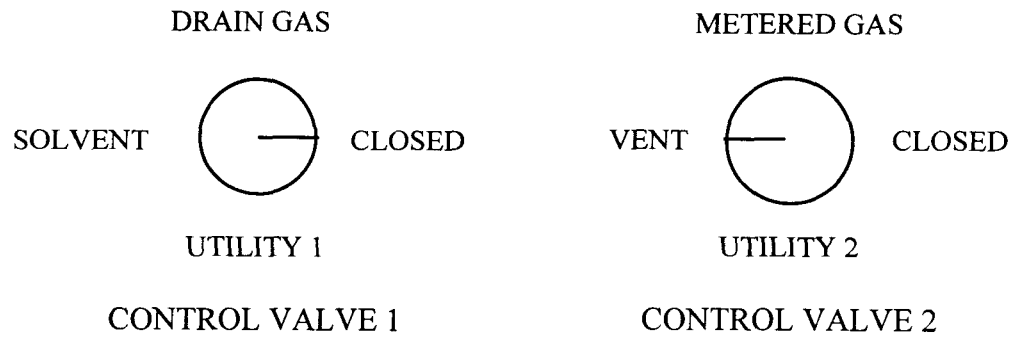

Figure 4-1 Control Valves set to the VENT position

3. Using the 7/64" hex driver, loosen the upper Reaction Vessel clamps. The clamps are located at the junction of the Reaction Vessels and the Upper Manifold.
4. Raise the Upper Manifold.

WARNING: Always vent the reactions vessels before removing a raising the Upper Manifold as contents may be under pressure.

   a. Lift the levers on both sides of the Upper Manifold so that they are parallel to the work surface and extend out to the sides of the Reactor Unit.
   b. Insert the levers into the cutouts on the Upper Manifold handles.
   c. Press the handle buttons and simultaneously use the levers to raise the Upper Manifold off the Reaction Vessels.

5. Remove the pin holding the Upper Manifold in place. Two pins hold each Upper Manifold onto the Reactor Unit. Always remove the pin that is on the opposite end of the Upper Manifold from the three tubing connections between the Upper Manifold and the Upper Reactor Unit. A cord attaches the pin to the Reactor Unit so it is not inadvertently dropped.
   a. Side A: Remove the pin that is on the right side of the Upper Manifold.
   b. Side B: Remove the pin that is on the left side of the Upper Manifold.

NOTE: The remaining pin should only be removed when the Upper Manifold must be removed for the Reactor Unit for servicing. Careful handling is required when the upper manifold is removed from the Reactor Unit because individual Reaction Vessels shut off bolts can easily be damaged.

6. Swing the Upper Manifold out as far as it will go.
7. Tilt the Upper Manifold to keep it open. This prevents the manifold from swinging back into the Reaction Vessels.
   a. Side A: Tilt the Upper Manifold to the left.
   b. Side B: Tilt the Upper Manifold to the right.
8. Use the 7/64" hex driver to loosen the lower Reaction Vessel clamps on the Lower Manifold.
9. Remove the Teflon-encapsulated agitation magnet from the Reaction Vessel using the magnet removal tool.

NOTE: Failure to remove the agitation magnet from the Reaction Vessel may cause the frit to fall out the Reaction Vessel during removal from the Reactor.

10. Carefully twist the Reaction Vessel with a slight upward pull until the vessel breaks free from the lower manifold and slowly pull the vessel upward through the heater block.

NOTE: Be careful not to bump the Upper Manifold when removing Reaction Vessels.

11. Once extracted, cap the bottom of the Reaction Vessel before further handling or discard the used Reaction Vessel in an appropriate waste container.

Installing New Reaction Vessels

NOTE: The Quest 205 Reactor Assembly has a Side A and Side B. Each side contains a bank of five Reaction Vessels. One side or both sides simultaneously can be used for synthesis. If less than five reactions are to be run on a particular side, place empty Reaction Vessels in the unused positions.

1. If the Upper Manifold is in place over the Reaction Vessel Bank, open it by following steps #3-#7 under Removing Used Reaction Vessels.
2. Clean the luer plugs, luer port adapters, and luer ports.
   a. Remove each luer plug and luer port adapter from the Upper Manifold.
   b. Clean each plug and adapter with solvent to remove any particulates.
   c. Rinse the luer ports with solvent to remove any residue remaining from the previous synthesis.
   d. Gently clean the luer ports with a cotton swab wetted with solvent.
   e. To install the luer port adapter, insert it into the Upper Manifold. Rotate the adapter in a clockwise direction until a slight resistance is felt and continue for an additional ¼ turn.

NOTE: Over tightening of the luer port adaptor will permanently distort the end of the fitting so it can not seal against the Upper Manifold. Distorted luer port adapters can result in gas and/or solvent leakage.

   f. Replace the luer plugs into the luer port adapters.
3. Clean the male Reaction Vessel fittings on the Upper and Lower Manifolds with a soft cloth and appropriate solvent. Ensure that there are no particulates or dust on the fittings.
4. Obtain a sufficient number of 100 mL Reaction Vessels.
5. Place a Reaction Vessel in the selected RV position and push it down through the heater clamp until the end of the Reaction Vessel is between the Lower Manifold and the lower Reaction Vessel clamps.

NOTE: Once installed, the tops of the Reaction Vessels should all be at the same height.

6. Using the 7/64" hex driver, tighten the Reaction Vessel clamps on the Lower Manifold.

7. For solid phase reactions, weigh out and add the synthesis support or ArgoCaps to the Reaction Vessels.

   The maximum amount of resin that can be used depends on the resin density, resin swelling characteristics, and solvents used for synthesis. As a general rule, up to 8 g ArgoGel, or similar gel type resin, can be used.

8. Place a clean Teflon-encapsulated agitation magnet into each Reaction Vessel.

   For proper orientation, look closely at the magnet to identify the end with the engraved "-"(minus) symbol. This end should be oriented down in the Reaction Vessel to provide a small space between the bottom of the magnet and the top of the Reaction Vessel frit.

9. Tilt the Upper Manifold and swing it into the closed position.

   a. Side A: Tilt the Upper Manifold to the right.

   b. Side B: Tilt the Upper Manifold to the left.

10. Push the hinge pin (attached by a cord to the Reactor Unit) through the hinge to keep the Upper Manifold in the closed position.

11. Insert the Upper Manifold levers into the cutouts on the Upper Manifold handles.

12. Push in on the Upper Manifold handle buttons and use the levers to slowly slide the Upper Manifold onto the top of the Reaction Vessels.

NOTE: Ensure that the restrictors and the Reaction Vessels are properly aligned. The restrictors are the two small tubes protruding out of the Upper Manifold in each Reaction Vessel position.

---

13. Continue to push down the Upper Manifold levers to press the Upper Manifold male fittings into the tops of the Reaction Vessels:

14. Using the 7/64" hex driver, tighten the Reaction Vessel clamps on the Upper Manifold.

15. Adjust the agitation stops to the appropriate height. Typically, the maximum magnet stroke height should be below the level of the reaction solution.

    The lower stop sets the maximum upward stroke and the upper stop sets the minimum stroke. The upper stop (located within the upper "shell") is pre-set and generally does not need adjustment.

    To set the lower stop:

    a. Use an 7/64" hex driver to loosen the lower agitation stops and retighten them at the desired position.

    b. Raise the stop to reduce the upper stroke position. This is a trial and error process.

       A typical mixing stroke range would be from just above the frit to just below the liquid level of the Reaction Vessels.

    These stops can also be adjusted later during the synthesis as liquid levels change due to reagent additions.

Shutting Off Individual Reaction Vessels

Each Reaction Vessel bank holds five Reaction Vessels. All five Reaction Vessels do not need to be used in each synthesis. If less than five Reaction Vessels are needed, the unused Reaction Vessels can be shut off.

1. If the Upper Manifold is in place over the Reaction Vessel bank, open it by following steps 3-7 under Removing Used Reaction Vessels.

WARNING: Always vent the reactions vessels before removing a raising the Upper Manifold as contents may be under pressure.

2. There are two hex socket bolts on the rear of the Upper Manifold for each Reaction Vessel position. Locate the bolts associated with the Reaction Vessel position to be closed.

3. Using the 3/32 hex driver, turn the two bolts until they are flush with the surface of the Lower Manifold. This physically presses the membrane against the solvent and vent ports for the selected Reaction Vessel.

NOTE: A Reaction Vessel should be placed in each position on a Reaction Vessel bank, any time that solvents are delivered to that bank.

4. If no other Reaction Vessel positions need to be shut off close the Upper Manifold (as described in step 9-14 in Installing New Reaction Vessels).

To reopen a Reaction Vessel position, perform steps 1 and 2. Using the 3/32 hex driver, turn the two hex socket bolts approximately 2 ½ turns counter-clockwise.

NOTE: After reopening a vessel position, toggle the membrane pressure valve on and listen for leaks. If a hissing sound is heard, the dummy RV screw has been unscrewed too much. Tighten the screw slightly to correct.

NOTE: During the next solvent delivery after reopening a vessel position verify that flow rate to each vessel is within +-10%. If the previously closed position has low flow, the dummy RV screw may not have been loosened enough.

Waste Tank

1. Ensure the waste tank is properly positioned under the Lower Manifolds (see Installing the Waste Tank in Section 2).
2. Check that the tube attached to the waste tank leads to an appropriate waste container.

WARNING: The waste tank is heavy when full of solvent. Use caution when handling.

Starting a Reaction

This section explains how to:

- Set the reaction temperature, temperature duration time, and agitation parameters.
- Close the Upper Manifold Membrane Switch.
- Perform manual parallel solvent additions.
- Manually add reagents or solvents to the Reaction Vessels through the luer ports.

Determine the steps that are needed to complete a liquid or solid phase chemistry reaction, then perform the corresponding procedures provided in this section as required.

Be sure to clean the instrument after the reaction is finished (see Section 5, Maintenance).

Setting the Reaction Temperature, Time, and Agitation

The reaction temperature, heating duration, and agitation parameters are set by changing the appropriate parameters on one of the Controller Unit display screens. The Mode button is used to access the different display screens. For detailed information on the contents of each display screen and how to use the Controller Unit buttons and other components, see Section 7: Control Box Display Screens.

Setting the Agitation Parameters

NOTE: Set the agitation parameters to minimize splashing of solution on the Upper Manifold male fittings. This prevents the build up of resin and/or particulates in the luer ports.

Three parameters are shown on the Agitation display screen.

- The MixEvery parameter is the agitation frequency expressed in seconds, or the elapsed time between consecutive upstrokes (see Figure 4-2).
- The UpStroke parameter is the amount of time the agitation bar will be in the upper position (see Figure 4-2). (This number is necessarily less than the agitation frequency value.)
- The % Upward parameter automatically changes when the UpStroke parameter is set.

The % Upward parameter controls the upstroke in the same manner as the Upstroke parameter, but is expressed in terms of a percentage of the agitation frequency rather than a time. If the % Upward parameter is set by the user, the UpStroke parameter automatically changes to match the new % Upward value.

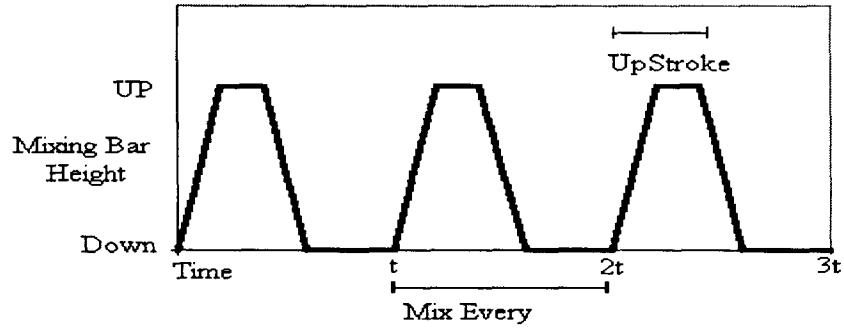

Figure 4-2 Example Agitation Cycle Plot

Consider these guidelines when setting the agitation parameters:

- If the reaction solution is viscous or there is a large amount of resin, use a lower stroke velocity (agitation needle valve).
- If the synthesis support is very delicate, decrease the stroke frequency to reduce the support exposure to mixing (MixEvery parameter).
- If a liquid-liquid extraction is being done, increase the stroke frequency and stroke velocity to increase the mixing efficiency (MixEvery parameter, agitation needle valve).

NOTE: It is advisable to keep the magnets in the up position when not mixing during a solid phase synthesis. This helps prevent a large mass of resin from settling down on top of the magnet and hindering mixing.

To set the parameters:

1. Use the Mode button to access the Agitation Control screen (See figure 3).

```
   - - Not Agitating - -

MixEvery   :    4.0 sec
UpStroke   :    3.8 sec
% Upward   :      95 %
```

Figure 4-3 Agitation Control Screen

2. Set the MixEvery parameter.
   a. Use the Forward and Back buttons to select the MixEvery parameter.
   b. Use the Parameter Setting buttons to increase or decrease the MixEvery parameter.
3. Set the Upstroke parameter.
   a. Press the Forward or Back buttons to select the Upstroke parameter.
   b. Use the Parameter Setting buttons to increase or decrease the Upstroke parameter.

      The % Upward parameter automatically changes to reflect the new value set for Upstroke.
4. To change the % Upward parameter (not necessary if Upstroke parameter is correctly set):
   a. Press the Forward or Back buttons to select the % Upward parameter.
   b. Use the Parameter Setting buttons to increase or decrease the % Upward parameter.

      The Upstroke parameter automatically changes to reflect the new value set for % Upward.
5. Press the Agitator ON/OFF button, located on the Controller Unit, to start the mixing.

NOTE: The agitator needle valve is set to CLOSED during shipment. Turn it counter clockwise to start agitation.

6. Modify the agitation speed by changing stroke velocity (if desired).
   Move the Controller Unit Agitator Needle Valve counter clockwise to increase the speed of the agitator bar or clockwise to decrease the speed.
7. Press the Agitator ON/OFF button to stop mixing.

Temperature Control

The reaction temperature range on the Quest 205 is –40°C to +130°C. For a particular reaction, do not program a temperature set point, which exceeds the boiling point of the reaction solvent.

Each side of the Quest 205 can have a different set point. To achieve sub-ambient temperatures, a user-supplied external recirculating chiller is required. Connect the chiller to only one side of the Quest 205 at one time.

WARNING: This symbol indicates a hot surface. Use caution when working near or on the Reactor Unit. When heating, the Reactor Unit becomes hot. Allow the Reactor Unit to cool before attempting to access the Reaction Vessels.

Prior to starting a heating step, set both Manifold Control Valves to CLOSED. This prevents solvent loss during heating.

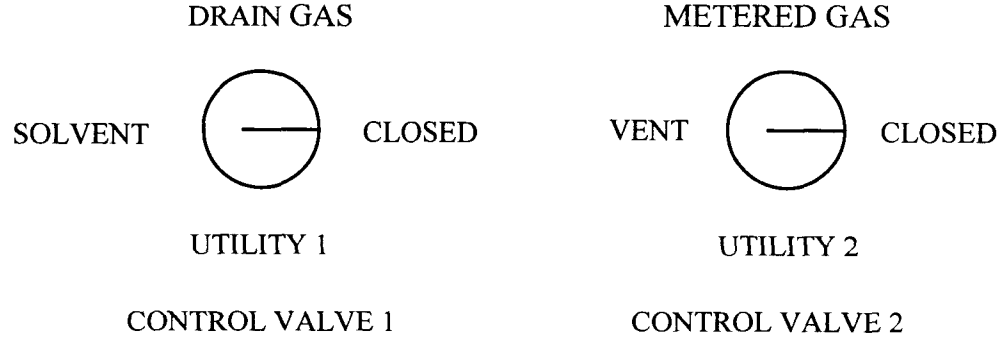

Figure 4-4 Control Valves set to the CLOSED position

Entering the Temperature Set-Point

1. On the keypad, press the MODE button until the Set Temperature screen is displayed (see figure 4-5).

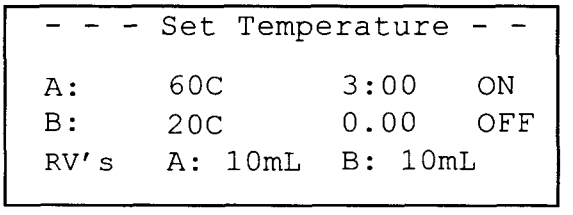

Figure 4-5 Set Temperature screen

2. Use the Forward and Back buttons to place the cursor over one of the digits of the setting in the temperature field.

NOTE: There is a separate temperature field for Side A and B

3. Use the Parameter Setting buttons to increase or decrease the temperature parameter for Side A and/or Side B.

WARNING: As a general rule, do not enter a temperature set point above the boiling point of the reaction solvent being used. This prevents against over pressurization of the system.

4. Use the Forward and Back buttons to place the cursor over one of the digits of the setting in the RV Volume field.

NOTE: There is a separate volume field for Side A and for Side B

5. Use the Parameter Setting buttons to select the reaction volume for the Reaction Vessels on Side A and/or Side B. The volume entered should be the total volume of reagents, solvent, and resin in the Reaction Vessels. This value can be changed during synthesis as the reaction volume changes.

6. Use the Forward and Back buttons to move to the time field. This is the duration at which the specified side will stay at the temperature set point.

7. Use the Parameter Setting buttons to increase or decrease the chosen time parameter for Side A and/or Side B.

8. To start heating the Reaction Vessels:

   a. Locate the cursor on the screen line for either Side A or Side B.

   b. Press the START/STOP button.

   c. Repeat for the other bank of Reaction Vessels, if desired.

   The Reaction Vessel Bank begins to heat up to the set point. On the initial heat-up period, the actual RV temperature may overshoot the set point by a few degrees, but the system will equilibrate at the selected set point.

NOTE: Breaking the seal on the Reaction Vessel during an elevated temperature reaction may cause a vacuum to form in the Reaction Vessel during cooling, collapsing it. Apply drain gas (using Control Valve 2) to re inflate the Reaction Vessel.

9. Set the Upper Manifold Membrane Switch to CLOSED. (For instructions, see Upper Manifold Membrane Switch in this section.)

10. The temperature set-point may be changed from an existing set-point by accessing the Set Temperature screen.

11. The heaters turn off when the time has elapsed or they can be manually stopped. To stop the heaters:

    a. Locate the cursor on the screen line for either Side A or Side B.

    b. Press the START/STOP button.

    d. Repeat for the other bank of Reaction Vessels, if desired.

    Pressing the START/STOP button while outside of the Set temperature screen will display the Start/Stop Heaters screen. This screen provides the option of starting or stopping the both heaters either individually or together.

12. Press the MODE button to view the Monitor screen, if desired. This screen displays the set-point temperature and the actual RV temperature.

Chilling the Reaction Vessels

For sub-ambient temperature set-points, an external recirculating chiller is required. A chiller can only be used on one side of the Quest 205. If a second chiller is available, then both sides of the Quest 205 can be chilled together.

A Chiller interface kit is available from Argonaut Technologies to simplify the connections to the chiller. This kit contains fitting to convert the chiller interface to a ¼" female NPT fitting.

WARNING: Disconnect the chiller when it is not in use. Purge the Quest 205 cooling channel of refrigerant liquid after the chiller is disconnected. Do not heat a Reaction Vessel bank with the chiller connected or with residual liquid in the cooling channel.

Upper Manifold Membrane Switch

The Upper Manifold Membrane Switch is typically set in the CLOSED position when running a reaction. In this position, the Membrane switch supplies 30 psi gas to the outside of a membrane located in the Upper Manifold. This membrane, when pressurized, flattens against the common pathways of the Upper Manifold. The flattened membrane closes the pathways between the Reaction Vessels on a bank and prevents any crossover of Reaction Vessel contents from vessel to vessel.

NOTE: The functions of the Manifold Control Valves are disabled when the Membrane Pressure switch is in the CLOSED position.

The Membrane switch should be set in the OPEN position when:

- The Quest 205 is connected to a gas bubbler.
- Utilizing Manifold Control Valve functions such as solvent delivery, draining, venting, and/or providing an inert gas blanket.

Parallel Solvent Addition and Vessel Draining

Parallel Solvent Addition

The Quest 205 is equipped with an external Solvent Bottle Cap Assembly that interfaces with a standard solvent bottle. From this bottle, parallel addition of solvent is possible.

Parallel solvent addition is typically done when adding solvent to a reaction mixture, performing resin wash steps, and for system clean-out. Parallel addition is accomplished utilizing the Manifold Control Valves to create a flow path from the solvent bottle to the Upper Manifold.

WARNING: Always wear gloves and safety glasses when operating the Quest 205.

To perform a parallel solvent addition:

1. Install the solvent bottle.
   a. Place the solvent bottle in a safety carrier (4L capacity for domestic instruments or 2.5L capacity for international instruments).
   b. Ensure that a new reagent inlet filter is installed on the solvent line and a Teflon bottle seal is present in the cap.
   c. Insert the long tube of the Bottle Cap Assembly into the bottle and screw down the cap.
   d. Turn the dial on the top of the bottle cap towards the tube marked "BTL PRESS."
   e. Wait about 1 minute for the bottle to pressurize.

WARNING: Always place the solvent bottle in the plastic safety carrier.

2. Toggle the Upper Manifold Membrane Switch to OPEN.
3. Initialize the solvent flow to the Reaction Vessels by setting Control Valve 1 to SOLVENT and Control Valve 2 to VENT (see figure 4-6).

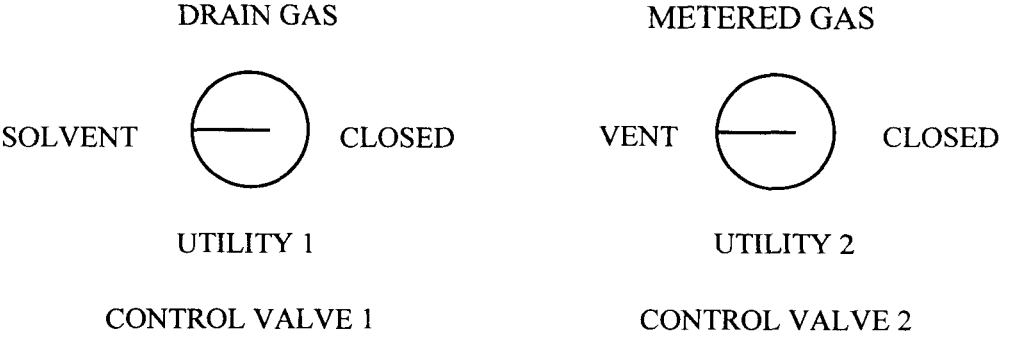

Figure 4-6 Control Valves set to the SOLVENT and VENT position

4. When the Reaction Vessels have been filled to the desired level, rotate Control Valve 1 from SOLVENT to DRAIN GAS. This will blow residual solvent from the Upper Manifold common path into the Reaction Vessels (requires about 1 second).

5. After blowing the residual solvent into the vessels, set both Manifold Control Valves to CLOSED.

Draining the Reaction Vessels

Draining the Reaction Vessels is typically done during the resin wash steps of a solid phase synthesis or when a reaction step is complete.

NOTE: before draining a solid phase reaction stop the magnet bar in the raised position to help prevent the agitation magnets from getting stuck in the resin

1. Verify that the waste tank is installed below the Reactor Unit.
2. Toggle the Upper Manifold Membrane Switch to OPEN.
3. Open the drain valves on the Lower Manifold by pushing down on the Drain Valve Levers.
4. Set the Control Valve1 to DRAIN GAS and CONTRL VALVE 2 to CLOSED (see figure 4-7).

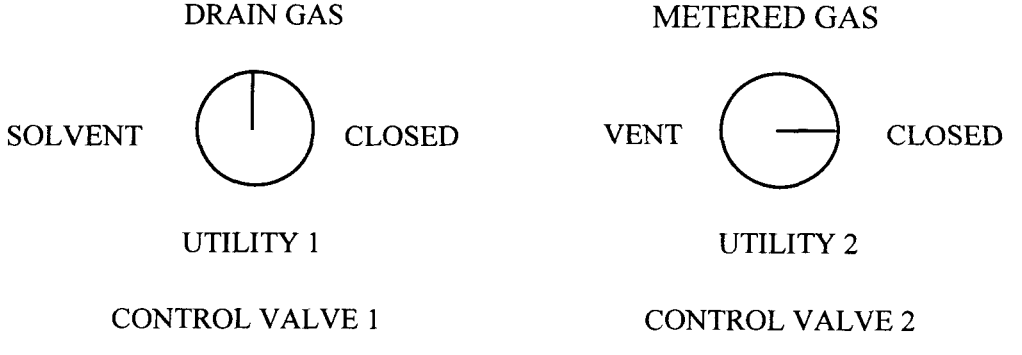

Figure 4-7 Control Valves set to DRAIN GAS and VENT

5. After draining the vessels, set both Manifold Control Valves to CLOSED.
6. Return the Drain Valve Levers to the CLOSED (up) position when finished.

Changing a Solvent Bottle

Changing the solvent bottle involves back-flushing the solvent delivery line, removing the bottle, and changing the end-line filter.

1. Ensure clean Reaction Vessels are in place on at least one side of the Quest 205.
2. On the side of the Reactor Unit with the Reaction Vessels installed, toggle the Upper Manifold Membrane Switch to OPEN
3. Turn the dial on the solvent bottle cap to the VENT position. Wait about 1 minute for the bottle to vent before proceeding.
4. Vent the Reaction Vessels by setting Control Valve 1 to CLOSED and Control Valve 2 to VENT (See figure 4-8).

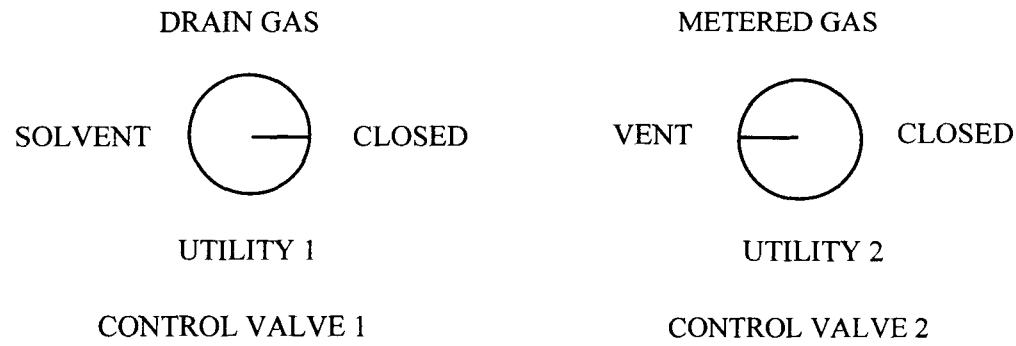

Figure 4-8 Control Valves set to CLOSED and VENT

NOTE: Ensure the RVs and manifolds are clean before performing the following steps or debris may be blown into the solvent line

5. Wait 5 seconds, then set Control Valve 1 to the SOLVENT and Control Valve 2 to METERED GAS. This setting uses the metered gas pressure to blow gas back through the solvent bottle liquid line and into the solvent bottle.
6. Increase the flow rate on the metered gas line by turning the metered gas needle valve(located on the top of the Reactor Unit) counter clockwise. Leave the valves in that configuration for 1 minute to completely empty the line.
7. Turn both Manifold Control Valves to CLOSED.

8. Unscrew the cap from the solvent bottle, change the solvent inlet filter, and install a new solvent bottle.

WARNING: Always place the solvent bottle in the plastic safety carrier.

Adding Solvent or Reagents Through the Luer Ports

Solvents, liquid reagents, and solids can be added to the Reaction Vessels through the luer ports located at the top of the Upper Manifold. Typically, these reagents are added via syringe and mechanical pipette (liquids) and modified funnel (solids).

Adding Solvent or Reagents

1. Prior to adding solvents or reagents through the luer ports, the system must be vented, as it may be under pressure.
   a. Set the Manifold Control Valve 2 to VENT. Slowly approaching the VENT setting on Control Valve 2 will gently equalize the pressure and avoid "bumping" the solution (see figure 4-8).
2. Slowly remove the luer plug by rotating the plug while pulling it out.

WARNING: Always wear safety glasses, gloves and appropriate clothing when working with the Quest 205.

WARNING: Do not open the upper luer ports when the Reaction Vessels are being heated. Turn off the heaters and allow the vessels to return to ambient temperature before opening the luer ports.

3. Add solvent or reagents to a Reaction Vessel.

   Adding liquid chemicals:

   a. Remove the luer port plug.
   b. Insert a needle and syringe or mechanical pipette through the luer port adaptor of the selected Reaction Vessel.

WARNING: Be careful not to score the interior surfaces of the luer port with the needle, as marring the surface can affect sealing the port.

Solid chemicals:

a. Remove the luer port adaptor.

b. Insert a funnel into the port.

c. Add the solid chemicals.

d. Rinse the solid down the funnel with the wash solution.

4. To install the luer port adapter, insert it into the Upper Manifold. Rotate the adapter in a clockwise direction until a slight resistance is felt and continue for an additional ¼ turn.

NOTE: Over tightening of the luer port adaptor will permanently distort the end of the fitting so it can not seal against the Upper Manifold. Distorted luer port adapters can result in gas and/or solvent leakage.

5. Replace the luer plugs into the luer port adapters.

6. Turn both Manifold Control Valves to CLOSED.

Adding Liquid Solvent or Reagents to an Air-Sensitive Chemistry

NOTE: To monitor inert gas flow while adding liquid chemicals to an air-sensitive reaction, a bubbler can be attached to the Utility Port 1 (see Section 9: Accessories).

To add liquid solvents or reagents to an air sensitive chemistry.

1. Start the synthesis.

2. When it is time to add the chemical, set Control Valve 1 to UTILITY 1 and CONTROL VALVE 2 to METERED GAS.

Turn the metered gas needle valve counter clockwise to allow a flow of inert gas across the Reaction Vessels.

NOTE: The standard luer plug can be replaced with the Septa luer plug (see Section 9: Accessories).

Remove the luer plug and insert a needle and syringe or mechanical pipette through the luer port adaptor of the selected Reaction Vessel

Reaction Vessel Bank-to-Bank Transfer

The contents of one Reaction Vessel on a particular side of the Reactor Unit (the "source" Reaction Vessel) can be transferred to a Reaction Vessel on the other side of the Reactor Unit (the "target" Reaction Vessel). A bank-to-bank transfer is achieved using a transfer cannula (in Accessory Kit). The transfer cannula is a Teflon tube with a 1/4"-28 female luer on one end and a pierced septa luer plug on the other.

NOTE: • Always wear safety glasses and gloves. Escaping gases may entrain small amounts of liquid.

1. Rotate the Quest 205 so that the "target" reactor vessel is easily accessible.
2. Set the Control Valve 1 to CLOSED and Control Valve 2 to VENT on the side with the "target" Reaction Vessel.
3. Remove the luer plug for the "target" Reaction Vessel.
4. Set Control Valve 2 to METERED GAS on the side with the "target" Reaction Vessel.
5. Insert the pierced septa luer plug into the luer port adapter of the "target" Reaction Vessel.

WARNING • Ensure the tubing does not go below any liquid level in the target Reaction Vessel. Keeping the end of the tubing above the liquid will prevent any liquid from being pushed out the tubing.

6. Toggle the Upper Manifold Membrane Switch to the OPEN position to purge the tubing in the transfer cannula with METERED GAS (to increase the flow rate of the metered gas turn the metered gas needle valve, located on the top of the Reactor Unit, counter clockwise).
7. Return the Upper Manifold Membrane Switch to the CLOSED position
8. Set Control Valve 1 CLOSED and Control Valve 2 to VENT on the side with the "target" Reaction Vessel.
9. Rotate the Quest 205 so that the "source" Reaction Vessel is easily accessible.
10. Insure all Lower Manifold drain valves are closed and remove the Waste Tank.

11. Locate the male luer fitting for the "source" Reaction Vessel below the Lower Manifold. Attach the female luer on the transfer cannula to the "source" Reaction Vessel male luer fitting.

12. Set Control Valve 1 to CLOSED and Control Valve 2 to METERED GAS on the side with the "source" Reaction Vessel.

13. Toggle the Upper Manifold Membrane Switch to the OPEN position to apply METERED gas to the "source" Reaction Vessel.

14. Open the "source" Reaction Vessel drain valve on the Lower Manifold (down lever position). Adjust the metered gas needle valve to control the flow rate of the solution from the "source" Reaction Vessel to the "target" Reaction Vessel.

15. Return the drain valve to CLOSED (up position) after the transfer is complete.

16. Remove the transfer cannula from the male luer fitting on the Lower Manifold.

17. Return the Upper Manifold Membrane Switch to the CLOSED position.

18. Rotate the Quest 205 so that the target Reaction Vessel is easily accessible.

19. Remove the transfer cannula from the "target" Reaction Vessels luer port adapter.

20. Replace the luer plug into the "target" Reaction Vessels luer port adapter.

21. Set all Control Valves to the CLOSED position.

Providing a Gas Sweep Over the Reaction Vessels

It is possible to provide a low flow rate sweep of the Reaction Vessel upper head space during reagent addition or while a reaction is in progress by using metered gas.

1. Toggle the Upper Manifold Membrane Switch to OPEN.

2. Set the Control Valve 1 to UTILITY 1 and Control Valve 2 to METERED GAS (The gas flow flows out of the Utility 1 port located at the top of the Reactor Unit).

   It is recommended that a bubbler (See Section 9: Accessories) be attached to the Utility 1 port with the outlet pointed away from the Quest 205 and towards the back of the fume hood.

3. To modify the gas flow rate, turn the Metered Gas Control Valve counter clockwise to increase the gas flow rate or clockwise to decrease the gas flow rate.

NOTE: The use of a gas sweep may result in solvent loss, especially when heating.

4. To stop the gas flow set both Control Valves to CLOSED and return the Upper Manifold Membrane Switch to the CLOSED position.

Collection of Liquid Reaction Products

Use the flask rack and appropriate flasks (pear-shaped or round bottom) to collect liquid reaction products from the Quest 205.

Draining Synthesis Products to Collection Flasks

WARNING: There may be a small amount of splashing when collecting product. Wear safety glasses, gloves, and appropriate clothing.

NOTE: Stopping the magnet bar in up position to will prevent agitation magnets from getting stuck in resin.

1. Toggle the Upper Manifold Membrane Switch to OPEN.
2. Vent the system to relieve any residual pressure that can cause splashing during product collection.
   a. Set the Control Valve 1 to CLOSED and Control Valve 2 to VENT.
   b. Slowly approach the VENT setting on the valve. The pressure must be vented slowly to avoid "bumping" the solution.
3. Lower the waste tank by grasping the waste tray handles, pressing the buttons on the handles, and moving the tray into its lowest position.
4. Carefully remove the waste tank and drain its contents to an appropriate waste container.
5. Place the flask rack (in Accessory Kit) with appropriate flasks (user supplied, pear-shaped or round bottom) on the waste tray. Ensure the front legs of the flask rack are placed in the indentations in the waste tray.

6. Use a flask adaptor to drain the selected Reaction Vessel into a flask. The Flask Adaptor Assembly (in the Accessory Kit) is a Teflon tube with a flask adaptor on one end and a 1/4"-28 female luer adaptor on the other end. The Flask Adaptor Assembly fits 14/20, 19/22, 24/40, 29/26, and 29/42 flasks.
   a. Connect the female luer adaptor to the male luer plug below the Lower Manifold for the chosen Reaction Vessel.
   b. Place the flask adaptor into the collection flask.
7. Set Control Valve 1to CLOSED and Control Valve 2 to METERED GAS to pressurize the head space over the Reaction Vessels:

NOTE: When collecting product, use the 10 psi metered gas to provide the head pressure for fluid transfer. Using the 30 psi drain gas can result in splashing.

6. Open the Reaction Vessel drain valve on the Lower Manifold (down lever position). Adjust the metered gas needle valve to control the flow rate of the solution into the collection flask. Collect sample from one Reaction Vessel at a time.
7. Return the valve to CLOSED (up position) after each collection.

5 Maintenance

Post Synthesis Cleaning

This procedure describes the steps for cleaning the Quest 205 Synthesizer after a synthesis has been completed.

1. Perform three solvent washes (solvent delivery, agitation, drain) on each Reaction Vessel bank used for synthesis.

   It may be desirable to run a pattern of solvents through this wash process, depending on the type of chemistry that was run and the possible residues or particulates that were generated. If a pattern of solvents is run through the system, do at least three wash iterations for each solvent.

   a. Select a solvent that will dissolve any solids or other residues that were generated during the synthesis.

   b. Fill the Reaction Vessels about 3/4 full.

   c. Mix for 1 minute prior to draining the solvent.

2. After the last solvent wash, let the system drain for a couple of minutes to flush residual solvent out of the Reactor Unit. A volatile solvent, such as acetone, may be desirable for this step.

3. With the Lower Manifold drain valves still open, turn off DRAIN GAS (set valve 1 to CLOSED) and turn on METERED GAS. This flushes out the other common channel of the Upper Manifold.

4. Clean the luer plugs, luer port adapters, and ports and close the valves.

   a. Place each Manifold Control Valve to the CLOSED position.

   b. Remove each luer plug and luer port adaptor and wipe clean with solvent, if necessary.

   c. Examine each luer port for residue or particulates. If present, either rinse out the port with a solvent and syringe or wipe clean with a cotton swab wetted with an appropriate solvent.

   d. Close the Lower Manifold drain valves.

5. Clean the Reaction Vessel Bank(s).
   a. Raise the Upper Manifold (see Removing Used Reaction Vessels in Section 4).
   b. Remove the Reaction Vessels (see Removing Used Reaction Vessels in Section 4).
   c. Remove the magnet mixers from the Reaction Vessels and clean.
   d. Discard the Reaction Vessels and resin.
6. Examine the male Reaction Vessel fittings on the Upper Manifold and the Lower Drain Manifold. Use a soft cloth and an appropriate solvent to wipe the fittings clean of any residue or particulates.

NOTE: • Do not allow any particulates to enter the through holes on the Lower Manifold male Reaction Vessel fittings.

7. Empty the waste tank and rinse clean. Do not leave the tank with waste in it when the system is not in use.
8. Examine the plastic plate on the Lower Manifold and above the waste tank. Wipe it clean of any residue.

Manifold Maintenance

It is recommended that the bolts on both the Upper and Lower Manifolds be checked for proper tightness every two weeks. The Upper and Lower Manifolds are large blocks of Teflon sandwiched between metal plates. The nature of Teflon causes it to expand and contract over time. Due to the size of the Manifolds this expansion and contraction causes the bolts on the front of the Manifolds to loosen. Heating and cooling of the system accelerates this phenomenon.

Check and tighten the Upper Manifold bolts using the 7/64" hex wrench. Check and tighten the Lower Manifold bolts using the 3/32" hex wrench. Both hex wrenches are included in the accessory kit shipped with the Quest 205. Moderate hand tightness is sufficient.

The tightness of these bolts must be checked every two weeks. Failure to maintain the proper tension on these bolts can lead to gas and/or solvent leakage from the Manifolds.

6 Glossary

Agitation: The Quest 205 agitation system consists of a pneumatically actuated magnet bar, which vertically oscillates behind the two Reaction Vessel banks. Small Teflon-encapsulated magnets are placed in the Reaction Vessels. As the magnet bar oscillates, the magnets in the Reaction Vessels vertically oscillate with it, causing mixing to occur.

Agitation Needle Valve: Controls the speed at which the agitator bar moves.

Bulkhead fitting: Female threaded ports located on the front of the Controller Unit and in various places on the Reactor Unit.

Controller Unit: Contains the LCD screen and keypad through which agitation and temperature parameters are set and controlled.

Drain gas: Drain gas port supplies 30 psi gas line from the Controller Unit to the Reactor Unit.

Ferrule: Yellow, conical-shaped piece which mates to the PPS fittingd. Used for Teflon tube connections.

Flask Rack: Holds up to five pear-shaped or round flasks to collect synthesis product.

Frit: Teflon filter that is placed in the bottom of each Reaction Vessel.

Heating block: Aluminum plate mounted behind the Reaction Vessel banks.

Interface Harness: Bundle of tubing and electrical wires which connects the Controller Unit to the Reactor Unit.

Lower Manifold Drain Valves: The Lower Manifold mates to the bottom of the Reaction Vessels. The drain valves mechanically seal the lower exit paths from the Reaction Vessels. Each drain valve has a lever to toggle to closed or drain positions.

Luer port adaptor: Teflon piece that screws into each luer port located at the top of the Upper Manifolds. The luer plug is inserted into the adaptor.

Luer ports: Found at the top of each Upper Manifold. Each port is a beveled hole with a corresponding adaptor and plug. Solvents, reagents, and solids may be added to the Reaction Vessels via the luer ports.

Magnet bar: Aluminum assembly with cylindrical magnets mounted along its length. The magnet bar oscillates vertically, moving magnets in the Reaction Vessels and causing mixing of the reaction solution.

Manifold Control Valves: Each side of the Reactor Unit contains two Manifold Control Valves which control gas and solvent flow to and from the Reaction Vessels.

Metered gas: Drain gas port supplies the 9 psi gas from the Controller Unit to the Reactor Unit and is flow-regulated by a needle valve on the Reactor Unit.

Metered Gas Needle Valve: Control knob that increases or decreases the flow rate of 10 psi gas into the Reaction Vessels.

Reaction Vessels: Fritted single-use Teflon tubes to which resin and reagents are added for synthesis.

Reactor Unit: Unit containing Teflon Reaction Vessels, manual solvent and gas control valves, and heating, cooling, and agitation components.

Teflon tubing: Semi-transparent, semi-rigid tubing (1/8" OD) used for gas and liquid connections.

Upper Manifold: Aluminum and Teflon block containing two common pathways: one for parallel solvent delivery drain gas, the other for venting and metered gas.

Upper Manifold Membrane Switch: Pressurizes a Teflon membrane which seals against the common paths of the Upper Manifold to prevent crossover of the fluid or gas contents of the Reaction Vessels.

Utility ports: Two ports that provide the ability to attach external accessories to the Quest 205. The port input lines are teed, with tubes going to the corresponding Manifold Control Valves on each side of the Quest 205.

Waste tank: A rectangular plastic container for waste collection. The waste tank is equipped with a drain valve, which is used to drain the waste to an appropriate external waste container.

7 Controller Unit Display Screens

The display is a LCD (liquid crystal display) screen located on the Controller Unit. Certain display screens show the current reaction temperature, time, and agitation parameters. Other display screens, with the aid of the Controller Unit buttons, allow the user to change the reaction temperature, time, and/or agitation frequency.

This section lists the various display screens and explains how to use the Controller Unit buttons to select a screen and change the parameters.

Sign-On Screen

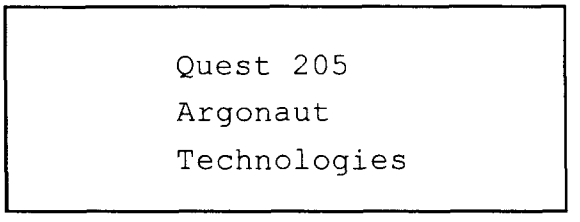

Figure 7-1 Sign-On Screen

The Sign-On screen identifies this instrument as the Argonaut Technologies Quest 205. Table 7-1 outlines the function of the Controller keypad buttons while at this screen.

Pressing this button...	Results in...
MODE	Firmware Version screen
FORWARD/BACK	N/A
PARAMETER	N/A
START/STOP	Start/Stop Heaters screen appearing
AGITATOR ON	Start/Stop agitation

Table 7-1 Sign-On Screen Control Button Functions

Firmware Version Screen

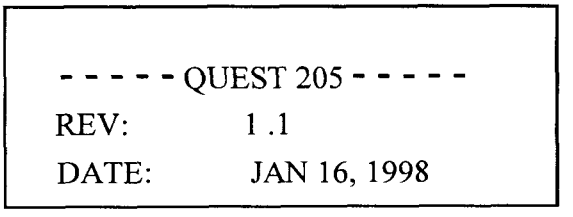

Figure 7-2 Firmware Version Screen

The Firmware Version screen shows the Quest 205 revision and the revision date. This screen is shown when the Mode button is pressed while the Sign-On screen is displayed. Otherwise, the Firmware Version screen must be accessed through the Other Functions screen (described later in this section). Table 7-2 outlines the function of the Controller keypad buttons while at this screen.

Pressing this button...	Results in...
MODE	Agitation Control screen appearing
FORWARD/BACK	N/A
PARAMETER	N/A
START/STOP	Start/Stop Heaters screen appearing
AGITATOR ON	Start/Stop agitation

Table 7-2 Firmware Version Screen Control Button Functions

Agitation Control Screen

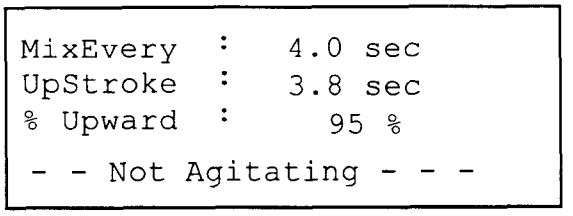

Figure 7-3 Agitation Control Screen

The agitation parameters are set using the Agitation Control screen.

The Agitation Control screen contains three parameters: MixEvery, UpStroke, and % Upward.

The MixEvery parameter is the agitation frequency expressed in seconds. The agitation frequency is defined as the elapsed time between consecutive upstrokes.

Use the Parameter Setting buttons to increase or decrease the MixEvery parameter.

The UpStroke parameter is the amount of time the agitation bar is in the upper position. (This number is necessarily less than the agitation frequency value.)

The % Upward parameter controls the upstroke in the same manner as the Upstroke parameter, but is expressed in terms of a percentage of the agitation frequency, rather than a time.

If the UpStroke parameter is changed, then the % Upward parameter automatically changes to correspond to the new UpStroke parameter. Likewise, if the % Upward parameter is changed, then the Upstroke parameter automatically changes to correspond to the new % Upward parameter.

For example, if the MixEvery parameter is set to 2.0 seconds and the % Upward parameter to 70%, the UpStroke parameter on the screen automatically changes to 1.4 seconds.

Notice that the agitation parameters that are set apply to both Side A and Side B. Table 7-3 outlines the function of the Controller keypad buttons while at this screen.

Pressing this button...	Results in...
MODE	Set Temperature screen appearing
FORWARD/BACK	Selecting a parameter on the screen
PARAMETER	Increasing or decreasing the value of the chosen parameter
START/STOP	Start/Stop Heaters screen appearing
AGITATOR ON	Start/stop agitation

Table 7-3 Agitation Control Screen Control Button Functions

Set Temperature Screen

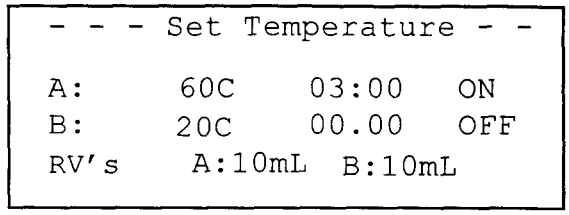

Figure7-4 Set Temperature Screen

The Set Temperature screen is used to set reaction temperatures, specify the duration of the heating step and the actual volume of the reactions in the Reaction Vessels. This screen is also used to start or stop the heating of the Reaction Vessels. Table 7-4 outlines the function of the Controller keypad buttons while at this screen.

Pressing this button...	Results in...
MODE	Monitor Temperature screen
FORWARD/BACK	Selecting a parameter on the screen
PARAMETER	Increasing or decreasing the value of the chosen parameter
START/STOP	Changing the status of the heater for the selected Reaction Vessel Bank. If the heater is on, it is turned off. If the heater is off, it is turned on.
AGITATOR ON	Start/stop agitation

Table 7-4 Set Temperature Screen Control Button Functions

Monitor Temperature Screen

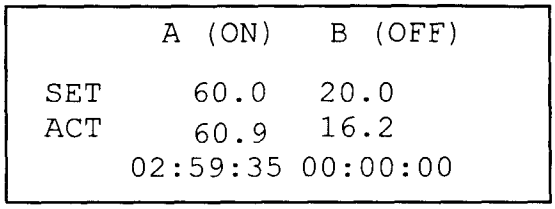

Figure7-5 Monitor Temperature Screen

The Monitor Temperature screen shows the temperature control status of each Reaction Vessel bank. Parameters displayed include the temperature at which the reactions are set, the actual temperature of the reaction, and whether the heaters are on or off. Table 7-5 outlines the function of the Controller keypad buttons while at this screen.

Pressing this button...	Results in...
MODE	Other Functions screen appearing
FORWARD	N/A
BACK	Set Temperature screen appearing
PARAMETER (+)	Set Temperature screen appearing
PARAMETER (–)	N/A
START/STOP	Start/Stop Heaters screen appearing
AGITATOR ON	Start/stop agitation

Table 7-5 • Monitor Temperature Control Button Functions

Other Functions Screen

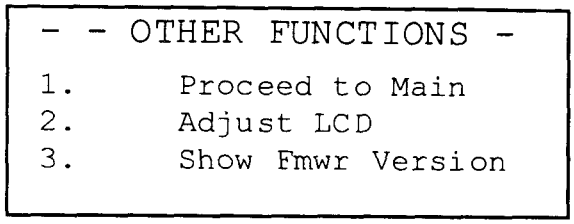

Figure7-6 Other Functions Screen

The Other Functions screen is used to select from a list of functions not available on the main screens. Five "other functions" are available and are described below. Only three of the five functions can be seen on the screen at one time. The screen scrolls by pressing the Forward button once the bottom of the current screen is reached. Table 7-6 outlines the function of the Controller keypad buttons while at this screen.

The five options areas are as follows.

- Proceed to Main: Returns to the first screen of the main screen loop, Agitation Control.
- Adjust LCD: Adjusts the screen contrast
- Show Fmwr (firmware) Version
- Perform Self Test
- Restore Defaults

Pressing this button...	Results in...
MODE	The screen choice (1-5) indicated by the cursor will be engaged.
FORWARD/BACK	Moving the cursor up or down to select one of the five screen options.
PARAMETER	Moving the cursor up or down to select one of the five screen options.
START/STOP	Start/Stop Heaters screen appears
AGITATOR ON	Start/stop agitation

Table 7-6 Other Functions Screen Control Button Functions

Contrast Control Screen

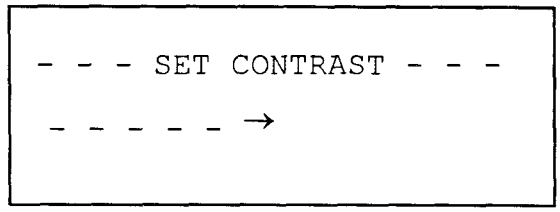

Figure7-7 Set Contrast Screen

The contrast of the display screen is adjusted through the Contrast Control Screen. Table 7-7 outlines the function of the Controller keypad buttons while at this screen.

Pressing this button...	Results in...
MODE	Returning to the Other Functions Screen
FORWARD/BACK	Increasing or decreasing the display screen contrast
PARAMETER	Increasing or decreasing the display screen contrast
START/STOP	Start/Stop Heaters screen appears
AGITATOR ON	Start/stop agitation

Table 7-7 Set Contrast Control Button Functions

Self Test Screen

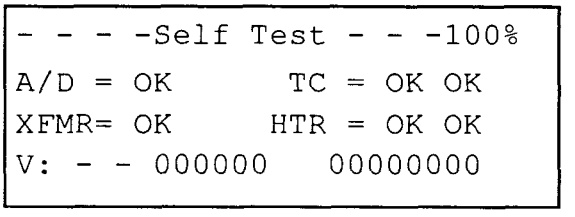

Figure7-8 Self Test Screen

The Self Test Screen appears when the Mode button is pressed after selecting option 4 (Perform Self Test) on the Other Functions Screen. This initiates a self test.

The self test procedure is normally executed in the factory to verify the basic hardware functions of the unit. The following results are displayed:

1. Success or failure of the A/D;
2. Success or failure of the two thermocouples, A and B;
3. Success or failure of the transformer sensor;
4. Success or failure of the two heaters, A and B; and
5. Status of the 16 valves.

While the self test is in progress, a % indicator at the top of the screen goes from 0 to 100 % to show the progress of the test. When the test is complete, the Self Test screen remains displayed until the Mode button is pressed.

Results are displayed as follows:

For the A/D, thermocouple, and transformer tests, either "OK", "ERR", or "??" is displayed. "??" means that a test was not performed because a prerequisite test failed. For example, if the A/D fails, then the thermocouples, transformer, and heaters will show "??".

The two heater tests also show "OK", "ERR", or "??" when the tests are complete. While the tests are in progress, however, temperature is displayed for each heater. Valve status is shown by two 8-character strings, which should be "– – OOOOOO OOOOOOOO" if all is well. Each character represents one valve. "–" means that the valve functions properly. "O" means the valve is open. "S" means there is a short in the valve.

In the current Quest 205, only two of the 16 valves are actually used,s which is why the self test normally shows two "–" characters, followed by "O's."

Table 7-8 outlines the function of the Controller keypad buttons while at this screen.

Pressing this button...	Results in...
MODE	Return to the Other Functions Screen.
FORWARD/BACK	N/A
PARAMETER	N/A
START/STOP	Start/Stop Heaters screen appears
AGITATOR ON	Start/stop agitation

Table 7-8 Self Test Screen Button Functions

Restore Defaults Screen

This screen appears momentarily after the MODE button is pressed, when option 5 (Restore Defaults) is selected on the Other Functions Screen.

Selecting this screen causes all user parameter settings (such as the agitation frequency parameters, LCD display contrast, etc.) to be reset to their factory preset default values. User settings are stored in a battery-backed-up memory, so that if the instrument is turned off, the user settings remain intact.

The Restore Defaults function need only be used on occasions when it is helpful to reset all the parameters to a standard state (such as when the unit is being delivered from one site to another).

Start/Stop Heaters Screen

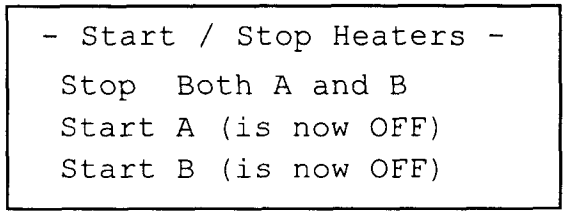

Figure7-9 Start/Stop Heaters Screen

The Start/Stop Heaters screen starts or stops the heaters. Pressing the START/STOP button while in a screen other than the Set Temperature screen brings up the Start/Stop Heaters screen.

Use the Forward and Back buttons to select one of the three options. After selecting an option, press the Mode button to activate the option. Table 7-9 outlines the function of the Controller keypad buttons while at this screen.

Pressing this button...	Results in...
MODE	Returning to previous screen
FORWARD/BACK	Selecting one of the three lines of the Start/Stop Heaters screen
PARAMETER	Selecting one of the three lines of the Start/Stop Heaters screen
START/STOP	Starting or stopping the heaters on Side A and/or B as specified by the option chosen with either the Forward/Back or Parameter buttons
AGITATOR ON	Start/stops agitation

Table 7-9 START/STOP Control Button Functions

8 Reactor Unit Plumbing Schematic

9 Accessories

This section provides desciptions and usage instructions for many of the accessories available for the Quest 205.

Quest 205 Magnet Stirrer (P/N 900200)

Description: The magnet stirrers are used in RV for both solution phase and solid-phase applications. The Teflon magnet stirrers consist of Teflon spikes that increase the mixing efficiency of resins.

Instruction: Drop a cleaned magnet into each new Reaction Vessel. Ensure that the magnets are placed into the RVs with the round indentation in the up position.

Quest 205 Magnet Extraction Bar (P/N 102288)

Description: The magnet extraction bar is used to remove the Teflon magnet stirrers from the RVs.

Instruction: To remove the Teflon magnet stirrers from an RV, place the magnet extraction bar next to the Reaction Vessels and slowly pull the magnet to the top of the RV.

Quest 205 Flask Rack (P/N 900199)

Description: The Quest 205 Flask Rack is used to support up to five 200-300 round bottom and pear-shaped flask.

Instruction: Place the up to five 200-300 mL round bottom and/or pear-shaped flasks into the flask rack and secure it into place. Remove the waste tank from the Quest 205 Reactor Unit and lower the waste tray to the lowest setting. Place the two front legs of the flask rack into the holes on the waste tray.

Quest 205 Restrictor Tubing (P/N 900201) and Insertion Tool (P/N 900202)

Description: The Quest 205 Restrictor tubing is used to restrict the solvent flow into each Reaction Vessel position. The Quest 205 Restrictor Insertion Tool is used to install new restrictor tubing into the upper manifold if the restrictors are blocked or damaged.

Instruction: Before installing the restrictor tubing, clean the upper manifold using the procedure described in the Quest 205 User Manual. Remove the blocked or damaged restrictor tubing with a needle nose plier. Once the restrictor is removed, check the inside of restrictor port for particulate. Rinse the port with some acetone and air dry. Once cleaned, place a new restrictor tubing into the top of the restrictor insertion tool. Use the tool to apply even pressure to the restrictor port to secure the new restrictor.

Quest 205 Weighing Funnel (P/N 900196)

Description: The Quest 205 Weighing Funnel is specifically designed for weighing out large amounts of solid or resin reagents and directly applying it to the Quest 205 Reaction Vessels. The Quest 205 Weighing Funnel can accommodate a maximum of 13-14 g of solid or resin reagents.

Instruction: Place and tare the Quest 205 Weighing Funnel onto a balance pan. Slowly add the appropriate amount of solid or resin reagents to the Weighing Funnel. Transfer the Weighing Funnel from the balance to the Quest 205 Reactor Unit. Unscrew the luer plug adapter and place the stout end of the weighing funnel into the luer port. Rest the weighing funnel on the upper manifold and rinse the weighing funnel with the appropriate solvent or use a thin spatula to guide the solid or resin reagents into the Reaction Vessel. If necessary, gently tap the funnel to dislodge the solid or resin reagents from the weighing funnel.

Quest 205 Addition Funnel (P/N 900197)

Description: The Quest 205 Addition Funnel is specifically designed for adding large amounts of liquid reagents or solvents directly to the Quest 205 Reaction Vessel. The flattened corner of the funnel allows for quick access to the upper manifold.

Instruction: Unscrew the luer plug adapter from the upper manifold of the Quest 205 reactor unit. Place the addition funnel into the luer port and slowly add the liquid reagent or solvent to the Reaction Vessel. After adding in the liquid reagent or solvent, replace the luer plug adapter to the upper manifold.

Quest 205 RV Tapered Caps (P/N 900203)

Description: The Quest 205 RV tapered caps allows the user to cap off the bottom of the Reaction Vessels post synthesis to provide increased support. Applications include lyophilization of resins and/or storage of the resins in a dessicator.

Instruction: After removing a used Reaction Vessel from the Quest 205, snuggly fit the Quest 205 RV tapered caps to the bottom of the Reaction Vessel.

Quest 205 RV Rack (P/N 900204)

Description: The Quest 205 RV rack can accommodate up to twelve 100 mL Reaction Vessels.

Instruction: Place the 100 mL Reaction Vessels into the Quest 205 RV rack.

Quest 205 Hex Ball Driver 3/32" Tool (P/N 900205)

Description: The Quest 205 Hex Ball Driver 3/32" Tool is used to stop the solvent flow to each Reaction Vessel.

Instruction: To restrict solvent flow to a Reaction Vessel, remove the cabled hinged pin from the side of the upper manifold without the supply tubing and rotate out the upper manifold. Lock the upper manifold by fully extending the manifold and tilt the upper manifold to the 1o'clock position by raising it slightly. This will allow the upper manifold not to swing out while adjusting the blanking screws. Use the Quest 205 Hex Ball Driver 3/32" Tool to tighten down the 3/32" hex screws on the back of the upper manifold. Repeat this process for each Reaction Vessel in which the user wants to restrict solvent flow.

Quest 205 Hex Ball Driver 7/64" Tool (P/N 900206)

Description: The Quest 205 Hex Ball Driver 7/64" Tool is used to adjust the agitation stops and clamps on the reactor unit.

Instructions: (Agitation Stops) Adjust the agitation bars by inserting the hex ball driver 7/64" tool and turn counterclockwise to loosen and clockwise to tighten the hex screws.

Instructions: (Clamps) Adjust the clamps by inserting the hex ball driver 7/64" tool and turn counterclockwise to loosen and clockwise to tighten the hex screws for both the upper and lower clamps.

Quest 205 Bubbler Accessory (P/N 900125)

Description: The Bubbler allows the user to visualize the gas flow rate on the Quest 205. The rate of bubble formation is the Bubbler will be directly related to the gas flow through the Reaction Vessels.

Instructions: Through the glass side arm, fill the Bubbler with enough oil to cover the end of the glass tube that runs down its center. Slide the large knurled fitting and ferrule over one end of the 1/8" "Teflon line supplied with the Bubbler. Insert the tubing and ferrule into the glass arm coming out of the top of the Bubbler and screw the fitting in. Fasten the Bubbler to the hood with the glass side arm facing towards the back of the hood. Slide a 1/8" Peek fitting and Tefzel ferrule onto the free end of the Teflon tubing. Screw this end into the UTILITY 1 port on the top of the Quest 205 Reactor Unit. To monitor the inert gas delivery, turn the Quest Control Valves to "UTILITY 1" an "METERED GAS". The inert gas flow rate can be adjusted by turning the Metered Gas Needle Valve clockwise to increase or counterclockwise to decrease the flow rate.

Quest 205 Transfer Cannula (P/N 900207)

Description: The Quest 205 Transfer Cannula is used to allow bank to bank transfer of reaction mixtures.

Instruction: Open the Upper Manifold Membrane by toggling it to the OPEN position. Attach the female luer adapter onto the lower male luer fitting on Bank A. Remove the Luer Plugs on Bank B and replace it with the appropriate Septum Luer Plugs (i.e. RV 1 to RV10, RV2 to RV 9, etc.). On Bank B, turn the Quest Control Valves to "CLOSED" and "VENT". On Bank A, rotate the Quest Control Valves to "CLOSED" and "METERED GAS". Adjust the metered gas flow rate by adjusting the Metering Gas Valve Needle. Individually drain each RV by opening the drain lever on Bank A. Leave all the drain levers on Bank B closed. Close the drain lever once the transfer of liquid is complete. Rotate the Quest Control Valves to "CLOSED" and "CLOSED".

Quest 205 Multi-Flask Adapter Kit (P/N 900209)

Description: The Quest 205 Multi-Flask Adapter Kit includes five multi-flask adapters, 1 ½" 18 G blunts tip needle, and polypropylene valves. The Multi-Flask Adapter can accommodate standard joint glassware sizes. The application of the Multi-Flask Adapters include product collection via collection Cannula and off-line SPE cartridge purification.

Instruction: (Product collection via collection Cannula) Securely position the multi-flask adapters onto the flasks. Place the exit tubing of the collection cannula into top of the multi-flask adapter.

Instruction: (Off-line SPE cartridge purification) Securely position the multi-flask adapters onto the flasks. Place the exit tubing of the collection cannula into top of the multi-flask adapter. Securely fit the 1 ½" blunt tip needle through the top of each multi-flask adapter. Then securely place the polypropylene valve onto the female luer fitting of the needle. Rotate the polypropylene valve to the opened or closed position.

Quest 205 SPE Cartridge Adapter Kit (P/N 900210)

Description: The SPE Cartridge Adapter Kit includes five SPE cartridge adapters and is used for off-line SPE cartridge purification of products. This adapter will accommodate 25, 60 and 75 mL SPE cartridges.

Instruction: Prepare and pack the SPE cartridges with the appropriate media. Attach the female luer adapter of the collection cannula to the lower luer male fitting. Place the exit tubing of the collection cannula into the SPE cartridge adapter. Snuggly fit the SPE cartridge adapter onto the top of the SPE cartridge. Then secure the cartridge onto the multi-flask adapter kit and flask.

Quest 205 Septum Luer Plugs (P/N 900145)

Description: Septum luer plugs allow quick and efficient delivery of reagents while maintaining a closed reaction environment. They are used in place of the standard luer plugs on the Quest Synthesizers. Using a syringe and needle, air and moisture-sensitive reagents can be added directly to the Reaction Vessels through the septum.

Instructions: Before installing the septum luer plugs, clean the upper manifold luer ports using the procedure described in the Quest 205 User Manual. Install the Septum Luer Plugs firmly into the upper manifold luer ports. To deliver reagents under inert conditions, turn the Quest Control Valves to "UTILITY 1" and "METERED GAS". Adjust the inert gas flow by adjusting the Metered Gas Needle Valve clockwise to increase the flow and counterclockwise to decrease the flow. To add reagent to the Reaction Vessel, use a syringe with a minimum needle length of 1 ½". Insert the needle through the septum of the septum luer plug and turn the Quest Control Valves to the "CLOSED" and "CLOSED" position. To ensure that the septum luer plugs maintain an inert environment, the septum and cap will require replacement as needed.

Replacement Parts:

- Cap with Septum (100/pkg) P/N 900148
- Septum (100/pkg) P/N 900149

10 User Tutorial

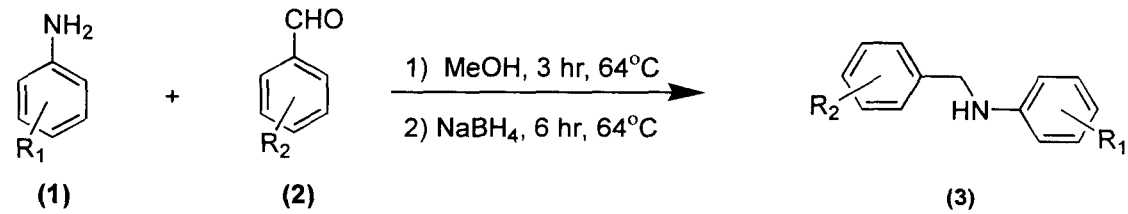

Figure 1-Solution Phase Reductive Amination to form the Corresponding Secondary Amines

Overview

The objective of the Quest 205 Organic Synthesizer Tutorial is to introduce new users to the instrument by performing a parallel solution phase reaction, work-up, and purification. The synthesis is a solution phase reductive amination to form the corresponding secondary amine. The reaction scheme for this synthesis is shown in **Figure 1**. Reagents required for the synthesis and purification are outlined in **Table 1**.

The tutorial is divided into the following sections, (A) Instrument and Solution Preparation, (B) Reductive Amination, (C) Product Work-Up and Collection, (D) Cleaning and Maintenance, and (E) Product Analysis. This experiment is performed on a single bank of five 100 mL Reaction Vessels (RVs) on the Quest 205 Organic Synthesizer. The RVs should be installed after the instrument is thoroughly cleaned (see section A). After the RVs are rinsed with MeOH, add the R_1-aniline (0.5 M in MeOH) and R_2-aldehyde (0.5 M in MeOH) solutions into the corresponding RVs and mix for three hours at 64°C under refluxing conditions. Cool the reaction mixture to room temperature and add the reducing agent, 0.5 M $NaBH_4$/EtOH, to each RV in two 6 mL portions over a thirty minute period. Once gas evolution ceases, reflux the reaction for six hours at 64°C.

The reaction mixtures are worked up with diH_2O and CH_2Cl_2. The organic layer can be dried and purified in parallel on-line by using the Quest Bank to Bank Transfer Cannula. The organic layer is drained via the Transfer Cannula to the top of the opposing RV filled with 12 g of neutral aluminum oxide and 7 g of $MgSO_4$. After ten minutes, drain the organic layer directly in a 250 mL round bottom flask.

$MgSO_4$. After ten minutes, drain the organic layer directly in a 250 mL round bottom flask.

An alternative purification technique allows the user to drain the organic layer into a SPE cartridge (either 60 mL or 75 mL) filled with 12 g of neutral aluminum oxide (activated) and 7 g of $MgSO_4$, and capped with a polypropylene stopcock (see figure). After ten minutes, gravity drain the organic layer into a 250 mL round bottom flask.

Concentrate the products using a rotary evaporator or concentration unit and calculate the product mass yields. Reconstitute the products in 6 mL of CH_2Cl_2, and analyze for product purity by HPLC and NMR analysis. NOTE: The results reported in **Table 3** (Page 10) are representative and may vary based on the purity of the actual reagents used for this synthesis.

Instrument and Solution Preparation

i. R_1-substituted aniline solutions in MeOH (0.5 M)

Prepare stock solutions as described in Table 1.

ii. R_2-substituted benzaldehyde solutions in MeOH (0.5 M)

Prepare stock solutions as described in Table 1.

iii. $NaBH_4$ solution in EtOH (0.5 M)

Prepare two 31 mL stock solutions, each five minutes before addition to the RVs. It is critical to add freshly prepared $NaBH_4$ solution to each RV.

iv. Installation of Bubbler Accessory (P/N 900125)

The Bubbler allows the user to visualize the gas flow rate on the Quest. Please follow the proper installation procedures outlined in the Quest 205 User Manual.

Material	Source	Part #	Comment	Total amount used
100 ml Reaction Vessels	Argonaut	900191	P/N 900087	**5 or 10***
Aniline	Aldrich	24,228-4	FW=93.13 d=1.022	2.8249 mL (in 62 mL MeOH)
Benzaldehyde	Aldrich	41,809-9	FW=106.12 d=1.044	660.7 µL (in 13 mL MeOH)
p-Anisaldehyde	Aldrich	A8,810-7	FW=136.15 d=1.119	790.9 µL (in 13 mL MeOH)
p-Tolualdehyde	Aldrich	T3,560-2	FW=120.15 d=1.019	766.4 µL (in 13 mL MeOH)
Salicylaldehyde	Aldrich	S35,6	FW=122.12 d=1.146	692.7 µL (in 13 mL MeOH)
m-Tolualdehyde	Aldrich	T3,550-5	FW=120.15 d=1.019	766.4 µL (in 13 mL MeOH)
Sodium Borohydride	Aldrich	21,346-2	FW=37.83	586.4 mg (2x 31 mL EtOH)
Methanol	Aldrich	27,047-4	FW=32.04	130 mL
Ethanol	Aldrich	27,074-1	FW=46.07	65 mL
diH_2O			FW=20.03	90 mL
Dichloromethane	Aldrich	27,056-3	FW=84.93	360 mL
Aluminum oxide, activated, neutral	Aldrich	19,997-4		12 g/cartridge
Magnesium Sulfate	Aldrich	24,697-2	FW=120.37	7 g/cartridge
Round Bottom Flask			250 mL	5
60 mL cartridge 20 micron PE frit**	Applied Separations	2446		5
OR				
75 mL extract clean cartridge (no frit)**	Alltech	210575		5
75 mL frit for extract clean cartridges**	Alltech	211775		5

Table 1. Materials and Reagents Required for the Quest 205 Solution Phase Tutorial

***NOTE: Ten Reaction Vessels will be needed if the Bank to Bank Transfer Cannula is used to purify the products on-line. If the cartridge method is to be used, only five Reaction Vessels are required.**

**** These items are optional for purification. These items are not needed if on-line purification is to be performed.**

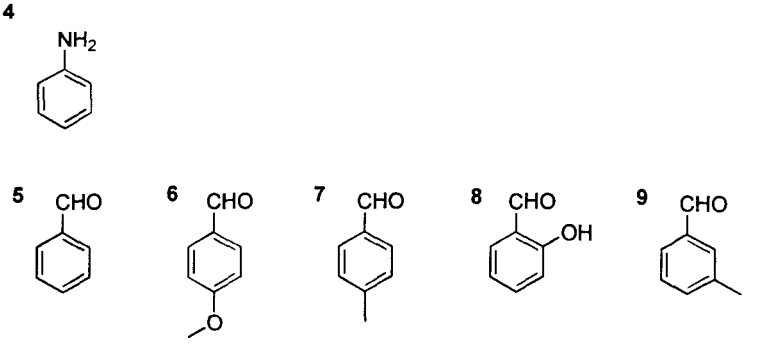

Figure 2-Stuctures of Anilines and Benzaldehydes Reagents

CAUTION: Always wear gloves, eye protection, and proper clothing when working with the Quest 205.

Prior to Starting the Synthesis:

- Read the Quest 205 User Manual.
- Verify that the Quest was installed according to the Quest Installation Procedure in the Quest 205 User Manual.
- For systems with a single inert gas supply, verify that the Quest Controller Unit input pressure is between 30-40 psi. For systems using both compressed and inert gas, verify that Controller Units agitation gas input pressure is 55-60 psi compressed gas supply and inert gas input pressure is 30-40 psi.
- Familiarize yourself with the nomenclature and various components of the Quest Reactor Unit.

RV Removal, Instrument Cleaning, and RV Installation

Use the following procedure to install and remove Reaction Vessels from the Quest 205 Organic Synthesizer

1. Loosen the upper clamp screws by using the hex ball driver 7/64" tool. Raise the upper manifold by rotating the two levers on either side of the Quest and hooking them into the slots of the upper manifold handles. Push in the two silver buttons on the upper manifold handles and slide the upper manifold up using the two levers. Once the seal between the upper manifold and RVs is broken, unhook the levers from the slots in the upper manifold handles and raise the upper manifold by hand until it is locked at its highest position.

2. Loosen the lower clamp screws by using the hex ball driver 7/64" tool. Remove the cabled hinged pin from the side of the upper manifold without the supply tubing and rotate out the upper manifold. Lock the upper manifold by fully extending the manifold and tilt the upper manifold to the 1o'clock position by raising it slightly. This will allow the upper manifold not to swing out while installing and removing the RVs.

3. Loosen the RVs from the lower clamp by twisting the RVs upwards. Once the RVs are free from the lower clamp, remove the RVs from the Quest. Remove the magnets by either turning the RVs upside down or by using the magnet removal tool. Rinse each magnet with acetone.

4. Before installing new RVs, remove each luer plug and luer plug adapter from the upper manifold and clean each one with acetone to remove any particulate. Rinse the luer ports with acetone to remove any residue remaining from the reaction. Gently clean the luer ports with a cotton swab wetted with acetone and replace the luer plugs and luer plug adapters. Also, clean the upper manifold male fittings with acetone to remove any particulate that may interfere with sealing.

5. Using a cotton swab with acetone, clean the male Teflon RV fittings of the lower manifold. Clean the RV clamps and remove any particulate around the lower manifold area with acetone.

6. To install new RVs, place new 100 ml RVs into the cleaned reaction bank. Apply even pressure onto each RV until the bottom of the frit seats against the male Teflon RV fitting of the lower manifold. Once installed, the tops of the RVs should be uniform in height. Tighten the lower manifold clamps using the hex ball driver 7/64" tool.

7. Drop a cleaned magnet into each RV. Ensure that the magnets are placed into the RVs with the round indentation in the up position.

8. Unhinge the upper manifold from the one o'clock position and swing out the upper manifold. Insert the upper manifold into position and replace the cabled hinge pin.

9. Push in the silver buttons on both upper manifold handles and slowly lower the upper manifold onto the top of the RVs. Check that the RVs are properly aligned with the upper clamps. Insert the two levers on both sides of the Quest into the slots in the upper manifold handles and apply gentle pressure to lower the upper manifold until the silver buttons snap out. This indicates the upper manifold is locked into place. Tighten the upper manifold clamps using the hex ball driver 7/64" tool.

Reductive Amination

Filling the Dead Volume Between the RV frit and the Lower Manifold Drain Valve

This procedure provides instructions on filling the dead volume between the bottom of the Reaction Vessel frit and the lower manifold drain valve with solvent. This ensures that any air that can affect the synthesis is eliminated from the system.

1. Open the Upper Manifold Membrane Switch by toggling the switch to the "OPEN" position.

2. Deliver MeOH in parallel to each RV by rotating the Quest Control Valves to "SOLVENT" and "VENT". When the solvent has reached the appropriate level (approximately 10 mL) stop the solvent flow by turning the left Control Valve from "SOLVENT" to "DRAIN GAS". The "DRAIN GAS" purges the residual solvent in the delivery pathway into the Reaction Vessels. After a few seconds rotate both Quest Control Valves to the "CLOSED" positions.

3. Rotate the Control Valves to "CLOSED" and "VENT". Turn the Metered Gas Needle valve completely clockwise to close it. Rotate the Control Valves to "CLOSED" and "METERED GAS" to supply a steady stream of inert gas to the RVs.

4. To fill the dead volume between the RV frit and lower manifold drain valve, open each drain valve and increase the inert gas flow to the RV by slowly turning the Metered Gas Needle Valve counterclockwise. Close the drain valve once the solvent has reached the top of the RV frit. Repeat this procedure for each RV. Between drainings, turn the Metered Gas Needle Valve completely clockwise to close valve and rotate the right control valve to "VENT" followed by "METERED GAS".

Addition of Reagents of RVs

1. To the corresponding RVs, add 12 mL of 0.5 M aniline/MeOH to the RVs via syringe. Next, add 12 ml of the appropriate 0.5 M R2-substituted benzaldehydes/MeOH to the RVs in the same manner. Table 2 illustrates the RV reagent scheme. After reagent addition, snugly screw in the luer plugs for each RV to ensure a tight seal.

RV	R^1-C_6H_4-NH_2 (1)	R^2-C_6H_4-CHO (2)
1	Aniline (4)	Benzaldehyde (5)
2	Aniline (4)	p-Anisaldehyde (6)
3	Aniline (4)	p-Tolualdehyde (7)
4	Aniline (4)	Salicyaldehyde (8)
5	Aniline (4)	m-Tolualdehyde (9)

Table 2- RV Reagent Scheme

2. Close the Upper Manifold Membrane Switch and rotate the Quest Control Valves to the "CLOSED" and "CLOSED" positions. **It is vital to close off the system while refluxing or solvent loss will occur.**

3. Using the hex ball driver 7/64 tool, lower or raise the agitation stops so that the magnets in the RVs are approximately 1 cm below the solvent level in the RVs.

4. Program the agitation parameters by pressing the mode key on the front panel of the Controller Unit until the LCD displays the AGITATION menu. The agitation parameters used are:

- MixEvery: 2.0 sec
- UpStroke: 1.4 sec
- % Upwards: 70%

MIXEVERY and % UPWARDS parameters are adjusted by moving the cursor using the right or left keys below the LCD screen to the desired position. The parameter settings are changed using the PARAMETER SETTING up and down keys to the left of the LCD screen.

5. Start the agitation by pressing the agitation "ON" button on the Controller Unit.

6. Program the heater parameters by pressing the mode key until the LCD displays the SET TEMPERATURE menu. Enter the following parameters for Bank A:

- A: 64 C 3:00 OFF
- B: 100 C 0:00 OFF
- RVs A: 20 mL B: 20 mL

7. The heating duration and temperature can be adjusted by moving the cursor using the right or left keys below the LCD screen to the desired position. The heating parameters can be change by using the PARAMETER SETTING up and down keys to the left of the LCD screen.

***NOTE: For accurate measurement of the RV temperature, enter the volume of solvent that is in the RVs. The firmware accepts volume settings from 10 to 80 mL in 10 mL increments.**

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8. Turn on the heater for bank A by moving the cursor to the line for Bank A and pressing the Start/Stop key on the Controller Unit. This will only turn on the heater for Bank A.

9. The reaction temperature can be monitored by pressing the mode key until the TEMPERATURE MONITOR display screen is shown. This screen displays the set and actual temperature of each Reaction Vessel bank, heater status, and remaining time in the heater program. With the current settings, the display should show the following:

• A: (ON)	B: (OFF)
• Set 64 C	100 C
• Act45 C	33 C
• 3:00:00	0:00:00

The timer for the heater will not start until the Reaction Vessel temperature reaches the set temperature.

10. Once the actual temperature is achieved and the timer is counting down, the temperature can be adjusted by going back to the set temperature display using the mode key and adjusting the temperature and time parameters.

11. Reflux the reaction for three hours at 64 °C. The heater will turn off after the when the heater program is complete. Allow the reaction bank to cool to room temperature (approximately 30 minutes).

Addition of $NaBH_4$ Solution to each RV

1. Open the Upper Manifold Membrane Switch by toggling the switch to the "OPEN" position.

2. To each RV, remove the upper manifold luer plug and slowly add 6 mL of freshly prepared 0.5 M sodium borohydride/EtOH solution. Snugly screw in the luer plugs to ensure a good seal. Rotate the Quest Control Valves to "UTILITY 1" and "CLOSED" to vent the gas evolved during the $NaBH_4$ addition.

3. Adjust the agitation stops so that the magnets in the RVs are approximately 1 cm below the solvent level in the RVs. Agitate for 30 minutes at room temperature.

4. After 30 minutes, stop the agitation and add the second addition (6 mL) of 0.5 M sodium borohydride/EtOH to the RVs in the same manner as the first. Snugly screw in the luer plugs to ensure a proper seal. Adjust the Quest Control Valves to "UTILITY 1" and "CLOSED" to vent the gas evolved during this addition. Once the gas evolution ceases, toggle the Upper Manifold Membrane Switch to "CLOSED" and rotate the Quest Control Valves to the "CLOSED" and "CLOSED". **It is vital to close off the system while refluxing or solvent loss will occur.**

5. Adjust the agitation stops so that the magnets in the RVs are approximately 1 cm below the solvent level in the RVs and turn the agitation on.

6. Program the heater parameters by pressing the Controller Unit mode key until the LCD displays the SET TEMPERATURE menu. Enter the following parameters for Bank A:

- A: 64 C 6:00 OFF
- B: 100 C 0:00 OFF
- RVs A: 40 mL B: 40 mL

7. Turn on the heater for bank A after the gas evolution has stopped.

8. Reflux the reaction for six hours at 64 °C using the closed system described above. The heater will turn off after temperature program is complete. Allow the RVs to cool to room temperature (approximately 30 minutes).

Product Work Up and Collection

In-Line Purification: Bank to Bank Transfer Cannulation (optional)

1. Install five new 100 mL Reaction Vessels onto Bank B. Follow the procedures described for RV installation. Open the Upper Manifold Membrane Switch by toggling it to the "OPEN" position. Attach the female luer adapter onto the lower male luer fitting on Bank A for RVs 1-5. Remove the Luer Plugs on Bank B and replace it with the appropriate Septum Luer Plugs (i.e. RV 1 to RV10, RV 2 to RV 9, etc.). On Bank B, turn the Quest Control Valves to "CLOSED" and "VENT". On Bank A, rotate the Quest Control Valves to "CLOSED" and "METERED GAS". Adjust the metered gas flow rate by adjusting the Metered Gas Needle Valve.

2. To each RV on Bank B, add 12 g of neutral aluminum oxide using the Quest 205 Weighing Funnel (P/N 900196). Weigh the neutral aluminum oxide directly into the Quest 205 Weighing Funnel, unscrew the luer plug adapter, and directly add it through the spout of the Weighing Funnel. Add a top layer of 7 g of $MgSO_4$ in the same manner.

3. Drain the organic layer into tared 250 mL round bottom flasks using the collection cannulas. Attach the female luer adapter onto the lower luer male fitting on Bank B. Place five tared 250 mL round bottom flasks into the flask rack and secure it into place. Remove the waste tank and lower the waste tray to the lowest setting. On Bank B, place the two legs of the flask rack into the holes on the waste tray. Raise the waste tray to the next setting to secure the rack into place. Once in position, snugly fit the multi-flask adapters onto the 250 mL round bottom flasks. Attach the exit tubing directly into the multi-flask adapter.

4. The products are worked up with diH_2O and extracted with CH_2Cl_2 three times. Add 18 ml of diH_2O and 18 mL of CH_2Cl_2 to each RV on Bank A. Agitate the RVs for three cycles and stop in the Agitation Down position. Once the layers have separated, drain the bottom organic layer using the Bank to Bank Transfer Cannulas. Individually drain each RV by opening the drain lever on Bank A. Leave all the drain levers on Bank B closed. The bottom organic layer should transfer over into the corresponding RV containing the neutral aluminum oxide and $MgSO_4$. Visually determine the end of the phase separation and close the drain lever once the organic layer is separated and cannulated over. Rotate the Quest Control Valves to "CLOSED" and "CLOSED". Repeat this process for each RV on Bank A.

5. Add 18 mL of CH_2Cl_2 to each RV on Bank A. Agitate the RVs for three cycles and stop it in the Agitation Down position. Once the layers have separated, drain the bottom organic layer using the Bank to Bank Transfer Cannulas. Use the process described above and repeat for each sample. Repeat this process two more times with CH_2Cl_2 only. If the RV volume is at its maximum, let the organic layer sit for ten minutes. Gravity drain the product by opening the drain levers and rotate the Quest Control Valves to "CLOSED" and "VENT".

6. Let the reaction mixture sit in the RVs of Bank B for ten minutes and drain into the 250 mL round bottom flask using the collection cannulas. Drain each RV by rotating the Quest Control Valves to the "CLOSED" and "METERED GAS" position. Drain each RV into the 250 mL round bottom flasks by opening the drain levers. After draining, rotate the Quest Control Valves to the "CLOSED" and "CLOSED" position after draining and close the drain levers.

7. Concentrate the products using a rotary evaporator or concentrator unit until dryness. Weigh the round bottom flasks and calculate the product mass yields. Reconstitute the samples in 6 mL of CH_2Cl_2, and analyze each sample by HPLC and NMR analysis for product purity.

Off-Line Purification: 60 mL or 75 mL SPE cartridge (optional)

1. Prepare five 60 mL or 75 ml SPE cartridges with frits with 12 g of neutral aluminum oxide (bottom layer) and 7 g of $MgSO_4$ (top layer). Place a small amount of glass wool on top of the packed cartridges to secure the matrix. Attach the female luer adapter of the collection cannula to the lower luer male fitting on Bank B. Place the exit tubing of the collection cannula into the SPE cartridge adapter (P/N 900210). Snugly fit the SPE cartridge adapter onto the top of the SPE cartridge.

2. Place five tared 250 mL round bottom flasks into the flask rack and secure it into place. Remove the waste tank and lower the waste tray to the lowest setting. On Bank B, place the two legs of the flask rack onto the holes on the waste tray. Raise the waste tray to the next setting to secure the rack into place. Once in position, snugly fit the multi-flask adapters onto the 250 mL round bottom flasks. Securely fit the 1 ½" blunt tip needle through the top of each multi-flask adapter. Then securely place the polypropylene stopcock valve onto the female luer fitting of the needle. Rotate the polypropylene valve to the closed position.

3. Place the SPE cartridge assembly including the collection cannula on to the female luer fitting of the polypropylene valve of the multi-flask adapter. Repeat this process for each tared 250 mL round bottom flask.

4. The products are worked up with diH_2O and extracted with CH_2Cl_2 three times. Add 18 ml of diH_2O and 18 mL of CH_2Cl_2 to each RV on Bank A. Agitate the RVs for three cycles and stop in the Agitation Down position. Once the layers have separated, drain the bottom organic layer directly into the SPE cartridges. Open the drain lever and rotate the Quest Control Valves to "CLOSED" and "METERED GAS". Adjust the Metered Gas Needle Valve to allow the sample to drain at moderate rate. Visually determine the end of the phase separation and close the drain lever once the organic layer is fully drained. Rotate the Quest Control Valves to "CLOSED" and "CLOSED". Repeat this process for each RV.

5. Add 18 mL of CH_2Cl_2 to each RV on Bank A. Agitate the RVs for three cycles and stop in the Agitation Down position. Once the layers have separated, drain the bottom organic layer into the SPE cartridge. Use the process described above and repeat for each sample. Repeat this process two more times with CH_2Cl_2 only. If the cartridge volume is at its maximum, let the organic layer sit for ten minutes and open up the polypropylene valves to gravity drain the product.

6. Let the organic layer sit for ten minutes and drain it directly into the 250 mL round bottom flasks by opening the polypropylene valves. Rotate the Quest Control Valves to the "CLOSED" and "VENT" positions. Rotate the Quest Control Valves to the "CLOSED" ad "CLOSED" position after draining.

7. Concentrate the products using a rotary evaporator or concentrator unit until dryness. Weigh the round bottom flasks and calculate the product mass yields. Reconstitute the samples in 6 mL of CH_2Cl_2, and analyze each sample by HPLC and NMR analysis for product purity.

Cleaning and Maintenance

After each synthesis the Quest should be thoroughly cleaned. This procedure flushes the Quest liquid delivery system and cleans the upper manifold, luers plugs, and luer ports to remove residual solvent or reagent from the system. This prevents contaminating the next reaction with solvents or reagents from the previous synthesis. **Routine cleaning the Quest after each synthesis will help ensure that the system is fully functional prior to each synthesis.**

Systems without the Automated Solvent Wash Option

1. After completing the synthesis, rinse the reaction bank(s) by delivering the last solvent used for the reaction (fill RV's approximately 30% full), agitate for approximately 5 minutes and then drain the RV's into the waste tank. Repeat this rinse three times.

2. After the last drain, leave the lower manifold drain valves open and rotate the Quest Control Valves to "DRAIN GAS" and "CLOSED" for 10 minutes to allow the RVs to drain thoroughly and to remove any residual solvent. Close the lower manifold valves and rotate the Quest Control Valves to the "CLOSED" and "CLOSED" positions.

3. Remove the luer plugs and luer plug adapters and clean them with acetone to remove any particulate. Rinse the luer ports with acetone and then gently wipe them clean with a cotton swab wetted with acetone to remove residue from the reaction.

4. Replace the luer plugs and luer plug adapters. Dry the RVs by rotating the Quest Control Valves to "DRAIN GAS" and "CLOSED" with the lower manifold drain levers opened. This allows the RVs to dry thoroughly to remove any residual solvent.

5. Return the Quest Control Valves to the "CLOSED" and "CLOSED" positions. Flush the upper manifold by turning the Quest Control Valves to "CLOSED" and "METERED GAS". After 10 minutes turn the Quest Control Valves to "CLOSED" and "CLOSED".

6. If the Quest unit is not going to be used immediately, leave the used RVs in the reactor unit. If the Quest unit is going to be used immediately, continue with the RV removal and installation procedures.

Systems with Automated Solvent Wash

1. After completing the synthesis, program the Automated Solvent Wash (ASW) unit to rinse the reaction bank(s) by delivering the last solvent used for the reaction (fill RV's approximately 30% full), agitate for approximately 5 minutes and then drain the RV's. Repeat this rinse three times. Leave the lower manifold drain levers opened for all RV positions.

2. Use the following program scheme:

• R S	ADD	MIX	PUL	
• 3xD	78	5:00	20	(D=dichloromethane)

3. After the last drain, leave the lower manifold drain valves open and rotate the Quest Control Valves to "DRAIN GAS" and "CLOSED" for 10 minutes to allow the RVs to drain thoroughly and to remove any residual solvent. Close the lower manifold valves and rotate the Quest Control Valves to the "CLOSED" and "CLOSED" positions.

4. Remove the luer plugs and luer plug adapters and clean them with acetone to remove any particulate. Rinse the luer ports with acetone and then gently wipe them clean with a cotton swab wetted with acetone to remove residue from the reaction.

5. Replace the luer plugs and luer plug adapters. Dry the RVs by rotating the Quest Control Valves to "DRAIN GAS" and "CLOSED" with the lower manifold drain levers opened. This allows the RVs to dry thoroughly to remove any residual solvent.

6. Return the Quest Control Valves to the "CLOSED" and "CLOSED" positions. Flush the upper manifold by turning the Quest Control Valves to "CLOSED" and "METERED GAS". After 10 minutes turn the Quest Control Valves to "CLOSED" and "CLOSED".

7. If the Quest unit is not going to be used immediately, leave the used RVs in the reactor unit. If the Quest unit is going to be used immediately, continue with the RV removal and installation procedures.

Product Analysis

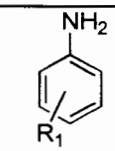
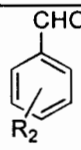
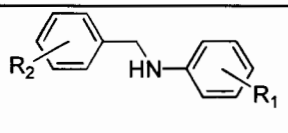
RV	 (1)	 (2)	 (3)	Yield (%)	HPLC Purity (%)
1	4	5	11	93.4	96%
2	4	6	12	96.9	74%
3	4	7	13	95.7	94%
4	4	8	14	98.9	92%
5	4	9	15	>99	90%

Table 3-Results of Solution Phase Reductive Amination

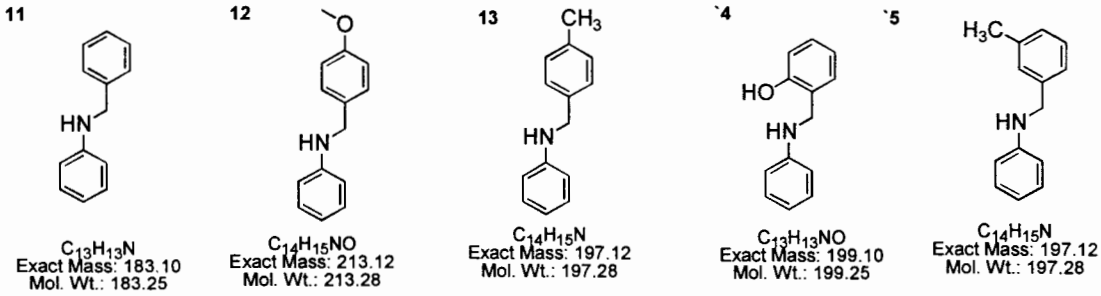


Figure 3- Structures of amine products

Spectroscopic Data

Table 3 illustrates the percent yield and HPLC purities for each amine product. Purities were determined by high-pressure liquid chromatography (area %) using a 3 μm C18 column (Microsorb-MV, 100 Å). The HPLC method used was a 2-90% ACN/H_20 with 0.1% TFA run over 9 minutes for quantitative analysis of reaction products, UV detection at 223 nm. HPLC retention time and ^{1}H NMR of representative compounds are provided below:

Compound **11**: HPLC retention time: 4.48 min. ^{1}H NMR ($CDCl_3$, 300 MHz):δ 7.40-7.16, 6.75-6.63 (m, 10 H, Ar-H), 4.34 (s, 2 H, CH_2), 4.03 (br s, 1 H, NH) ppm.

Compound **12**: HPLC retention time: 4.47 min. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.38-7.14, 6.88-6.86, 6.74-6.63 (m, 9 H, Ar-H), 4.25 (s, 2 H, CH_2), 3.79 (s, 3 H, CH_3), 3.32 (s, 1 H, NH) ppm.

Compound **13**: HPLC retention time: 4.74 min. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.29-7.11, 6.75-6.63 (m, 9 H, Ar-H), 4.29 (s, 2 H, CH_2), 3.98 (br s, 1 H, NH), 2.36 (s, 3 H, CH_3) ppm.

Compound **14**: HPLC retention time: 4.12 min. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.26-7.15, 6.92-6.84 (m, 9 H, Ar-H), 4.42 (s, 2 H, CH_2), 3.96 (br s, 1H, NH), 1.55-1.54 (s, 1 H, OH) ppm.

Compound **15**: HPLC retention time: 4.81 min. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.27-7.09, 6.75-6.64 (m, 9 H, Ar-H), 4.29 (s, 2 H, CH_2), 4.00 (br s, 1 H, NH), 2.37-2.36 (s, 3 H, CH_3) ppm.