Supporting information

Rapid Chemical Reaction Workup Based on Rigid Solvent Extraction

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1. General

^{1}H and ^{13}C NMR spectra were recorded at 500 MHz and 126 MHz (or 400 MHz and 101 MHz) respectively, using $CDCl_3$ as a solvent. The chemical shifts were reported in δ (ppm) values (^{1}H and ^{13}C NMR relative to $CHCl_3$, δ 7.26 ppm for ^{1}H NMR and δ 77.0 ppm for ^{13}C NMR and $CFCl_3$ (δ 0 ppm for ^{19}F NMR), multiplicities were indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and br (broad). Coupling constants (*J*), were reported in Hertz (Hz). All reagents and solvents were employed without further purification. TLC was developed on silica gel 60 F254 aluminum sheets. A CombiFlash Rf 200 (Teledyne Isco) was used for chromatographic separation. All chemicals were purchased from Aldrich, Alfa Aesar or Acros.

2. Preparation of porous polymer support (Porelite®)

Organic phase: A solution of divinylbenzene (DVB) (160 mL) and Span 80 (8 mL).

Aqueous phase: A solution of water (1600 mL), calcium chloride dehydrate (20 g) and potassium persulfate (4 g).

Under mechanic stirring (D-shaped PTFE paddle, 300-350 r.p.m), the aqueous phase was slowly added to the organic phase (c.a. 30 min) at room temperature. After addition, the emulsion was further stirred for 15 min. The resultant emulsion, having a consistency similar to that of mayonnaise, was transferred to a 2000 mL polyethylene bottle that was heated at 60°C for 48 hours. After this, the block polymer was removed from its container and extracted in a Soxhlet for 24 hours with 80% ethanol. The block polymer was dried in air and was crushed to powder form (35-120 mesh size) using commercial laboratory blender (from Waring®) and standard sieves.

3. General procedure for rigid solvent workup

Step 1. Reaction quenching. The reaction is conducted in the usual way and is quenched with a suitable aqueous solution (e.g. $NaHCO_3$ solution).

- If the reaction is conducted in a water immiscible solvent (e.g. toluene, DCM), in general no extra solvent is needed.
- If the solvent used in the reaction is water-miscible (eg., DMF, methanol, etc.), add a minimum amount (e.g. 3 mL solvent for every 1 g of product) of water immiscible solvent (e.g. ether).

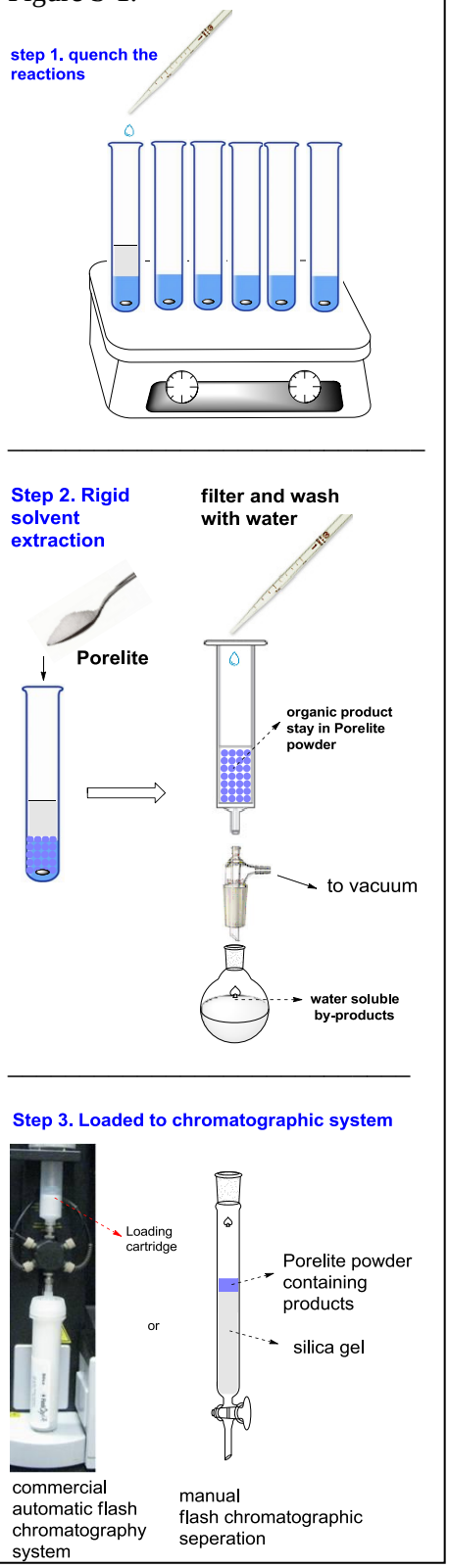
Step 2. Rigid solvent extraction. In this step, aqueous-soluble components (starting materials, by-products, etc.) are removed.

- Porelite® (typically 3 - 6 mL for every 1 gram of product) is added to reaction mixture under stirring, then excess amount of solvent is removed by vacuum (rotavapor) or nitrogen/air purging (no need to remove water in the mixture).
- The reaction mixture is filtered, washed with water (or HCl or Na_2CO_3 solution to remove basic or acidic byproducts). Allow the vacuum to dry the filter for 2 minutes to remove any remaining aqueous phase and volatile solvents. (*For automatic flash chromatographic separation, an empty loading cartridge can be used, which can be directly attached to the commercial system. For manual chromatographic separation, a regular Buchner filter can be used*).

Step 3. Loading to chromatographic system.

- Loading cartridge can be directly attached to the commercial flash chromatographic system (e.g., CombiFlash Rf series).
- For manual chromatographic separation, the polymer powder is loaded directly onto a manual flash silica gel column (dry loading).
- Because the polymer pad may contain air, it is recommended to start with least polar solvent (e.g. hexane) during chromatographic separation to remove the air.

Figure S-1.



Alternative method 1: If quenching of the reaction is not required, Porelite® can simply be added to reaction mixture, and, after vacuum drying, the polymer powder can be loaded directly into the flash column.

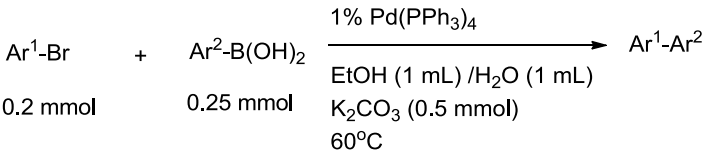
Alternative method 2: The addition of Porelite® (step 2) and the quenching of the reaction (step 1) may be conducted in a reversed order. Sometimes doing this gives more uniform mixing.

Alternative method 3:or parallel operations, a commercial filtration station can be used (Figure S-2).

Figure S-2. Use of commercial filtration station.

4. Typical examples of rigid solvent workup

4.1 Suzuki reaction (using manual flash chromatographic separation)



The Suzuki reaction was conducted according to the condition above.

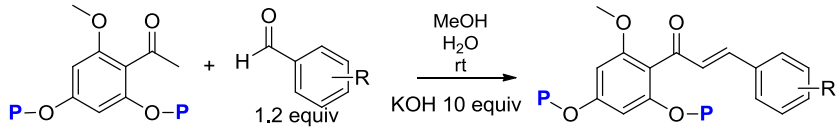
1. Water (2 mL) (*to quench the reaction and dissolve the inorganic salts*) and 1 mL ether (*because the solvent used in the reaction is water soluble; otherwise, no additional solvent is needed. Only minimum amount of ether is needed*) was added to the reaction mixture.

2. Porelite® (0.5 mL) was added to reaction mixture under stirring, the majority of organic solvents in the reaction was removed in vacuum (*using rotavapor, no need to remove aqueous phase*). The reaction mixture was filtered, a small amount of water (2 mL) can be used to help transfer the polymer powder to the filtration device. Then the polymer pad was washed with small amounts of water (3 mL). The filter was purged with air by using vacuum to remove residual aqueous phase and organic solvents for 2 min.

3. The polymer powder was transferred to the top of a flash column loaded with silica gel and the loaded polymer bed was covered with sea sand. It is then ready for flash chromatographic separation.

4.2. Chalcone library synthesis (using automatic flash chromatographic system)

Table S-1. Synthesis of chalcone library using traditional and new methods.



P	aldehyde (R)	yields % (traditional)	Yields % (new method)
Allyl	4-Methoxy	73	82
Allyl	2,4-Dimethoxy	90	92
Allyl	3,4,5-Trimethoxy	97	97
Allyl	4-Pyridinyl	55	65
Allyl	2-Pyridinyl	84	84
Allyl	2-Furanyl	87	87
MOM	4-Methoxy	91	92
MOM	3,4-Methylenedioxy	61	62
MOM	3,4,5-Trimethoxy	78	76

Traditional method (1.2-1.6 gram scale):

After completion of reaction, deionized water was added and the solution was extracted twice with EtOAc (2 x 40 mL), the combined organic layer was washed with water and then dried over $MgSO_4$ and then filtered. After evaporation, the crude extract was subjected to column chromatography.

Work-up time for each sample: around 0.5 h, parallel operation is difficult.

New method (1.2-1.6 gram scale):

After completion of the reactions, 6 mL EtOAc was added to each reactors (*amount of solvent depends on the solubility of product, in general using a minimum amount of solvent is preferred because most of this solvent will be removed later anyway*), and then 5 mL Porelite® was added under stirring. The majority of organic solvents in the reaction was removed in vacuum (*using rotavapor, no need to remove the aqueous phase*). The reaction mixture was filtered through an empty loading cartridge (Figure S-1), washed with water (10 mL). After quick vacuum drying, the cartridge was directly connected to a commercial flash chromatography system (CombiFlash Rf 200).

Work-up time for each sample: around 10 min. Parallel operation is easy (Figure S-2), which leads to greater time saving.