Electronic Supplementary Material (ESI) for Green Chemistry.

Supporting Information

Use of a switchable-hydrophilicity solvent as both a solvent and a catalyst in aldol condensation

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Table of Contents

Materials and methods

Materials and Characterization of Products

All reagents were purchased from either Fischer Scientific or Sigma-Aldrich and used without further purification unless noted. $CDCl_3$ was dried over 4 Å molecular sieves. Carbon dioxide gas, 4.8 supercritical fluid chromatography grade, was purchased from Praxair. Silica gel used for chromatographic separations was purchased from Sigma-Aldrich. Thin Layer Chromatography was performed using silica gel TLC plates. ^{1}H NMR spectra were recorded using a Bruker 400 MHz Spectrometer.

Methods

General Procedure Method for Aldol Condensation Method A.

A solution containing acetone (34.4 mmol, 2.0 ml) and 0.10 g of the corresponding aldehyde (0.66-0.94 mmol) from Table 1 method A, was added to a biphasic solution containing 2.0 ml water and 1.0 ml N,N-dimethylcyclohexylamine in a 25 ml round bottom flask at room temperature. The resulting mixture was then heated at reflux with a 18 cm condenser for 24 hr at 70 °C; after which the reaction mixture was cooled to room temperature. The reaction mixture was acidified using a 5 % aqueous HCl solution until the pH ≤ 3, and then extracted using ethyl acetate (3 x 1.0 ml). The ethyl acetate extracts were combined, dried over anhydrous sodium sulphate and filtered through a pipette containing a cotton plug. The volatiles were removed under vacuum. The resulting crude product mixture was purified by column chromatography using mixtures of hexane:ethyl acetate (9:1 for entry 1 and 3, and 1:1 for entry 2). Entries as indicated in Table 1. The product was analysed by ^{1}H NMR spectroscopy recording using a Bruker 400 MHz Spectrometer.

General Procedure Method for Aldol Condensation Method B

A solution containing acetone (34.4 mmol, 2.0 ml) and 0.10 g of the corresponding aldehyde (0.73-7.38 mmol) from Table 1 method B, was added to a biphasic solution containing 2.0 ml water and 1.0 ml N,N-dimethylcyclohexylamine in a 25 mL round bottom flask at room temperature. The resulting mixture was then heated at reflux with a 18 cm condenser for 24 hr at 70 °C; after which the reaction mixture was cooled to room temperature. The reaction mixture was transferred to a 23 ml scintillation vial (23X85 mm), then CO_2 was bubbled through the mixture with continuous stirring (approximately 30 min) until the solution appeared monophasic. The product was separated using vacuum filtration for a solid product or separatory funnel for a liquid product. The solid was dried under vacuum for an additional 10 min. The product was analysed by ^{1}H NMR spectroscopy recording using a Bruker 400 MHz Spectrometer.

General Procedure Method for Aldol Condensation Trial 1

A solution containing acetone (34.4 mmol, 2.0 ml) and 0.10 g of *p*-anisaldehyde (0.73 mmol), was added to a biphasic solution containing 2.0 ml water and 1.0 ml N,N-dimethylcyclohexylamine in a 25 ml round bottom flask at room temperature. The resulting mixture was then heated at reflux with a 18 cm condenser for 24 hr at 70 °C; after which the reaction mixture was cooled to room temperature. The reaction mixture was transferred to a 23 ml scintillation vial (23X85 mm), then CO_2 was bubbled through the mixture with continuous stirring (approximately 30 min) until the solution appeared monophasic and formed a pale yellow precipitate. The mixture was separated using vacuum filtration. The solid dried under vacuum for an additional 10 min. The solid product was analysed by ^{1}H NMR spectoscopy recording using a Bruker 400 MHz Spectrometer. The separated filtrate was further added to a round bottom flask and heated at reflux with a 18 cm condenser at 70 °C until the mixture contained two liquid phases (approximately 10 min). This resulting mixture was used in place of the biphasic mixture (2.0 ml water and 1.0 ml N,N-dimethylcyclohexylamine) in repeating the aldol condensation. The mixture was cooled to room temperature and acetone (34.4 mmol, 2.0 ml) and p-anisaldehyde (0.73 mmol) was added. The mixture was then heated at reflux with a 18 cm condenser for 24 hr at 70 °C for the next cycle.

General Procedure Method for Aldol Condensation Trial 2

A solution containing acetone (34.4 mmol, 2.0 ml) and 0.10 g of *p*-anisaldehyde (0.73 mmol), was added to a biphasic solution containing 2.0 ml water and 1.0 ml N,N-dimethylcyclohexylamine in a 25 ml round bottom flask at room temperature. The resulting mixture was then heated at reflux with a 18 cm condenser for 48 hr at 70 °C; after which the reaction mixture was cooled to room temperature. The reaction mixture was transferred to a 23 ml scintillation vial

(23X85 mm), then CO_2 was bubbled through the mixture with continuous stirring (approximately 30 min) until the solution appeared monophasic and formed a pale yellow precipitate. The mixture was separated using vacuum filtration. The solid dried under vacuum for an additional 10 min. The solid product was analysed by ^{1}H NMR spectroscopy recording using a Bruker 400 MHz Spectrometer. The separated filtrate was further added to a round bottom flask and heated at reflux at reflux with a 18 cm condenser at 70 °C until the mixture contained two liquid phases (approximately 10 min). This resulting mixture was used in place of the b-phasic mixture (2.0 ml water and 1.0 ml N,N-dimethylcyclohexylamine) in repeating the aldol condensation. The mixture was cooled to room temperature and acetone (34.4 mmol, 2.0 ml) and p-anisaldehyde (0.73 mmol) was added. The mixture was then heated at reflux with a 18 cm condenser for 48 hr at 70 °C for the next cycle.

General Procedure Method for Aldol Condensation Trial 3

A solution containing acetone (34.4 mmol, 2.0 ml) and 0.10 g of *p*-anisaldehyde (0.73 mmol), was added to a biphasic solution containing 2.0 ml water and 1.0 ml N,N-dimethylcyclohexylamine in a 25 ml round bottom flask at room temperature. The resulting mixture was then heated at reflux with a 18 cm condenser for 24 hr at 70 °C; after which the reaction mixture was cooled to room temperature. The reaction mixture was transferred to a 23 ml scintillation vial (23X85 mm), then CO_2 was bubbled through the mixture with continuous stirring (approximately 30 min) until the solution appeared monophasic and formed a pale yellow precipitate. The mixture was separated using vacuum filtration. The solid dried under vacuum for an additional 10 min. The solid product was analysed by ^{1}H NMR spectroscopy recording using a Bruker 400 MHz Spectrometer. The separated filtrate was further added to a round bottom flask and heated at reflux at reflux with a 18 cm condenser at 70 °C until the mixture contained two liquid phases (approximately 10 min). Addition water and N,N-dimethylcyclohexylamine were added to the mixture to maintain the 2.0 ml water and 1.0 ml N,N-dimethylcyclohexylamine that was in the original cycle in repeating the aldol condensation. The mixture was cooled to room temperature and acetone (34.4 mmol, 2.0 ml) and p-anisaldehyde (0.73 mmol) was added. The mixture was then heated at reflux with a 18 cm condenser for 24 hr at 70 °C for the next cycle.

General Procedure Method for Aldol Condensation Trial 4

A solution containing acetone (34.4 mmol, 2.0 ml) and p-anisaldehyde (0.73 mmol) was added to a biphasic solution containing 2.0 ml of water and 1.0 ml N,N-dimethylcyclohexylamine in a 23 ml scintillation vial (23X85 mm). The vial was put in a 70 °C water bath and heated for 24 hr; after which it was cooled to room temperature. CO_2 was bubbled through the mixture with continuous stirring (approximately 30 min) until the solution appeared as a single liquid with a yellow precipitate. The mixture was separated using cotton pipet filtration and both the precipitate and filtrate were collected. Product was collected from the cotton by passing acetone through the pipette. The volatiles were removed under vacuum. No further purification of the solid product was performed. The solid product was analysed by ^{1}H NMR spectroscopy recording using a Bruker 400 MHz Spectrometer. The filtrate was added to a round bottom flask and heated at reflux with a 18 cm condenser 70 °C until the mixture contained two liquid phases (approximately 10 min). The mixture was cooled to room temperature and acetone (34.4 mmol, 2.0 ml) and p-anisaldehyde (0.73 mmol) was added. The mixture was then placed again in a 70 °C water bath and heated for 24 hr for the next cycle.

Figures

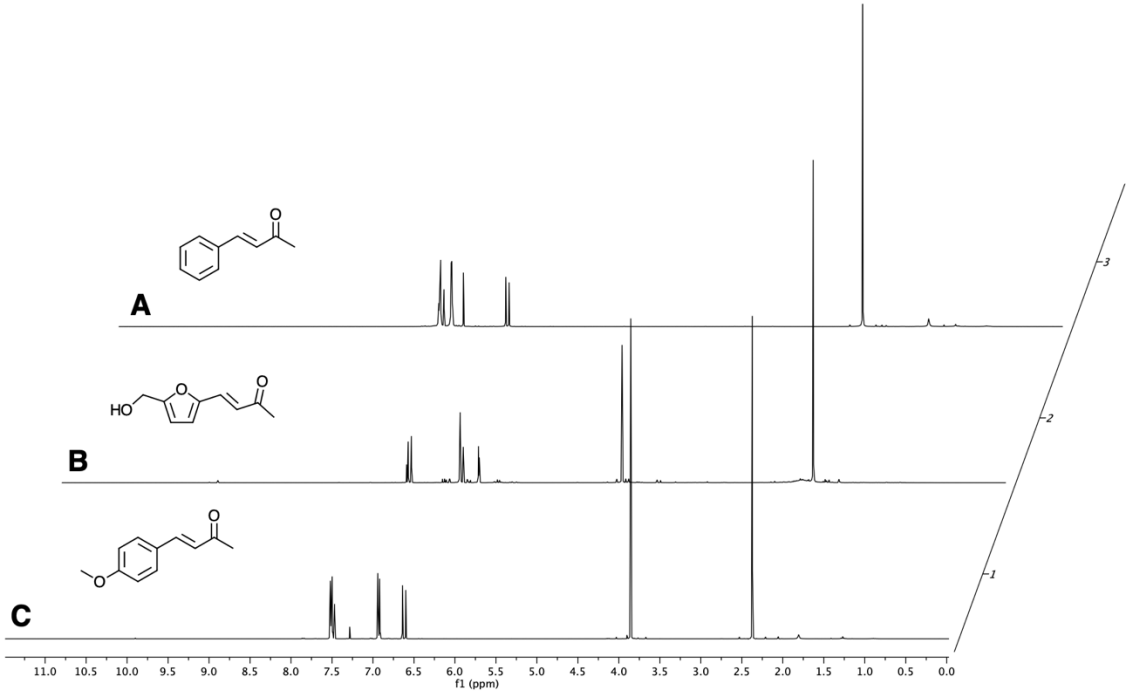


Figure S1.Table 1 method A: ^{1}H NMR spectra of the filtered product after DMCHA -promoted aldol condensation of A) benzaldehyde B) HMF C) p-anisaldehyde with acetone using hydrochloric acid workup and purification. Given that the starting materials and the products from the aldol condensation are well known, the peaks assigned to the aldol condensation products were comparable to literature data.[1,2] This indicates that selectivity to the mono-aldol product is high with no double addition products note.

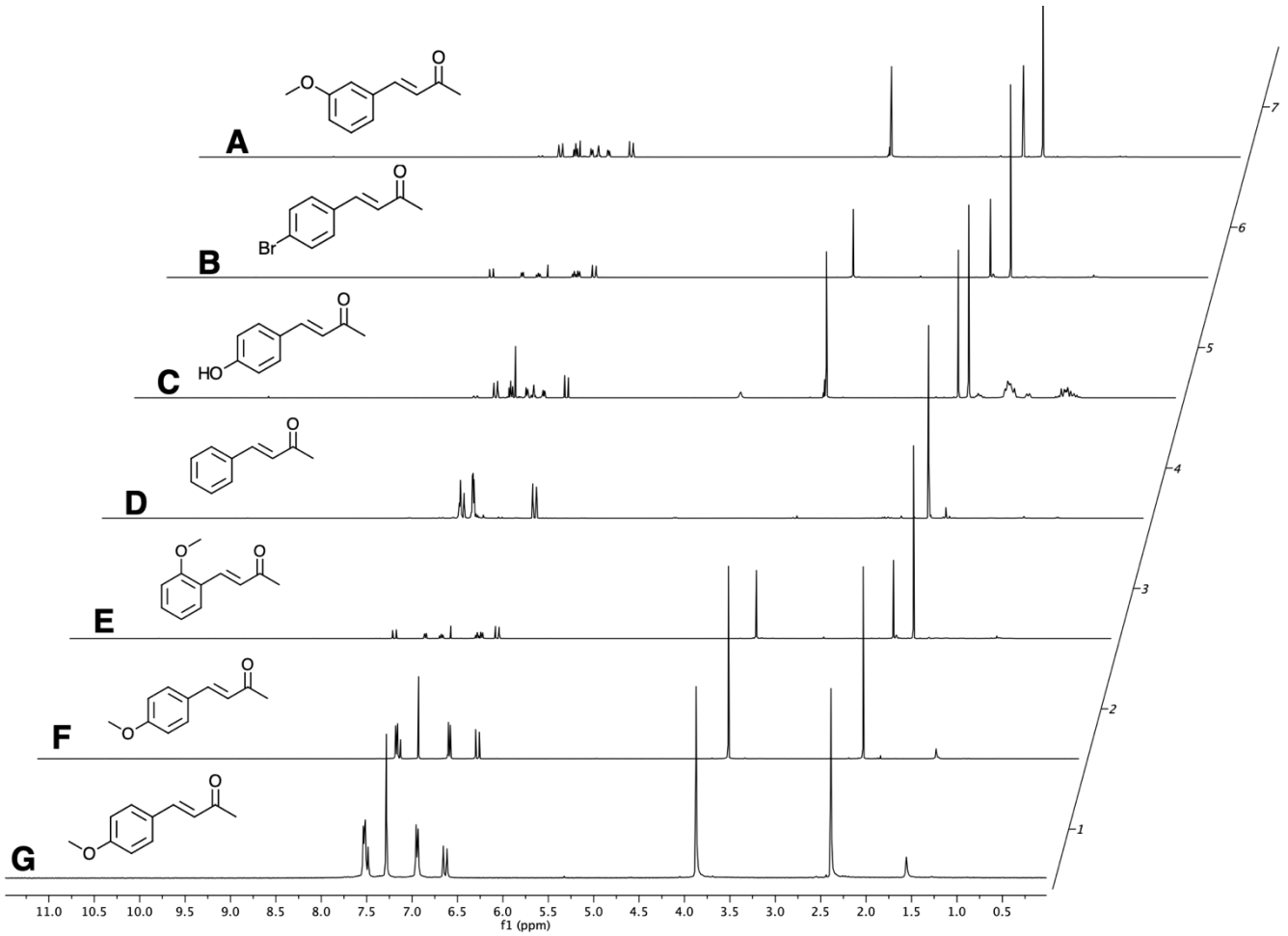
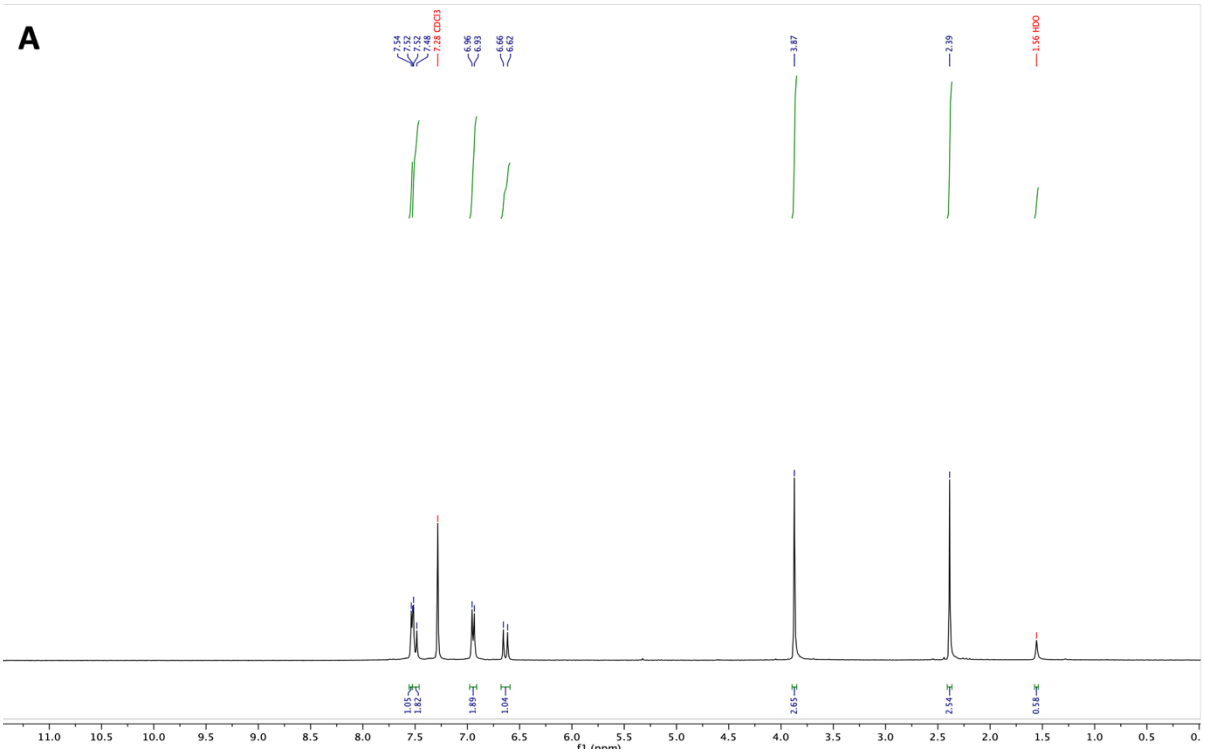


Figure S2. Table 1 method B: ^{1}H NMR spectra of the filtered product after DMCHA-promoted aldol condensation of A) 3-methoxybenzaldehyde B) 4-bromobenzaldehyde C) 4-hydroxybenzaldehyde D) benzaldehyde E) o-anisaldehyde F) p-anisaldehyde G) p-anisaldehyde (large scale) with acetone using CO_2 separation. Given that the starting materials and the products from the aldol condensation are well known, the peaks assigned to the aldol condensation products were comparable to literature data.[1,2,3,4] This indicates that selectivity to the mono-aldol product is high with no double addition products noted.

A



B

$$P[\%] = \frac{1.04\ (176.21)}{1.04(176.21)+(0.29)(18)}\ X\ 100$$

Figure S3. qHNMR *of the product mixture of DMCHA aldol condensation of p-anisaldehyde (large scale) with acetone using CO_2 separation. A) ^1H NMR spectra with incorporated peaks and integrals. B) calculation for % purity.*[5]

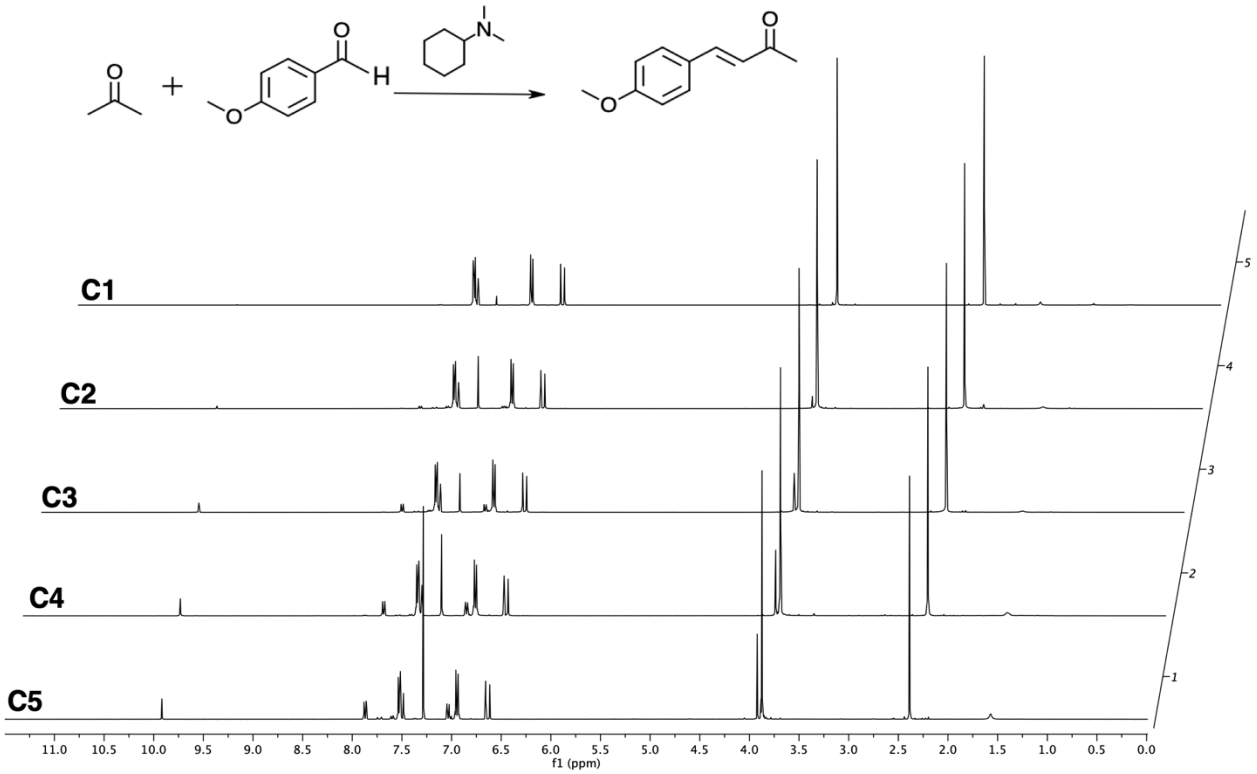


Figure S4: [1]H NMR spectra of the filtered product after DMCHA-promoted aldol condensation of p-anisaldehyde with acetone using repeatedly recycled DMCHA and the CO2-triggered separation protocol. Trial 1 cycle 1 (top) – cycle 5 (bottom). Given that the starting materials and the products from the aldol condensation are well known, the peaks assigned to the aldol condensation products were comparable to literature data.[1] This indicates that selectivity to the mono-aldol product is high with no double addition products noted.

Figure S5: [1]H NMR spectra of the filtered product after DMCHA-promoted aldol condensation of p-anisaldehyde with acetone using repeatedly recycled DMCHA and the CO2-triggered separation protocol. Trial 2 cycle 1 (top) – cycle 5 (bottom). Given that the starting materials and the products from the aldol condensation are well known, the peaks assigned to the aldol condensation products were comparable to literature data.[1] This indicates that selectivity to the mono-aldol product is high with no double addition products noted.

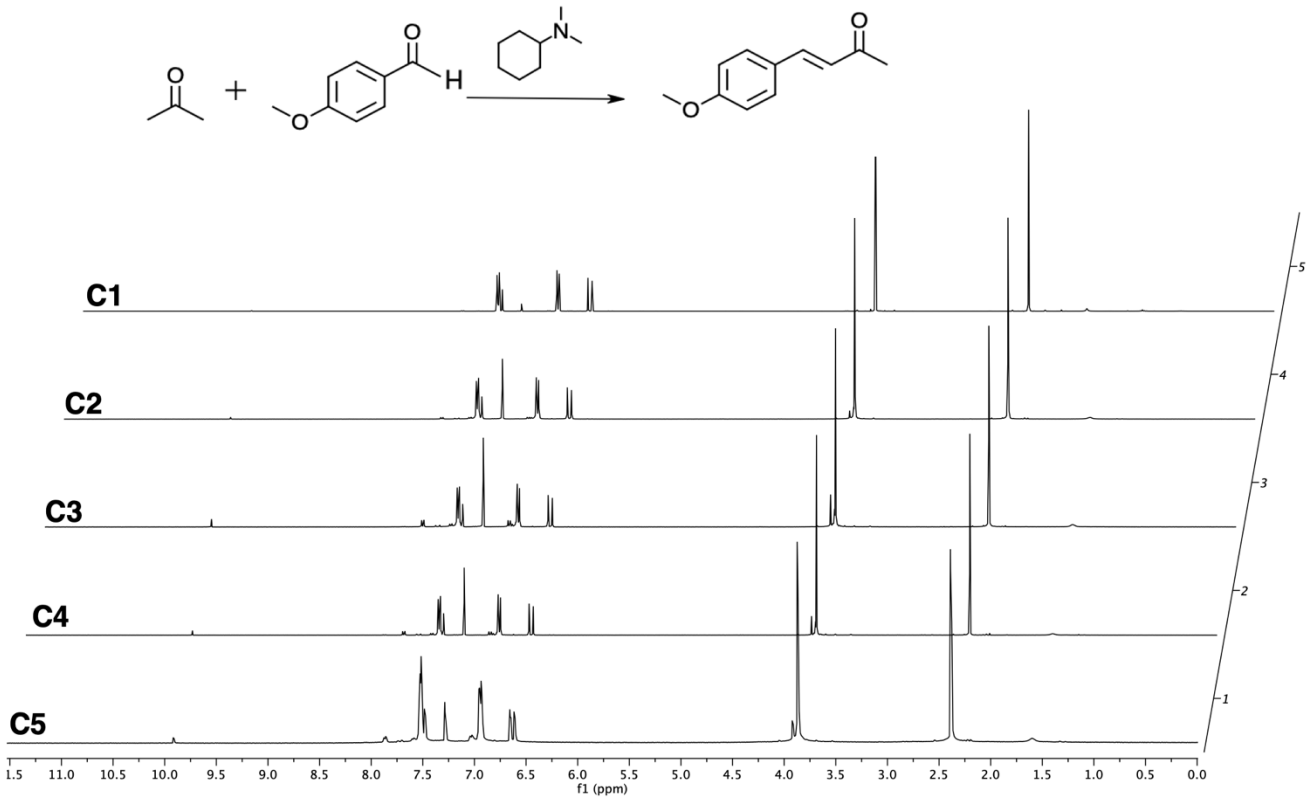


Figure S6: [1]H NMR spectra of the filtered product after DMCHA-promoted aldol condensation of p-anisaldehyde with acetone using repeatedly recycled DMCHA and the CO2-triggered separation protocol. Trial 3 cycle 1 (top) – cycle 5 (bottom). Given that the starting materials and the products from the aldol condensation are well known, the peaks assigned to the aldol condensation products were comparable to literature data.[1] This indicates that selectivity to the mono-aldol product is high with no double addition products noted.

References

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