Evaluation of Silica-H₂SO₄ as an Efficient Heterogeneous Catalyst for the Synthesis of Chalcones

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Abstract: We report an efficient silica-H₂SO₄ mediated synthesis of a variety of chalcones that afforded the targeted compounds in very good yield compared to base catalyzed solvent free conditions as well as acid or base catalyzed refluxing conditions.

Keywords: silica-H₂SO₄; solvent free conditions; chalcone; arylidene indanone; arylidene tetralone; Claisen-Schmidt condensation

1. Introduction

The generic term chalcones refer to compounds with a main 1,3-diphenylprop-2-enone core. Chemically chalcones are open chain flavonoids with two aromatic rings linked via a three carbon α,β-unsaturated enone system. These compounds are widely found in numerous species of plant, which are used as traditional folk medicines for treatment of a large number of diseases. Whether synthetic or
isolated from plants, chalcones have been found to be associated with diverse biological applications such as antiinflammatory [1], antipyretic, antimutagenic [2], antioxidant [3], cytotoxic, antitumor [4] and a large list yet to be mentioned.

Owing to their diverse biological activities, many synthetic strategies toward these compounds have been developed that involve Claisen-Schmidt condensations of substituted acetophenones with aldehydes. Different reagents employed for the chalcone synthesis include aq. alcoholic alkali [5], dry HCl [6], anhydrous AlCl₃ [7], POCl₃ [8], aqueous Na₂B₄O₇·10H₂O [9], HClO₄ [10], BF₃ [11], Mg(OtBu)₂ [12], graphite oxide [13,14] hydroxyapatite [15,16], phosphate derivatives [17], organo Cd compounds, SnCl₄ and the use of animal bone meal (ABM) as a heterogeneous catalyst [18]. In addition to these Gupta and Boss et al., in their separate studies synthesized chalcones under microwave irradiation in the presence of NaOH [19,20]. Seedhar et al., carried out chalcone synthesis in polyethylene glycol (PEG) as an environment friendly solvent [21]. Boukhvalov et al. carried out a computational investigation of the potential role of graphene oxide as a heterogenous catalyst [22].

With increasing concerns about environmental pollution, synthetic strategies are been developed that involve the use of less or no solvent. Similarly the heterogeneous catalysis is preferred over homogenous catalysis because of the work-up, economical and environmental advantages of the former. Silica-H₂SO₄ (SSA) is a versatile, selective and a powerful catalyst that has been explored for various organic transformations, such as the synthesis of heterocyclic compounds [23–27], cross-aldol condensations [28], Michael additions [29], protection [30,31], deprotection [32] and oxidation reactions [33]. The major advantages of SSA include: ease of preparation, ease of removal from reaction mixtures, comparatively mild conditions as compared to H₂SO₄ as well as NaOH. Since it requires no use of solvent, therefore it is economical as well as environmentally friendly and most important thing is that it can be recycled.

In this article, we wish to report an efficient and versatile procedure for the synthesis of chalcones in the presence of SSA and a comparison of the results of our synthesis to different methods in order to evaluate the effectiveness of the SSA-mediated synthesis of chalcones.

2. Results and Discussion

For the preparation of chalcones, four different reagents/reaction conditions were chosen: refluxing conditions using MeOH as a solvent in the presence of stoichiometric amount of H₂SO₄ or NaOH, grinding the reactants with NaOH pallets under neat conditions (SF) and by heating the reactants with SSA in the absence of any solvent.

The SSA was prepared by two different reported methods. One method involves the addition of H₂SO₄ to a suspension of silica gel in Et₂O, followed by the evaporation of the solvent under reduced pressure and heating the resulting silica gel at 120 °C for 3 h [34]. The other method involves the addition of silica gel to HSO₃Cl along with subsequent trapping of HCl produced during the reaction [35]. The SSA obtained by both methods was similar in form, i.e., a white solid, and showed similar results.

In order to determine the optimum amount of SSA required for a given transformation, the simplest chalcone 3a (obtained by condensing PhAc with PhCHO in the presence of varying amounts of SSA from 0.005 to 0.1 g) was synthesized (Scheme 1).
Scheme 1. SSA-assisted synthesis of chalcone 3a.

\[
\begin{align*}
\text{1a (1 eq)} & \quad \text{PhCHO} \\
\text{+} & \\
\Rightarrow & \\
\text{3a} & \quad \text{Ph}
\end{align*}
\]

It is observed that best results are obtained with 0.02 g of SSA. If less than 0.02 g of SSA was employed the yield of the product was low or the transformation was incomplete. An increase in amount of SSA resulted in a slight increase in yield, but decomposition of the product and difficult isolation of the product was observed upon increasing (≥0.05 g) the amount of SSA (Table 1).

Table 1. Determination of optimum amount of SSA for the preparation of chalcone 3a.

| Entry | SSA (g) | Solvent | Time (Temperature, °C) | %Yield |
|-------|--------|---------|------------------------|--------|
| 1     | 0.005  | MeOH    | 4 h (reflux)           | *      |
| 2     | 0.01   | CH₂Cl₂  | 6 h (reflux)           | *      |
| 3     | 0.01   | -       | 2 h (65)               | 28     |
| 4     | 0.02   | -       | 8 h (rt)               | -      |
| 5     | 0.02   | -       | 1 h (65)               | 91     |
| 6     | 0.02   | -       | 0.5 h (100)            | #      |
| 7     | 0.05   | -       | 0.5 h (65)             | 94     |
| 8     | 0.1    | -       | 0.5 h (65)             | ^      |

* A number of spots were observed on TLC along with reactants; # the SSA became a black powder and reaction workup afforded a number of spots on TLC; * no product could be isolated and TLC of the reaction mixture indicated the formation of a number of compounds; ^ All yields reported above are isolated yields.

In order to confirm the effectiveness of SSA three control experiments were performed, which include heating reactants with silica gel under solvent free conditions, using H₂SO₄ (without silica gel) in MeOH (at 65 °C) and by heating the aldehyde and ketone in the presence of silica gel and H₂SO₄ at 65 °C both in the presence and absence of methanol (used as a solvent). No product formation was observed when only silica gel was used. When the reactants were heated together with silica and H₂SO₄ in the absence of solvent, blackening of the contents of reaction flask was observed with no transformation occurred, even after 4 h. Heating the reactants with silica and H₂SO₄ in MeOH yielded 1,3-diphenylprop-2-enone (3a) in less than 10% yield after 5 h. Heating the reactants in H₂SO₄ using MeOH at 65 °C afforded the chalcone 3a in 28% yield after 4 h; however, refluxing the methanolic solution of reactants with H₂SO₄ afforded chalcone 3a in 38% after 4 h.

The catalyst is not only removed easily, but can be recycled. The catalyst was recovered by simple filtration after the addition of CH₂Cl₂ followed by partitioning between H₂O and the organic layer. The residual catalyst was washed with acetone in order to extract any remaining product adsorbed on the catalyst surface, and it was then reactivated by placing in an oven for 30 min at 100 °C. The recovered catalyst was used three times for the synthesis of 1,3-diphenylprop-2-enone and almost the same yield was obtained as observed in the first run.
2.1. Synthesis of Open Chain Chalcones 3a–o

When substituted PhAc 1 and ArCHO 2 were condensed in the presence of different reagents, the capricious yield of the products 3 depends upon the nature of reagent used. In general, the base-catalyzed reaction under refluxing conditions gave the lowest yields in almost all cases. The effect was more pronounced when either substrate (i.e., 1 or 2) contains –I and +R groups (such as OH, NMe₂) or –I and –R groups (such as NO₂). The acid catalyzed reaction also suffered the problem of low yields. The low yield with base-catalyzed refluxing conditions was attributed to the oxidation of aldehydes to their corresponding carboxylic acids via the Cannizarro reaction, which results in an overall decrease in the active concentration of aldehyde 2. The oxidation of aldehydes to carboxylic acids was much pronounced with para-substituted 2. The solvent free (SF) conditions led to quite a high yield of the product; however, the yields were quite low when either or both of the reactants contains –I and +R–R groups. The yields of such substrates under SSA conditions are quite higher (Scheme 2, Table 2). The formation of the chalcones 3a–o was confirmed by ¹H-NMR that indicated the presence of $J_{trans}$ (14.9–17.4 Hz). The mass spectra were also in agreement with the formation of the targeted chalcones.

**Scheme 2.** Synthesis of chalcones 3 under different reaction conditions.

**Table 2.** Comparison of yield using different reagents and $\delta$ of olefinic protons in 3a–o.

| Entry | R  | Ar     | 3     | % Yield | ¹H-δ § ($J$ ¹) |
|-------|----|--------|-------|---------|----------------|
|       |    |        |       | $\text{H}_2\text{SO}_4^*$ | $\text{NaOH}$ § | SF § | SSA § | $\text{H}^2$ | $\text{H}^3$ |
| a     | H  | Ph     | 3a    | 54      | 45             | 77  | 91  | 7.60 (16.4) | 8.12 (16.4) |
| b     | 3'OH | Ph | 3b    | 25      | 51             | 82  | 95  | 7.58 (15.9) | 7.98 (15.9) |
| c     | 3'-OH | 2-furyl | 3e    | 38      | 43             | 71  | 83  | 7.35 (16.8) | 7.59 (16.8) |
| d     | 4'-OH | Ph | 3d    | 48      | 24             | 73  | 88  | 7.43 (15.6) | 7.81 (15.6) |
| e     | 4'-OH | 2-furyl | 3e    | 45      | 41             | 85  | 88  | 7.54 (17.1) | 7.83 (17.4) |
| f     | 4'-OH | 4-MeOPh | 3f    | 58      | 32             | 89  | 92  | 7.43 (15.4) | 7.79 (15.4) |
| g     | 4'-Me | Ph | 3g    | 62      | 73             | 92  | 89  | 7.56 (17.4) | 7.88 (17.4) |
| h     | 4'-Me | 2-furyl | 3h    | 54      | 79             | 86  | 94  | 7.55 (15.6) | 7.88 (15.6) |
| i     | 4'-Me | 4-Me₂NPh | 3i    | <10     | 13             | 29  | 80  | 6.86 (14.9) | 7.58 (14.9) |
| j     | 3'-NO₂ | Ph | 3j    | <10     | -              | 35  | 83  | 7.62 (16.0) | 8.02 (16.0) |
| k     | 3'-NO₂ | 2-furyl | 3k    | 15      | -              | 40  | 87  | 7.50 (16.8) | 7.77 (16.8) |
| l     | 3'-NO₂ | 4-Me₂NPh | 3l    | 23      | -              | 25  | 76  | 7.54 (15.8) | 7.83 (15.8) |
| m     | 3'-NO₂ | 4-MeOPh | 3m    | 19      | -              | 33  | 74  | 7.38 (16.0) | 7.79 (16.0) |
| n     | 4'-Cl | Ph | 3n    | 78      | 68             | 83  | 96  | 7.61 (16.6) | 8.18 (16.5) |
| o     | 4'-Cl | 2-MeOPh | 3o    | 75      | 64             | 76  | 92  | 7.63 (16.1) | 8.03 (16.1) |

* 1.5 equivalent to 1, 5 h reflux in MeOH; § 1.15 equivalents to 1, 3 h reflux; ‡ SF (NaOH mediated solvent free) 3 equivalents of NaOH to 1, grinding in neat conditions; † SSA heating at 65 °C for 1.5 h under neat conditions; ‡ chemical shifts are reported in ppm; § coupling constants are reported in Hz (both protons showed doublets in all cases).
2.2. Synthesis of Tetralone- and Indanone-Based Chalcones 5a–m

After the successful synthesis of various substituted chalcones 3a–o, the effect of reagent on the yield of tetralone- and indanone-based chalcones was studied. For this purpose the tetralone and/or indanone was allowed to condense with various aldehydes in the presence of acid, base, solvent free conditions and SSA. The trends were almost similar as observed in case of 3a–o. In most cases a molecular ion 6a or 6b was observed as a stable radical cation (Scheme 3, Table 3).

Scheme 3. Synthesis of arylidene tetralone and arylidene indanones 5 under different conditions.

Table 3. Comparison of yield using different reagents, δ of H′ and m/z of [M]+ in 5a–m.

| Entry | n | Ar       | 5   | %Yield | δ (H′) | [6a]+ or [6b]+ (m/z) |
|-------|---|----------|-----|--------|--------|----------------------|
| a     | 0 | Ph       | 5a  | 35     | 41     | 83 87 7.93 220 (64)  |
| b     | 0 | 4-furyl  | 5b  | 48     | 52     | 78 91 7.44 210 (100) |
| c     | 0 | 4-Me2NPh| 5c  | 12     |        | 85 82 6.97 263 (100) |
| d     | 0 | 4-MeOPh | 5d  | 73     | 35     | 82 97 8.13 250 (76)  |
| e     | 0 | 3-MeOPh | 5e  | 75     | 56     | 79 90 7.64 250 (100) |
| f     | 0 | 3-NO2Ph | 5f  | 13     |        | <10 53 72 8.53 265 (42) |
| g     | 0 | 3,4-((OMe)2)Ph | 5g | 75     | 63     | 80 86 7.18 280 (100) |
| h     | 1 | Ph       | 5h  | 66     | 54     | 76 80 6.98 234 (56)  |
| i     | 1 | 2-furyl  | 5i  | 72     | 68     | 85 87 7.56 224 (100) |
| j     | 1 | 4-Me2NPh| 5j  | 21     | 17     | 62 94 7.82 277 (52)  |
| k     | 1 | 4-MeOPh | 5k  | 76     | 71     | 85 89 6.69 264 (100) |
| l     | 1 | 3-NO2Ph | 5l  | 20     | 19     | 71 85 8.27 279 (29)  |
| m     | 1 | 3-ClPh  | 5m  | 78     | 42     | 79 87 6.81 268, 270 (38, 12) |

* 1.5 equivalent to 1, 5 h reflux in MeOH; ^ 1.01 equivalents to 1, 3 h reflux; SF (NaOH mediated solvent free) 3 equivalents of NaOH to 1, grinding under neat conditions; SSA (0.02 g), heating at 65 °C for 1.5 h under neat condition; chemical shifts are reported in ppm.

The change in ring size of tetralone and indanone didn’t affect the yield of the product(s). The formation of arylidene indanone/tetralones was confirmed by 1H-NMR that indicated the presence of an olefinic proton that appeared as a singlet (6.69–7.82 ppm) in most of the cases depending upon the –I and –R/+R effect of the locants at 2 (Figure 3). The XRD of a couple of products (5g and 5i, one from each case) confirmed the formation of a new C=C bond (1.337Å between C1 & C10 and 1.340Å between C10 & C11 respectively) (Figure 1) [36].
Figure 1. The ORTEP diagram of (a) 5g. (b) 5i.

An aldol product 7b was isolated as a major product in case of H$_2$SO$_4$-mediated condensation of 4 with 2-Cl-5-NO$_2$PhCHO; whereas the base or SSA catalyzed reactions afforded the desired enone 7a. Due to steric factors no $o$-substituted substrate was used in any previous case. The H-bonding, forming a six member ring, between Cl or carbonyl O and alcoholic H would probably be the reason of the failure of the dehydration in 7b (Figure 2a). The XRD of 7b showed a new C-O (1.418Å) and O-H (0.821Å) bond formation instead of C=C (Figure 2b) [37].

Figure 2. (a) Formation of 7a and 7b under different reaction conditions: i) NaOH reflux (7a, 43%), SF (7a, 71%); SSA (7a, 82%); ii) H$_2$SO$_4$ reflux (7b, 73%). (b) The ORTEP diagram of 7b.

3. Experimental

The TLC was carried out on pre-coated silica gel (0.25 mm thick layer over Al sheet, Merck, Darmstadt, Germany) with fluorescent indicator. The spots were visualized under UV lamps (λ 365 and 254 nm) of 8 W power or KMnO$_4$ dip and heating. The compounds were purified either on a glass column packed silica gel (0.6–0.2 mm, 60Å mesh size, Merck) or by crystallization. All solutions were concentrated under reduced pressure (25 mm of Hg) on a rotary evaporator (Laborota 4001, Heidolph, Germany) at 35–40 °C. Melting points were determined using a MF-8 (Gallenkamp, Burladingen, Germany) instrument and are reported uncorrected. The IR-spectra are recorded on Prestige 21 spectrophotometer (Shimadzu, Japan) as KBr discs. The LREIMS are carried out on a Fisons Autospec Mass Spectrometer (VG, New Jersey, USA). The $^1$H (300, 400 and 500 MHz) and $^{13}$C-NMR (75 MHz) are recorded on AM-300, 400 and 500 MHz instruments (Bruker, Massachusetts, USA) in CDCl$_3$ using TMS as internal standard.
3.1. Preparation of SSA

**Method A:** The H$_2$SO$_4$ was added to a stirred suspension of silica gel in Et$_2$O. After stirring for 1 h, the solvent was evaporated under reduced pressure. The resulting SSA was placed in an oven at 120 °C for 3 h, which afforded SSA as a white solid.

**Method B:** The silica gel was added to HSO$_3$Cl along with subsequent trapping of HCl produced during the reaction. The suspension thus formed was stirred at room temperature for 3 h and the resultant product was dried in fume-hood to remove any trapped HCl produced during the reaction. The SSA obtained in this manner was white sand-like solid.

3.2. Representative Procedure for H$_2$SO$_4$ Catalyzed Synthesis of Chalcones under Reflux

The PhAc (1 mL, 0.90 g, 7.53 mmol, 1 eq.) and PhCHO (0.84 g, 7.91 mmol, 1.05 eq.) were added to a stirred solution of H$_2$SO$_4$ (0.5 mL, 0.86 g, 8.66 mmol, 1.15 eq.) in MeOH (15 mL) and the resulting reaction mixture was refluxed for 3 h. After the completion of reaction, the solvent was evaporated under a stream of N$_2$. The resulting reaction mixture was neutralized with 10% aq. NaHCO$_3$ and partitioned between H$_2$O (50 mL) and EtOAc (3 × 25 mL). The combined organic extract was dried over anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure to afford product as white amorphous solid. Crystallization from CH$_2$Cl$_2$ afforded product as colorless needles (0.89 g, 54%).

3.3. Representative Procedure for NaOH Catalyzed Synthesis of Chalcones under Reflux

The PhAc (1 mL, 0.90 g, 7.53 mmol, 1 eq.) and PhCHO (0.84 g, 7.91 mmol, 1.05 eq.) were added to a stirred solution of NaOH (0.35 g, 8.66 mmol, 1.15 eq.) in MeOH (15 mL) and the resulting reaction mixture was refluxed for 3 h. After the completion of reaction, the solvent was evaporated under a stream of N$_2$. The resulting reaction mixture was acidified with dil. aq. HCl and partitioned between H$_2$O (50 mL) and EtOAc (3 × 25 mL). The combined organic extract was dried over anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure to afford product as white amorphous solid. Crystallization from CH$_2$Cl$_2$ afforded product as colorless needles (0.74 g, 45%).

3.4. Representative Procedure for NaOH Catalyzed Synthesis of Chalcones under Solvent Free Conditions

The PhAc (1 mL, 0.90 g, 7.53 mmol, 1 eq) and PhCHO (0.84 g, 7.91 mmol, 1.05 eq) were ground together in a mortar and pestle in the presence of NaOH (0.30 g, 7.60 mmol, 1.01 eq) for 30 min. The reaction mixture was neutralized and extracted with Et$_2$O (3 × 25 mL). The combined organic extract was dried over anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure to afford the enone as colourless solid (1.27 g, 77%).

3.5. Representative Procedure for the SSA Catalysed Synthesis of Chalcones

The SSA (0.02 g) was added to a well stirred suspension of PhAc (1 mL, 0.90 g, 7.53 mmol, 1 eq.) and PhCHO (0.84 g, 7.91 mmol, 1.05 eq.) and the resulting mixture was heated at 65 °C for 1.5 h. The
reaction mixture was cooled to room temperature and partitioned between brine (25 mL) and CH₂Cl₂ (3 × 15 mL) and solid SSA was filtered off. The SSA was washed with acetone (25 mL) to ensure desorption of product on SSA surface. The combined organic extract was washed with brine (3 × 25 mL) and the organic extract was dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure to afford the chalcone as colorless solid (1.48 g, 91%).

1,3-Diphenylprop-2-eneone (3a): Rf: 0.58 (EtOAc/n-hexane, 1:3); M.p.: 57 °C (Lit. 56–57 °C)[38]; IR (KBr): νmax (cm⁻¹) 2930 (C-H), 1679 (C=O); ¹H-NMR (400 MHz, CHCl₃, δ in ppm): 7.18–7.32 (5H, m, H²-H⁵), 7.46–7.55 (3H, m, H³, H⁴), 7.60 (1H, d, J = 16.4 Hz, H²), 7.89 (2H, d, J = 7.8 Hz, H⁴), 8.12 (1H, d, J = 16.4 Hz, H³); ¹³C-NMR (75 MHz, CDCl₃, δ in ppm): 123.3 (d, C²), 125.4, 126.9, 128.4, 129.2 (2 × d, C², C³, C⁴, C⁵), 127.1, 133.8 (d, C⁶, C⁷), 134.2, 135.5 (s, C⁸, C⁹), 144.1 (d, C³), 187.5 (s, C¹); EI-MS (m/z, amu): 208 [M⁺] (54%), 131 [M−Ph⁺] (100%), 105 [PhCO⁺] (98%).

3-(4′-Hydroxyphenyl)-1-phenylpropenone (3d): Rf: 0.48 (EtOAc/ n-hexane, 3:1); M.p.: 44 °C (Lit. 35–45 °C)[38]; IR (KBr): νmax (cm⁻¹) 3320 (O-H, bs), 2885 (C-H), 1669 (C=O); ¹H-NMR (400 MHz, CHCl₃, δ in ppm): 6.87 (2H, d, Δ = 7.6 Hz, H³), 7.14–7.28 (5H, m, Ph-H), 7.43 (1H, d, Δ = 15.6 Hz, H²), 7.65 (2H, d, Δ = 7.5 Hz, H²), 7.67 (2H, d, Δ = 15.6 Hz, H³), 10.10 (1H, bs, OH); ¹³C-NMR (75 MHz, CDCl₃, δ in ppm): 112.8 (2 × d, C³), 121.0 (d, C²), 126.2, 128.1, 129.9 (2 × d, C₂, C⁴, C⁵), 129.4 (s, C⁶), 128.3 (d, C⁶), 132.8 (s, C⁷), 140.8 (d, C⁸), 158.3 (s, C⁹), 187.6 (s, C¹); EI-MS (m/z, amu): 224 [M⁺] (54%), 131 [PhCH=CHCO⁺] (100%, A), 121 [M−A⁺] (94%).

3-(Furan-2′-yl)-1-p-tolylpropenone (3h): Rf: 0.53 (EtOAc/ n-hexane, 1:3); M.p.: 64–67 °C (Lit. 62–64 °C)[39]; IR (KBr): νmax (cm⁻¹) 3130, 2852, 2935, 2677, 1675 (C=O); ¹H-NMR (400 MHz, CHCl₃, δ in ppm): 2.27 (3H, s, Me), 6.57 (1H, dd, Δ = 3.2, 1.8 Hz, H⁴), 6.78 (1H, d, Δ = 3.2 Hz, H³); 7.22 (2H, d, Δ = 7.5 Hz, H³), 7.55 (1H, d, Δ = 15.6 Hz, H²), 7.67 (2H, d, Δ = 7.5 Hz, H²), 7.82 (1H, d, Δ = 15.6 Hz, H³); ¹³C-NMR (75 MHz, CDCl₃, δ in ppm): 16.8 (q, CH₃), 110.4, 111.9, 128.3, 129.2, 129.4, 129.6, 129.9 (2 × d, C², C³, C⁴, C⁵, C⁶, C⁷, C⁸), 134.1 (s, C²/C⁴), 141.8 (d, C⁵/C⁶), 142.9 (s, C⁷/C⁸), 143.5 (d, C³/C⁶), 154.8 (s, C⁴), 189.3 (s, C¹); EI-MS (m/z, amu): 212 [M⁺] (79%), 121 [M−C₆H₄Me⁺] (94%), 119 [MeC₆H₄CO⁺] (100%).

3-(4′-Dimethylaminophenyl)-1-(3′-nitrophenyl)propenone (3i): Rf: 0.46 (EtOAc/ n-hexane, 1:1); M.p.: 107–111 °C (Lit. 110–111 °C)[40]; IR (KBr): νmax (cm⁻¹) 2999 (C-H), 1663 (C=O), 1545 (N-O); ¹H-NMR (400 MHz, CHCl₃, δ in ppm): 2.94 (6H, s, N(CH₃)₂), 6.54 (2H, d, Δ = 7.8 Hz, H³), 7.18 (2H, d, Δ = 7.8 Hz, H²), 7.54 (1H, d, Δ = 15.8 Hz, H³), 7.68 (1H, t, Δ = 6.8 Hz, H⁵), 7.83 (1H, d, Δ = 15.8 Hz, H²); 7.96 (1H, dd, Δ = 6.8, 2.4 Hz, H⁴), 8.31 (1H, d, Δ = 6.8 Hz, H⁵); 8.66 (1H, t, Δ = 2.4 Hz, H³); ¹³C-NMR (75 MHz, CDCl₃, δ in ppm): 42.7, 42.9 (q, N-CH₃), 112.9 (2 ×, d, C³), 120.2 (d, C²), 122.4 (s, C⁵), 126.7 (2 ×, d, C²), 129.9, 130.4, 130.8, 133.6 (d, C², C⁴/C⁶), 135.1 (s, C¹), 140.2 (s, C⁴), 144.4 (d, C³), 149.0 (s, C³), 188.2 (s, C¹); EI-MS (m/z, amu): 296 [M⁺] (18%), 174 [M−C₆H₄NO₂⁺] (100%, A), 150 [NO₂C₆H₄CO⁺] (23%), 146 [A−CO⁺] (100%).

1-(4′-Chlorophenyl)-3-(4′-methoxyphenyl)propenone (3o): Rf: 0.57 (EtOAc/n-hexane, 1:1); M.p.: 67–68 °C (Lit. 68–70 °C)[41]; IR (KBr): νmax (cm⁻¹) 3007 (C-H), 1658 (C=O), 766 (C-Cl); ¹H-NMR (400 MHz, CHCl₃, δ in ppm): 3.73 (3H, s, OMe), 6.65 (2H, d, Δ = 7.8 Hz, H³), 6.98 (2H, d,
2-(Furan-2′-yl)methyleneindan-1-one (5b): Rf: 0.55 (EtOAc/ n-hexane, 1:3); M.p.: 116 °C (Lit. 118–119 °C)[42]; IR (KBr): $\nu_{\max}$ (cm$^{-1}$) 2991 (=C-H), 1616 (C=O); $^1$H-NMR (CDCl$_3$, 400 MHz, $\delta$ in ppm): 4.04 (2H, s, H$^3$), 6.53–6.54 (1H, m, H$^4$), 6.75 (1H, d, J = 3.2 Hz, H$^5$), 7.41 (1H, t, J = 7.2 Hz, H$^6$), 7.44 (1H, s, H$^1$), 7.53 (1H, d, J = 7.2, H$^4$), 7.57-7.61 (2H, m, H$^5$, H$^6$), 7.87 (1H, d, J = 7.2 Hz, H$^7$); $^{13}$C-NMR (75 MHz, CDCl$_3$, $\delta$ in ppm): 20.9 (t, C$^3$), 110.4, 112.3 (d, C$^{1''}$, C$^{4''}$), 125.1, 127.8, 128.2, 129.9 (d, C$^{4}$), 136.1 (d, C$^1$), 136.9, 137.5, 138.3 (s, C$^2$, C$^{3a}$, C$^{7a}$), 142.8 (d, C$^{3}$), 154.1 (s, C$^2$), 188.7 (s, C$^3$); EI-MS (m/z, amu): 210 [M]$^+$ (100%), 182 [M – CO]$^+$ (18%, A), 181 [A – H]$^+$ (84%).

2-(4′-Dimethylaminobenzylidene)indan-1-one (5c): Bright yellow solid; Rf: 0.52 (EtOAc/n-hexane, 1:1); M.p.: 167 °C (Lit. 168 °C)[43]; IR (KBr): $\nu_{\max}$ (cm$^{-1}$) 2933 (=C-H), 1656 (C=O); $^1$H-NMR (CDCl$_3$, 400 MHz, $\delta$ in ppm): 3.07 (6H, s, NMe$_2$), 4.00 (2H, s, H$^5$), 6.97 (1H, s, H$^3$), 7.41 (1H, d, J = 6.4 Hz, H$^4$), 7.54–7.63 (6H, m, H$^5$, H$^6$, H$^{2''}$, H$^{3''}$), 7.88 (1H, d, J = 6.8 Hz, H$^7$); $^{13}$C-NMR (75 MHz, CDCl$_3$, $\delta$ in ppm): 24.5 (t, C$^3$), 43.2, 43.4 (q, N-CH$_3$), 112.8 (2x, d, C$^3$), 123.8 (s, C$^1$), 125.2 (2x, d, C$^{5''}$), 126.7, 128.5, 129.4, 130.2 (d, C$^{1''}$), 133.9 (d, C$^1$), 134.0, 137.2, 137.8 (s, C$^2$, C$^{3a}$, C$^{7a}$), 143.5 (d, C$^4$), 186.9 (s, C$^3$); EI-MS (m/z, amu): 263 [M]$^+$ (100%), 235 [M – CO]$^+$ (43%, A), 234 [A – H]$^+$ (71%).

2-(3′-Methoxybenzylidene)indan-1-one (5e): Colorless solid; Rf: 0.58 (EtOAc/ n-hexane, 1:3); M.p.: 135 °C (Lit. 138 °C)[44]; IR (KBr): $\nu_{\max}$ (cm$^{-1}$) 2948 (=C-H), 1679 (C=O); $^1$H-NMR (CDCl$_3$, 300 MHz, $\delta$ in ppm): 3.86 (3H, s, OCH$_3$), 4.04 (2H, s, H$^3$), 6.94 (1H, dd, J = 8.1, 1.8 Hz, H$^6$), 7.18 (1H, bs, H$^2$), 7.26 (1H, d, J = 8.0 Hz, H$^5$), 7.37 (1H, t, J = 7.8 Hz, H$^6$), 7.41 (1H, t, J = 7.2 Hz, H$^7$), 7.54 (1H, d, J = 7.2 Hz, H$^4$), 7.58–7.63 (2H, m, H$^5$, H$^6$), 7.90 (1H, d, J = 7.5 Hz, H$^7$); $^{13}$C-NMR (75 MHz, CDCl$_3$, $\delta$ in ppm): 25.2 (t, C$^3$), 56.8 (q, O-CH$_3$), 110.5, 112.4, 117.5 (d, C$^1$), 125.8, 126.5, 127.5, 128.9, 130.0 (d, C$^{3}$), 135.4 (d, C$^{3'}$), 135.8, 136.2, 137.9, 138.5 (s, C$^2$, C$^{3a}$, C$^{7a}$), 159.9 (s, C$^{3}$), 187.9 (s, C$^3$); EI-MS (m/z, amu): 250 [M]$^+$ (100%), 249 [M – H]$^+$ (56%).

2-(3′-Nitrobenzylidene)indan-1-one (5f): Pale yellow solid; Rf: 0.54 (EtOAc/ n-hexane, 3:1); M.p.: 119–121 °C; IR (KBr): $\nu_{\max}$ (cm$^{-1}$) 2987 (=C-H), 1679 (C=O), 1565 (N-O); $^1$H-NMR (CDCl$_3$, 500 MHz, $\delta$ in ppm): 4.11 (2H, s, H$^3$), 7.45 (1H, t, J = 7.5 Hz, H$^6$), 7.60 (1H, d, J = 7.5 Hz, H$^4$), 7.64 (2H, t, J = 8.0 Hz, H$^5$, H$^{2''}$), 7.68 (1H, dd, J = 2.0, 2.0 Hz, H$^{3''}$), 7.92 (1H, d, J = 7.5 Hz, H$^7$), 7.93 (1H, d, J = 7.5 Hz, H$^6$/H$^7$), 8.24 (1H, dd, J = 8.0, 1.5 Hz, H$^6$/H$^7$), 8.53 (1H, s, H$^1$); $^{13}$C-NMR (75 MHz, CDCl$_3$, $\delta$ in ppm): 24.8 (t, C$^3$), 122.2, 124.0, 125.8, 126.5, 127.5, 128.9, 129.7, 130.0 (d, C$^{4}$), 134.3, 135.9 (d, C$^1$), 136.0, 136.2, 136.5, 137.4 (s, C$^2$, C$^{3a}$, C$^{7a}$), 147.7 (s, C$^{3''}$), 188.6 (s, C$^3$); EI-MS (m/z, amu): 265 [M]$^+$ (42%), 219 [M – NO$_2$]$^+$ (35%, A), 218 [A – H]$^+$ (53%).

2-(3′,4′-Dimethoxybenzylidene)indan-1-one (5g): off-white solid; Rf: 0.58 (EtOAc/n-hexane, 1:3); M.p.: 182 °C (Lit. 183-185 °C)[45]; IR (KBr): $\nu_{\max}$ (cm$^{-1}$) 3018 (=C-H), 1652 (C=O); $^1$H-NMR (CDCl$_3$, 400 MHz, $\delta$ in ppm): 3.93 (3H, s, OMe), 3.95 (3H, s, OMe), 4.02 (2H, s, H$^3$), 6.95 (1H, d,
2-Benzylidene-3,4-dihydro-2H-naphthalen-1-one (5h): Pale yellow solid; Rf: 0.64 (EtOAc/n-hexane, 1:3); M.p.: 96 °C (Lit. 96 °C)[46]; IR (KBr): \( \bar{\nu}_{\text{max}} \) (cm\(^{-1}\)) 3016 (=C-H), 1656 (C=O); \(^1\)H-NMR (CDCl\(_3\), \( \delta \) in ppm): 2.99 (1H, t, \( J = 7.2 \) Hz, H\(^7\)), 3.13 (2H, t, \( J = 7.2 \), H\(^4\)), 6.98 (1H, bs, H\(^1\)), 7.21–7.66 (8H, m, H\(^5\)-H\(^7\), H\(^2\)-H\(^6\)), 7.85 (1H, d, \( J = 7.6 \) Hz, H\(^8\)); \(^1^3\)C-NMR (75 MHz, CDCl\(_3\), \( \delta \) in ppm): 27.2, 28.9 (t, C\(^3\), C\(^4\)), 127.1, 128.3 (2x, d, C\(^2\), C\(^3\)), 128.5, 128.6, 129.5 (d, C\(^5\), C\(^7\), C\(^8\)), 131.8, 132.5, 136.0 (d, C\(^6\), C\(^8\)), 136.7 (3x, s, C\(^{2a}\), C\(^2\), C\(^1\)), 144.2 (s, C\(^{4a}\)), 188.6 (s, C\(^1\)); EI-MS (m/\( z \), amu): 234 [M\(^+\)] (56%), 206 [M – CO\(^+\)] (23%).

2-(Furan-2′-yl)methylene-3,4-dihydro-2H-naphthalen-1-one (5i): Colourless solid; Rf: 0.54 (EtOAc/n-hexane, 1:3); M.p.: 129–131 °C; IR (KBr): \( \bar{\nu}_{\text{max}} \) (cm\(^{-1}\)) 2965 (=C-H), 1621 (C=O); \(^1\)H-NMR (CDCl\(_3\), 300 MHz, \( \delta \) in ppm): 3.01 (2H, t, \( J = 6.6 \) Hz, H\(^3\)), 3.33 (2H, ddd, \( J = 5.1, 5.1, 1.8 \) Hz, H\(^5\)), 6.53 (1H, dd, \( J = 3.3, 1.8 \) Hz, H\(^4\)), 6.71 (1H, d, \( J = 3.3 \) Hz, H\(^3\)), 7.27 (1H, d, \( J = 7.5 \) Hz, H\(^5\)), 7.38 (1H, t, \( J = 7.5 \) Hz, H\(^5\)), 7.48 (1H, ddd, \( J = 7.5, 7.5, 1.5 \) Hz, H\(^6\)), 7.56 (1H, s, H\(^1\)), 7.60 (1H, d, \( J = 1.5 \) Hz, H\(^8\)), 8.11 (1H, dd, \( J = 7.5, 1.2 \) Hz, H\(^8\)); \(^1^3\)C-NMR (75 MHz, CDCl\(_3\), \( \delta \) in ppm): 26.7, 28.4 (t, C\(^3\), C\(^4\)), 112.2 (d, C\(^{2+}\)), 116.6 (s, C\(^3\)), 122.8, 127.0 (d, C\(^5\), C\(^7\)), 128.1 (2x, d, C\(^6\)), 131.9 (s, C\(^{4a}\)), 133.1 (d, C\(^1\)), 133.6 (s, C\(^{4a}\)), 143.5 (s, C\(^2\)), 144.4 (d, C\(^5\)), 152.5 (s, C\(^{2+}\)), 187.4 (s, C\(^1\)); EI-MS (m/\( z \), amu): 224 [M\(^+\)] (100%), 223 [M – H\(^+\)] (42%), 196 [M – CO\(^+\)] (26%).

2-(4′′-Dimethylaminobenzylidene)-3,4-dihydro-2H-naphthalen-1-one (5j): Bright yellow solid; Rf: 0.54 (EtOAc/n-hexane, 1:3); M.p.: 35 °C (Lit. 35 °C)[46]; IR (KBr): \( \bar{\nu}_{\text{max}} \) (cm\(^{-1}\)) 2889 (=C-H), 1665 (C=O); \(^1\)H-NMR (CDCl\(_3\), 400 MHz, \( \delta \) in ppm): 2.93 (4H, m, H\(^3\), H\(^4\)), 3.11 [6H, s, N(CH\(_3\))\(_2\)], 7.07–7.47 (7H, m, H\(^5\)-H\(^7\), H\(^2\), H\(^3\)), 7.82 (1H, s, H\(^1\)), 8.09 (1H, d, \( J = 7.2 \) Hz, H\(^8\)); \(^1^3\)C-NMR (75 MHz, CDCl\(_3\), \( \delta \) in ppm): 27.8, 28.7 (t, C\(^3\), C\(^4\)), 40.1 [2x, q, N(CH\(_3\))\(_2\)], 111.6 (s, C\(^1\)), 123.6 (2x, d, C\(^3\)), 127.3, (2x, d, C\(^2\)), 126.8, 127.8, 128.0, 131.0, 132.1 (d, C\(^6\), C\(^8\), C\(^3\), C\(^5\)), 132.7, 134.5, 142.9 (s, C\(^2\), C\(^{4a}\)), 150.6 (s, C\(^{4a}\)), 187.8 (s, C\(^1\)); EI-MS (m/\( z \), amu): 277 [M\(^+\)] (53%), 276 [M – H\(^+\)] (33%), 249 [M – CO\(^+\)] (8%).

2-(4′′-Methoxybenzylidene)-3,4-dihydro-2H-naphthalen-1-one (5k): Yellow solid; Rf: 0.54 (EtOAc/n-hexane, 1:3); M.p. 92 °C (Lit. 92 °C)[46]; IR (KBr): \( \bar{\nu}_{\text{max}} \) (cm\(^{-1}\)) 2949 (=C-H), 1654 (C=O); \(^1\)H-NMR (CDCl\(_3\), 400 MHz, \( \delta \) in ppm): 2.94 (2H, t, \( J = 7.2 \) Hz, H\(^3\)), 3.10 (2H, t, \( J = 7.2, 7.2 \) Hz, H\(^5\)), 3.75 (3H, s, OMe), 6.69 (1H, s, H\(^1\)), 6.82 (2H, d, \( J = 6.8 \) Hz, H\(^3\)), 7.15 (2H, d, \( J = 6.8 \) Hz, H\(^2\)), 7.24–7.35 (2H, m, H\(^2\), H\(^5\)), 7.44 (1H, ddd, \( J = 7.2, 7.2, 1.8 \) Hz, H\(^6\)), 7.90 (1H, dd, \( J = 7.2, 1.8 \) Hz, H\(^8\)); \(^1^3\)C-NMR (75 MHz, CDCl\(_3\), \( \delta \) in ppm): 27.8, 28.7 (t, C\(^3\), C\(^4\)), 66.1 (q, OCH\(_3\)), 111.6 (s, C\(^1\)), 121.8 (2x, d, C\(^3\)), 127.9 (2x, d, C\(^5\)), 125.4, 127.2, 128.5, 131.0, 132.7, (d, C\(^6\), C\(^8\), C\(^7\), C\(^{4a}\)), 134.0 (s, C\(^2\)), 142.9, 147.8 (s, C\(^{4a}\), C\(^{4a}\)), 187.4 (s, C\(^1\)); EI-MS (m/\( z \), amu): 264 [M\(^+\)] (100%), 236 [M – CO\(^+\)] (88%).

2-(3′′-Chlorobenzylidene)-3,4-dihydro-2H-naphthalen-1-one (5m): Bulk-brown solid; Rf: 0.56 (EtOAc/n-hexane, 1:3); M.p.: 71–74 °C (Lit. 72 °C)[46]; IR (KBr): \( \bar{\nu}_{\text{max}} \) (cm\(^{-1}\)) 2948 (=C-H), 1662
(C=O), 785 (C-Cl); \(^1\)H-NMR (CDCl\(_3\), 300 MHz, \(\delta\) in ppm): 2.98 (2H, t, \(J = 7.2\) Hz, H\(^1\)), 3.08 (2H, t, \(J = 7.2\) Hz, H\(^4\)), 6.81 (1H, s, H\(^\text{H}^1\)), 7.18–7.24 (3H, m, H\(^2\prime\), H\(^4\prime\), H\(^5\prime\)), 7.33-7.47 (4H, m, H\(^5\)-H\(^7\), H\(^6\)), 7.86 (1H, d, \(J = 7.2\) Hz, H\(^8\)); \(^{13}\)C-NMR (75 MHz, CDCl\(_3\), \(\delta\) in ppm): 27.2, 28.7 (t, C\(^3\), C\(^4\)), 123.1, 124.2, 127.3, 128.4, 129.6, 133.1, 133.6, 133.8 (d, C\(^5\), C\(^6\), C\(^7\), C\(^8\), C\(^2\prime\), C\(^4\prime\), C\(^5\prime\), C\(^6\prime\)), 134.4, 135.8, 137.5, 137.8, 148.3 (s, C\(^\text{C}^1\), C\(^\text{C}^7\), C\(^\text{C}^4\), C\(^\text{C}^8\)), 187.3 (s, C\(^1\)); EI-MS (m/z, amu): 268, 270 [M]+ (38, 12%), 240, 242 [M – CO]+ (18, 7).

(\(\text{E}-\))2-(\(2{\prime}\)-\(\text{Chloro}-5{\prime}\)-\(\text{nitrobenzylidene})-3,4-\(\text{dihydronaphthalen}-1(2\text{H})\)-\(\text{one}\) \(\text{(7a)}\)): Off-white solid; Rf: 0.57 (EtOAc/n-hexane, 1:3); M.p.: 97 °C (Lit. 97 °C[47]); IR (KBr): \(v_\text{max} \text{ (cm}^{-1}\)) 2968 (=C-H), 1681 (C=O), 1519 (N=O), 738 (C-Cl); \(^1\)H-NMR (300 MHz, CDCl\(_3\), \(\delta\) in ppm): 2.99 (4H, s, H\(^1\), H\(^4\)), 7.24 (1H, m, H\(^3\)), 7.38 (1H, t, \(J = 7.2\) Hz, H\(^7\)), 7.51 (1H, t, \(J = 7.2\) Hz, H\(^6\)), 7.62 (1H, d, \(J = 8.8\) Hz, H\(^8\)), 7.82 (1H, s, H\(^1\prime\)), 8.14-8.19 (3H, m, H\(^3\prime\), H\(^4\prime\)& H\(^5\prime\)); \(^{13}\)C-NMR (75 MHz, CDCl\(_3\), \(\delta\) in ppm): 24.2, 28.4 (t, C\(^3\), C\(^4\)), 123.5, 123.8, 126.4, 128.5, 128.9, 129.4, 132.5, 133.6 (d, C\(^5\)-C\(^6\), C\(^1\prime\), C\(^3\prime\), C\(^4\prime\), C\(^5\prime\), C\(^6\prime\)), 136.4, 136.8, 137.3, 137.5, 139.4, 143.4 (s, C\(^2\), C\(^8\), C\(^\text{C}^1\), C\(^\text{C}^7\), C\(^\text{C}^4\), C\(^\text{C}^8\)), 187.8 (s, C\(^1\)); EI-MS (m/z, amu): 315, 317 [M]+ (21, 6%), 280 [M – Cl]+ (81%).

4. Conclusions

The higher yields (72%–97%) of chalcones are obtained by SSA-mediated coupling over other reported strategies. Furthermore, the slightly lower yields of the hydroxyl substituted chalcones from solvent free NaOH mediated condensation make SSA the method of choice for the synthesis of chalcones.

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Conflicts of Interest

The authors declare no conflict of interest.

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*Sample Availability*: Samples of the compounds 3a–o, 5a–m and 7a–b are available from the authors.

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