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# A concise synthesis of 2-benzoyl-1-indanones and 1-indanones from 2-aryl-1-tetralones

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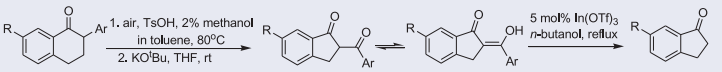
**ABSTRACT**

Methyl-2-(3-oxo-3-aryl) benzoates derived from acid catalyzed air oxidative fragmentation of 2-aryl-1-tetralones were efficiently undergone intramolecular-Claisen condensation in the presence of potassium tertiary butoxide. The resulting 2-benzoyl-1-indanones formed in two-step ring contractions were further subjected to indium triflate mediated retro-Claisen condensation to get 1-indanones.

**GRAPHICAL ABSTRACT**

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**KEYWORD**
Air oxidation; 2-benzoyl-1-indanones; 1-indanone; retro-Claisen condensation

## Introduction

1-Indanone and structurally related moieties are widely found in bioactive natural products, drugs and agrochemicals.[1,2] 2-benzoyl derivatives of 1-indanones belongs to an important class of $\beta$-dicarbonyl compounds which along with tautomeric 2-hydroxbenzylidene-1-indanones and structurally related 2-arylidene-1-indanones show diverse biological activities.[3] On the other hand, metal chelates of $\beta$-dicarbonyl compounds are well known to have significant material science application potential.[4] Recently transition metal complexes of 2-benzoyl-1-indanones have been reported to be anticarcinogenic and also shown properties suitable for potential photovoltaic and luminescence applications.[5] There are several synthetic procedures available to get 2-benzoyl-1-indanones, however, given the dependence of both biological and material properties on their structural variation, novel synthetic methods are required.[1,2,5]

## Results and discussions

Recently our group has reported an acid catalyzed auto oxidative fragmentation of 2-aryl-1-tetralones **1** in presence of methanol and air to generate methyl-2-(3-oxo-3-aryl) benzoates **2** (Scheme 1).[6]

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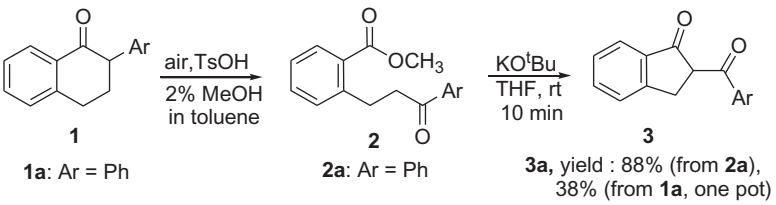


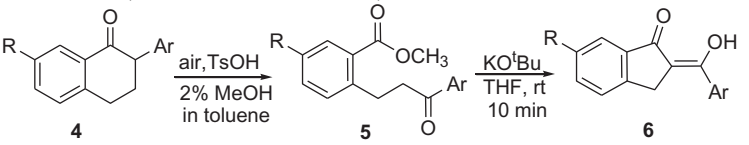

**Scheme 1.** Auto oxidative fragmentation of 2-aryl-1-tetralones followed by intramolecular-Claisen condensation

The 1,6-dicarbonyl compounds **2** thus obtained should in principle undergo intramolecular-Claisen condensation.[7] Indeed, when **2a** was subjected to a stoichiometric amount of potassium *tert*-butoxide in THF, 2-benzoyl-1-indanone **3** formed almost instantly at room temperature with high yield. This condensation allows a two-step formal ring contraction of 2-aryl-tetralone to 2-benzoyl-1-indanone. The ring contraction has been a widely used strategy in synthesis.[8] In particular; synthesis of 1-indanone derivatives via ring contraction of 1-tetralone has been reported via photofavorsky reaction and through a multistep sequence involving stoichiometric thallium (III) nitrate.[9] In this context, the current method involving air oxidation provides a green alternative synthesis. The excellent yield obtained under ambient condition obviates further optimization of the condensation reaction (**2a**→**3a**). However, reaction did not occur when the solvent was changed to toluene which posed difficulty to carry out a one-pot conversion of **1**–**3**. A one-pot two-step protocol in which evaporation of solvent from the fragmentation reaction (**1a**→**2a**) followed by the condensation reaction (**2a**→**3a**) in THF gave the desired compound **3a** albeit in lower 38% yield. Hence, we decided to carry out the condensation step separately.

The two-step auto oxidative fragmentation of 2-aryl-1-tetralones[10] followed by intramolecular-Claisen condensation reaction was then carried out in substrates with various substituents both in tetralone as well as in α-aromatic group and summarized in Table 1. The fragmentation reaction (**4**→**5**) via known procedure gave good yields of **5**.[11] Whereas all the condensation reactions (**5**→**6**) were found to be fast and completed within 10 minutes in room temperature with excellent yield. The later reaction was however found to be sensitive to moisture and a dry solvent is necessary to get optimum yield. No significant effect of both electron-donating and electron-withdrawing substituents on the outcome of the condensation reaction was observed. The resulting indanone derivatives exist exclusively as 2-hydroxyarylidene-1-indanone form **6** in the solid state but in equilibrium with 2-benzoyl-1-indanones **6′** in solution with varying ratios depending on the substitution on aromatic rings (Scheme 2).[5] Compared to the 2-benzoyl-1-indanone **3a** the enol form was lower in **6c** and higher in both **6b** and **6f** as observed by $^1$H NMR in $CDCl_3$. The rich chemistry of *β*-dicarbonyl compounds especially catalytic asymmetric transformations can be applied for further conversion of **6** to various indanone and indane moieties.[12] One of the straightforward conversion of *β*-dicarbonyl compounds is their reaction with alcohols in the presence of lewis acids to produce esters via retro-Claisen condensation.[13,14]

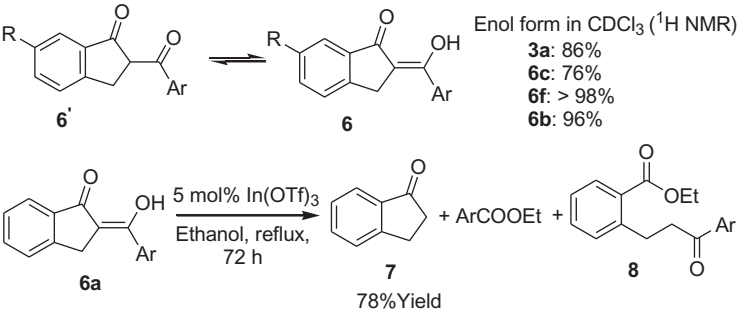
When compound **6a** was reacted with ethanol in the presence of catalytic $In(OTf)_3$, it chemoselectively yielded 1-indanone **7** as no significant amount of **8** was observed.

**Table 1.** 2-Benzoyl-1-indanones from 2-aryl-1-tetralones.




| entry | **4** (Ar) | R | Products (yield[a] in %) |
|---|---|---|---|
| 1 | **4a** (*p*-Me-Ph) | H | **6a** (93%) |
| 2 | **4b** (*o*-Me-Ph) | | **6b** (90%) |
| 3 | **4c** (*p*-OMe-Ph) | | **6c** (92%) |
| 4 | **4d** (*p*-Cl-Ph) | | **6d** (96%) |
| 5 | **4e** (3-pyridyl) | | **6e** (92%) |
| 6 | **4f** (Ph) | OMe | **6f** (93%) |
| 7 | **4g** (*p*-Me-Ph) | | **6g** (94%) |
| 8 | **4h** (Ph) | F | **6h** (94%) |

All the reactions were run with 0.05 M concentration of the **5** in THF.
[a]yields reported are isolated yield. Isolated yields for the conversion of **4** to **5** are 82–90%.




**Scheme 2.** Retro-Claisen condensation of 2-benzoyl-1-indanones/2-hydroxyarylidene-1-indanone.

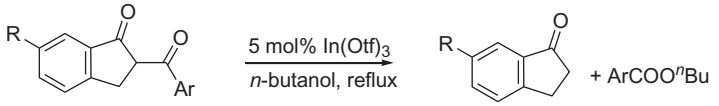
However, the reaction requires a long time even under the refluxing condition. The importance of 1-Indanone derivatives continues to attract the attention of the synthetic community for the development of novel methods of their preparation.[15] The observed selective retro-Claisen condensation with high yield makes it an attractive method for the synthesis of 1-Indanones from 2-aryl-1-tetralones.

Retro-Claisen condensation of various substituted 2-benzoyl-1-indanones with *n*-butanol in the presence of catalytic $In(OTf)_3$ are summarized in Table 2. As expected the reaction time shortened under reflux in higher boiling *n*-butanol compare to ethanol. The reaction was also found to be faster with electron-deficient α-aryl group (entries 4 and 5) compare to electron-rich aryl group (entry 2). However, no significant effect of substitution in 6-substituted indanones was observed. The byproduct *n*-butyl esters were also isolated in moderate yield (data not shown).

## Conclusions

In conclusion, air oxidative fragmentation of 2-aryl-1-tetralones allows a concise and novel synthesis of 2-benzo yl-1-indanones and 1-indanone in overall two and three steps respectively with moderate to good yield. The ring contraction thus achieved could be a useful strategy in the synthesis of complex molecules.

**Table 2.** 1-Indanones from 2-benzoyl-1-indanones.




**6**

**7**, R= H
**8**, R= OMe
**9**, R= F

| entry | Substrate | time | Products (yield[a] in %) |
|---|---|---|---|
| 1 | **6a** | 6 h | **7** (86%) |
| 2 | **6b** | 6 h | **7** (88%) |
| 3 | **6c** | 12 h | **7** (85%) |
| 4 | **6d** | 6 h | **7** (90%) |
| 5 | **6e** | 4 h | **7** (86%) |
| 6 | **6f** | 6 h | **8** (92%) |
| 7 | **6g** | 6 h | **8** (93%) |
| 8 | **6h** | 6 h | **9** (81%) |

All the reactions were run with 0.05 M concentration of the **6** in *n*-butanol.
[a]yields reported are isolated yields.

## Experimental procedures

### *General procedure for the synthesis of 2-hydroxyarylidene-1-indanones (2-benzoyl-1-indanones) 3a, 6a–h*

To a solution of Methyl-2-(3-oxo-3-aryl) benzoates (1.00 mmol) in dry THF (20 ml) in a round bottom flask was added KO$^{t}$Bu (130 mg, 1.16 mmol) at room temperature. The reaction flask was then fitted with septa and argon filled balloon and stirred for 10 minutes. The reaction was then quenched with saturated $NH_4Cl$ solution (10 ml) and extracted with ethyl acetate (2 × 50 ml). The combined organic layer was washed with brine (10 ml) and dried over anhydrous sodium sulfate. Evaporation of solvent gave crude product which upon column chromatography with 5% EtOAc/Hexane gave 2-hydroxyarylidene-1-indanones (2-benzoyl-1-indanones).

*2-(Hydroxy-phenyl-methylene)-indan-1-one* **3a** (known)[5a] Yield 208 mg (88%); light yellow solid; $R_f$ = 0.40 (10% EtOAc/hexane); mp. 92 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 15.06 (1H,br), 7.92–7.98 (2H, m), 7.90 (1H, d, $J$ = 7.6 Hz), 7.60–7.45 (5H, m), 7.44 (1H, dd, $J$ = 7.6 Hz, 7.6 Hz), 3.94 (2H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 195.9, 171.0, 148.7, 138.1, 135.0, 133.5, 131.4, 128.8, 128.3, 127.6, 125.7, 123.6, 109.6, 32.4.

### *General retro-Claisen reaction procedure for synthesis of 1-indanones*

To a solution of 2-hydroxyarylidene-1-indanones (0.50 mmol) in n-butanol (10 ml) was added $In(OTf)_3$ (15 mg, 0.027 mmol) and the reaction was refluxed until the starting material is consumed as observed by TLC. Then water (5.0 ml) was added to the reaction followed by extraction with ethyl acetate (2 × 50 ml). The combined organic layer was washed with brine (10 ml) and dried over anhydrous sodium sulfate. Evaporation of solvent gave crude product which upon column chromatography with 5% EtOAc/Hexane gave 1-indanones.

*1-Indanone* **7**. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.76 (1H, dd, $J = 7.5$ Hz), 7.59 (1H, td, $J = 7.5$ Hz, 1.2 Hz), 7.48 (1H, td, $J = 7.5$ Hz, 0.9 Hz), 7. 37 (1H, td, $J = 7.5$ Hz, 0.9 Hz), 3.15 (2H, dd, $J = 6.0$ Hz, 6.0 Hz), 2.66–2.74 (2H, m).

General Information, experimental, analytical data, $^1$H, $^{13}$C NMR spectra and characterization data of all the synthesized compounds are available as Supporting Information.

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