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## Note

# Synthesis of α,α'-bis (arylmethylidene) cycloalkanones catalyzed by molecular iodine: An improved procedure for the Claisen-Schmidt condensation

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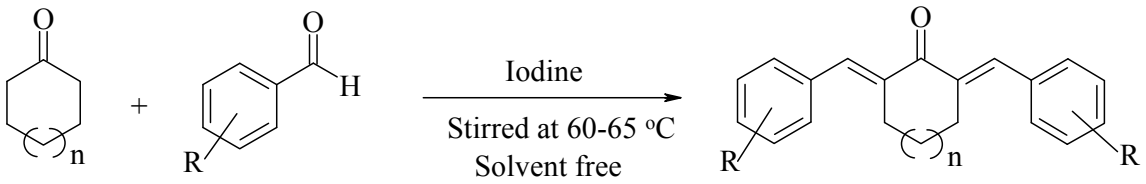
Molecular iodine efficiently catalyzes the two-component condensation of cycloalkanones and araldehydes to afford the corresponding α,α'-bis (arylmethylidene) cycloalkanones. The new protocol for the Claisen-Schmidt condensation reaction works well in the absence of the solvent. The yields are high and reactions go to completion 10-15 min under mild condition.

**Keywords**: α,α'-Bis(arylmethylidene)cycloalkanones, cycloalkanones, aldehydes, Claisen-Schmidt condensation, iodine

There is considerable interest in the formation of α,α'-bis (arylmethylidene) cycloalkanones and related compounds are precursors for the synthesis of bioactive pyrimidine derivatives[1]. The synthesis of this kind of compound is usually realized with the aid of strong acid or base catalyst. However, these strong catalysts often lead to side reactions such as self-condensation of the ketone and dimerisation of aldehyde. In addition, the harsh reaction conditions employed make it even more unattractive for the synthesis of complex molecules, which usually contain acid or base sensitive functional groups. The synthesis of α,α'-bis (arylmethylidene) cycloalkanones is usually achieved *via* a Claisen-Schmidt condensation between the cycloalkanones and aromatic aldehydes catalyzed by solid base[2,3], $BF_3{\cdot}OEt_2$ (ref. 4), $InCl_3$ (ref. 5), $InCl_3$/TMSCl[6], bis (*p*-ethoxyphenyl)telluroxide (BOMPTO)[7], TMSCl/NaI[8a], $Yb(OTf)_3$ (ref. 8b), $RuCl_3$ (ref. 9a), $FeCl_3$ (ref. 9b), $SmI_3$ (ref. 10), $Cp_2ZrH_2/NiCl_2$ (ref. 11), $Cp_2TiPh_2$ (ref. 12), $TiCl_3(SO_3CF_3)$[13], KF/inorganic solid support[14] and metal complexes[15]. Under microwave irradiation in the presence of solid catalysts such as KF- $Al_2O_3$ (ref. 16) and NaOH[17]. However, the yields of some examples are not satisfactory and the mentioned methods usually involve expensive reagents and relatively harsh conditions are employed for the reaction and longer time durations are required for completion. Others involve tedious experimental procedures and complex reaction mixtures and the yields are low. To avoid these limitations we started searching new catalysts, with high catalytic activity, easy availability, short reaction time, simple work-up and molecular iodine attracted our attention. Recently, we have reported the synthesis of α-iodoacetates from alkenes/ammonium acetate/$I_2$ (ref. 18) and synthesis of *N, N'*-disubstituted urea/thiourea catalyzed by iodine[19].

## Results and Discussion

In continuation with the search for the simple non-hazardous methods for the transformations in organic synthesis using iodine, herein we report a highly versatile and efficient synthesis of α,α'-bis (arylmethylidene) cycloalkanones **3** using cyclopentanone or cyclohexanone **1** and araldehydes **2** with catalytic amounts of iodine. A mixture of **1** and **2** (1:2) equivalents respectively was taken in a 50 mL round bottomed flask and heated for 10-15 min on a preheated oil-bath, stirred at 60-65ºC under solvent free condition to get **3a-k** in good to excellent yield (**Scheme I**).




n = 0, 1 R = H, Cl, OMe, $CH_3$, $NO_2$

**1** **2** **3 a-k**

**Scheme I**

In order to standardize the reaction conditions firstly we carried out the reaction with different amount of iodine and temperature and the results are summarized in **Table I**. In the absence of any catalyst, the desired α,α'-bis-arylmethylidene cyclopentanone was obtained in a very trace amounts even after 1 hr at 60−65 ºC. Secondly the conventional Lewis acids such as $ZnCl_2$, $CuCl_2$, $FeCl_2$, $NiCl_2$, $CoCl_2$, $MnCl_2$ and $AlCl_3$ showed poor effect, they promoted the self-condensation of ketones and aldehydes rather than the cross aldol reaction. The yields were also not satisfactory. We treated 0.1 mmole of iodine as catalyst with reaction substrates, heated on a preheated oil-bath at 60−65ºC for 10−15 min to obtain high yield of the products **Table II**.

## Conclusion

In conclusion, a reliable, improved and practical procedure for the synthesis of α,α'-bis (arylmethylidene) cycloalkanones from cycloalkanones and araldehydes has been developed, the method involves the use of catalytic amounts of inexpensive readily available iodine metal. In our opinion the present method is superior to some of the existing methods as shown in **Table III**.

## Experimental Section

Melting points were determined on a Büchi melting point apparatus. IR and NMR spectra were recorded on Nicolet 400D FT-IR spectrophotometer and 400 MHz Brucker spectrometer respectively. Cyclopentanone, cyclohexanone, all aldehydes and iodine were all commercial products and used without further purification.

**General procedure for the preparation of α,α'-bis (arylmethylidene) cycloalkanones**. Cyclopentanone (5 mmoles), benzaldehyde (10 mmoles) and iodine (0.1 mmole) were mixed. The mixture was stirred at 60-65ºC for 10 min to complete the reaction (monitored on TLC). After the reaction was complete

**Table I** — Optimization of the catalytic activity of iodine and reaction conditions[a] and the yield of α,α'-bis (arylmethylidene) cycloalkanones

| Entry | Amount of iodine (mmoles) | Temp(°C) | Time(min) | Yield (%)[b] |
|---|---|---|---|---|
| 1 | 10 | 25 | 60 | 20 |
| 2 | 10 | 40 | 40 | 30 |
| 3 | 5 | 50 | 30 | 32 |
| 4 | 5 | 50 | 60 | 45 |
| 5 | 2.5 | 55 | 30 | 50 |
| 6 | 2.5 | 60 | 30 | 56 |
| 7 | 1 | 60 | 20 | 72 |
| 8 | 1 | 65 | 20 | 75 |
| 9 | 0.5 | 60-65 | 20 | 86 |
| 10 | 0.1 | 70 | 15 | 88 |
| 11 | 0.1 | 60-65 | 10 | 92 |
| 12 | None | 60-65 | 60 | trace amount |

[a]Reaction conditions: cyclopentanone (10 mmoles), benzaldehyde (20 mmoles), catalyst and temperature as shown in table. [b] Isolated product

**Table II** — Iodine catalyzed synthesis of α,α'-bis (arylmethylidene) cycloalkanones **3a-k**

| Entry | Ketone **1** | R-CHO (R=)/ **2** | Product[a] (**3a-k**) | Yield[b] (%) | Time (min) | m.p(ºC) Found | m.p(ºC) Reported[c] |
|---|---|---|---|---|---|---|---|
| **a** | Cyclopentanone | $C_6H_5$ | **3a** | 92 | 10 | 188−90 | 188−90 |
| **b** | Cyclopentanone | 4-$NO_2C_6H_4$ | **3b** | 85 | 10 | 228−30 | 229−31 |
| **c** | Cyclopentanone | 4-$CH_3OC_6H_4$ | **3c** | 90 | 10 | 212−13 | 212−13 |
| **d** | Cyclopentanone | 4-$ClC_6H_4$ | **3d** | 92 | 10 | 229 | 228−29 |
| **e** | Cyclopentanone | 4-$CH_3C_6H_4$ | **3e** | 90 | 10 | 243−44 | 243−44 |
| **f** | Cyclopentanone | $C_6H_5CH$=CH | **3f** | 92 | 15 | 145 | 145−46 |
| **g** | Cyclopentanone | Furyl | **3g** | 90 | 10 | 204−05 | 203−04 |
| **h** | Cyclohexanone | $C_6H_5$ | **3h** | 93 | 10 | 155 | 156 |
| **i** | Cyclohexanone | 4-$NO_2C_6H_4$ | **3i** | 84 | 15 | 170 | 171 |
| **j** | Cyclohexanone | 4-$CH_3OC_6H_4$ | **3j** | 85 | 15 | 210−12 | 213 |
| **k** | Cyclohexanone | $C_6H_5CH$=CH | **3k** | 94 | 15 | 130−32 | 132 |

[a] All the products are known, characterized by IR & $^1$HNMR spectral analysis and compared with the authentic samples. [b] Isolated yields. [c] Melting points of compounds are consistent with reported values (Refs. 5, 8b, 14 and 16b).

**Table III** — Comparison of results of reactions carried out with different catalysts for the synthesis of α,α'-bis (arylmethylidene) cycloalkanones

| Entry | Catalysts | Time | Temp.ºC | Yield (%)[b] |
|---|---|---|---|---|
| 1 | $InCl_3$ (ref. 5) | 6-12 hr | 110 / Sealed tube | 89-95 |
| 2 | $RuCl_3$ (ref. 9a) | 4-24 hr | 120 / Sealed tube | 82-95 |
| 3 | KF-$Al_2O_3$ (ref. 16b) | 5 min | MW | 73-82 |
| 4 | $InCl_3$/ionic liquid[6] | 5-6 hr | 100 | 78-82 |
| 5 | $Cp_2ZrH_2$ /$NiCl_2$ (ref. 11) | 8 hr | 130 | 75-80 |
| 6 | TMSCl/NaI[8a] | 60-80 min | 25 | 78-92 |
| 7 | $TiCl_3(SO_3CF_3)$[13] | 15 min-2.5 hr | 25 | 94-99 |
| 8 | Iodine[a] | 10 min | 60-65 | 92 |

[a]Present method: reaction condition: cyclopentanone (10 mmoles), benzaldehyde (20 mmoles) and iodine (0.1 mmoles), [b] isolated yields.

conversion, the system was cooled to room temperature, the mixture was washed with 10% $Na_2S_2O_3$ solution and then taken into diethyl ether, dried over anhydrous $Na_2SO_4$, evaporation of the solvent afford a crude solid product, which was purified by successive washings with petroleum ether to get **3a** in 92% yield.

**2,6-dibenzylidene-cyclopentanone**, **3a**: IR (KBr): 3052, 3017, 2910, 1688, 1625, 1600 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 7.58-7.60 (m, 6H), 7.35-7.45 (m, 6H), 3.12 (s, 4H); $^{13}C$ NMR ($CDCl_3$): δ 188.1, 144.4, 133.3, 128.5, 127.5, 126.7, 122.6.

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