Efficient Condensation of Cycloketones and Acetone Using SOCl$_2$/EtOH

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INTRODUCTION

2-(1-Cyclohexenyl)cyclohexanone (1) (Scheme 1) is an important intermediate for the synthesis of OPP (o-C$_6$H$_5$C$_6$H$_4$OH) which is used as antiseptic. Both 1 and bicyclopentyliden-2-one (2) (Scheme 1) are original materials for the synthesis of some unsymmetrical trisannulated benzenes (4) and (5$^1$) (Scheme 3). 4-Methyl-3-penten-2-one (3) (Scheme 2) is a common solvent for some colophony and fibrin, an important intermediate of some drugs and pesticides.

Cyclohexanone has long been known to undergo self-condensation to 1.$^2$ The condensation can be catalyzed by acids, bases, or by heat alone. A few methods, for instance, using tetraalkoxysilane in the presence of fluoride ions,$^3$ RuCl$_3,^4$ CuCl$_2,^{15}$ as catalyst have been reported for the synthesis of 1 and 2, and several methods have been described for the

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\begin{align*}
\text{CH}_3\text{COCH}_3 & \xrightarrow{\text{SOCl}_2/\text{EtOH} \quad 24\text{h}} \quad \xrightarrow{\text{r. t.}} \\
& \text{H}_3\text{C} & \text{C}=\text{HCCOCH}_3 \\
& 3
\end{align*}
\]

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\begin{align*}
1: & n=1; 2: n=0
\end{align*}
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The literature synthetic methods involve some disadvantageous reaction conditions such as too high or too low temperature, high pressure and long reaction time.

**Result and Discussion**

On the basis of our previous reports the synthesis of 1, 3, 5-triarylbenzene, 7 asymmetrical 1, 3, 5-triarylbenzene, 8 chalcones 9 and α, α'-bis(substituted benzyldiene) ketones 10 catalyzed by SOCl₂/EtOH, we expanded this method to the synthesis of symmetrical trisannulated benzenes and 1, 3, 5-trimethyl benzene. During the study of synthesizing the symmetrical trisannulated benzenes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12-dodecahydro-triphenylene (6) and 2, 3, 4, 5, 6, 7, 8, 9-octahydro-1H-trindene (7) (Scheme 4), we noticed that oil with high boiling point could be obtained as the main product (see the synthesis of compounds 1 and 2) if the amount of SOCl₂ was reduced and the reaction time was prolonged. The oil was isolated by distillation and characterized by GC-mass and 1H NMR, and the analytical data showed that it was the intermediate of the triple condensation reaction. We optimized the reaction conditions and found that SOCl₂/EtOH reagent is also a good catalyst for synthesizing the dimers of these ketones.

Furthermore, we found that the alcohol serving as reaction solvent was indispensable for the catalyst system. Other solvents such as toluene and pyridine were not efficient for the reaction, only alcohol catalysed the condensation reaction. There is no significant variation of yields between anhydrous CH₃OH and anhydrous C₂H₅OH. On the basis of these results, we think the reaction proceeds via the reaction of the enol sulfite ester of the ketones, and the byproduct HCl may accelerate the reaction. 19, 10 The detailed mechanistic investigation and further applications of this reaction are under study in our laboratory.

**Conclusion**

In this paper, an efficient and simple method for the synthesis of the dimers of cycloketones and acetone in the presence of thionyl chloride and anhydrous ethanol has been reported. Comparing with other methods, this method is easily available with cheap catalyst, simple manipulation under mild conditions. We believe this reaction will expand the application of the thionyl chloride in organic synthesis.

**Experimental**

Melting points were determined on the kofler micro melting point apparatus without correction. Infrared spectra were recorded on a PTS-40 IR spectrophotometer in KBr. 1H NMR spectra were measured in CDCl₃ using TMS as internal standard on a BRUKER 80 MHz NMR spectrometer. The mass spectra were performed on an Agilent GC-MS spectrometer.

Synthesis of 2-[(1-cyclohexenyl)-cyclohexanone (4)]

To a stirred mixture of cyclohexanone (15.54 mL, 0.15 mol; freshly distilled) and anhydrous ethanol (43.7 mL, 0.75 mol), thionyl chloride (7.28 mL, 0.1 mol) was added dropwise. The mixture was stirred...
for 24 hours, saturated aqueous Na₂CO₃ solution was added. The mixture was extracted with ethyl ether (20 mL) three times, and the combined solution was dried over anhydrous MgSO₄. After evaporation of the volatiles on a rotovap, the residue was distilled at reduced pressure (140-142°C/13 mmHg), total yield: 60%. b.p.: 140-142°C/13 tor. (lit.): 142°C/13 tor.; IR (KBr, cm⁻¹): 2950, 2870, 1717, 1450, 920, 830; ¹H NMR (CDCl₃, ppm): 1.9-2.4(m, 16H), 2.9(m, 1H), 5.5(m, 1H); Mass (m/z, %): 178(M⁺, 60), 149(100).

Synthesis of 4-terphenylidene-2-one (2):
To a stirred mixture of cyclohexanone (13.27 mL, 0.15 mol; freshly distilled) and anhydrous ethanol (43.7 mL, 0.75 mol), thionyl chloride (1.82 mL, 0.025 mol) was added dropwise. In a similar experiment as described for 1, the residue was distilled at reduced pressure (120-122°C/12mmHg), total yield: 55%. b.p.: 120-122°C/12 tor. (lit.): 120-124°C/12 tor.; IR (KBr, cm⁻¹): 2950, 2850, 1700, 1445, 1120; ¹H NMR (CDCl₃, ppm): 1.9-2.3(m, 12H), 2.8(m, 1H), 5.5(m, 1H); Mass (m/z, %): 150(M⁺, 55), 121(100).

Synthesis of 4-methyl-3-penten-2-one (3):
To a stirred mixture of acetone (11 mL, 0.15 mol) and anhydrous ethanol (35 mL, 0.6 mol), thionyl chloride (3.64 mL, 0.05 mol) was added dropwise. In a similar experiment as described for 1, the residue was purified by column chromatography on silica gel using petroleum ether as eluent, isolated yield: 52%. m.p.: 95°C (lit. 97.5°C); IR(KBr, cm⁻¹): 2837, 1448, 1424, 1300, 1275; ¹H NMR (CDCl₃, ppm): 2.7(t, 12H, J=7.3Hz), 1.9-2.4(m, 6H); Mass (m/z, %): 198(M⁺, 100).

REFERENCES
11. IR spectrum is compatible with the Sadler Reference Spectra (Vol. 19-20, 18001K); ¹H NMR spectrum is compatible with the Sadler Reference Spectra (Vol. 19-21, 13213M).