

InCl₃·4H₂O Catalyzed Aldol Condensation of Cycloalkanones with Aromatic Aldehydes

Gui Sheng DENG*, Tie Gang REN

College of Chemistry and Chemical Engineering, Hunan Normal University, Changsha 410081

Abstract: InCl₃·4H₂O catalyzes the cross-aldol condensation of cycloalkanones with aromatic aldehydes in sealed tube under solvent free condition to afford an efficient method for the synthesis of α , α' -bis(substituted)benzylidenecycloalkanones.

Keywords: Aldol condensation, cycloalkanone, indium trichloride, catalysis.

α , α' -Bis (substituted) benzylidenecycloalkanones are widely used as precursors for synthesis of bioactive pyrimidine derivatives and their synthesis have attracted considerable attention¹. Aldol condensation of cyclopentanone or cyclohexanone with aldehydes is employed, and the reactions were carried out in the presence of strong acids or bases². Recently, the application of metal ions as catalyst in this type of reaction has been reported³. For example, RuCl₃ has been reported to be an excellent catalyst, which can promote these reactions in neutral conditions⁴. The disadvantage is that RuCl₃ is expensive. These reactions can also be catalyzed with TiCl₃ (SO₃CF₃) in excellent yields⁵. However, TiCl₃ (SO₃CF₃) can be hydrolyzed in the presence of water, which was resulted in the aldol-condensation reaction⁶. Here, we report a novel procedure for cross-condensation reaction of cycloalkanones with aromatic aldehydes. In our procedure indium trichloride promotes this condensation reaction as an efficient catalyst under solvent free condition heated at 110°C without any self-condensation of cycloalkanones and hydrolyzation of InCl₃ (**Scheme 1**). The yields of the aldol products are excellent. The results for cross-aldol condensation of cycloalkanones with aromatic aldehydes are list in **Table 1**. Di-aldol products are only obtained without mono-aldol products.

Typical procedure for the synthesis of compound **3a**. Cyclohexanone 0.490 g (5 mmol), benzaldehyde 1.061 g (10 mmol) and InCl₃·4H₂O 0.034 g (0.1 mmol) were placed in a glass tube and sealed. The sealed tube was placed in an oil bath and heated at 110°C for 6 hours. After cooling to room temperature, the reaction mixture was ground with ethanol (20 mL), and filtered. The crude product was washed with water, saturated brine and ethanol in turn. After drying in vacuum and recrystallization from ethanol, the crystalline product was afforded **3a** in 95% yield, mp. 116-117°C (Lit.⁷ 117°C), ¹H NMR (200MHz, CDCl₃, TMS) δ ppm: 7.81 (s, 2H, =C-H), 7.50-7.30 (m, 10H, Ar-H), 2.94 (t, 4H, J=6Hz, 3, 5-CH₂), 1.86-1.74 (m, 2H, 4-CH₂). IR (KBr) cm⁻¹:

1663 (w), 1605 (m), 1445 (m), 1275 (m), 1146 (m), 772 (m), 696 (s).

Scheme 1

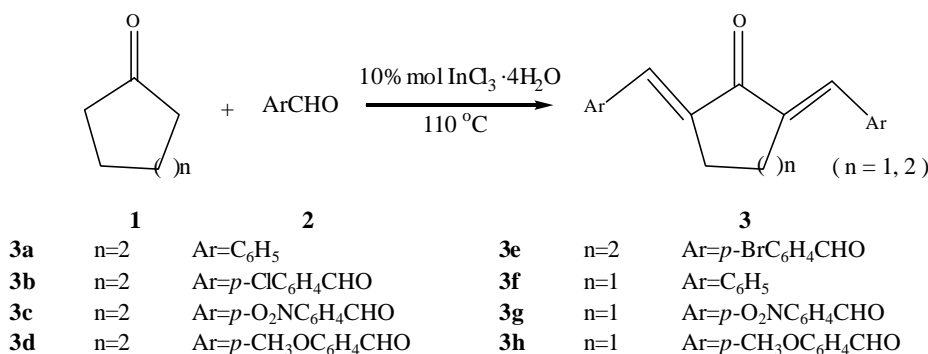


Table 1 Cross-aldol condensation reaction of cycloalkanones with aromatic aldehydes in the presence of 10% molar equivalents of InCl₃·4H₂O in sealed tube at 110 °C

Entry ^a	Reaction Time(h)	Yield (%) ^b
3a	6	95
3b	10	93
3c	24	93
3d	10	90
3e	12	93
3f	10	89
3g	24	91
3h	12	94

a) All compounds were confirmed by ¹H NMR and IR. b) Isolated yield.

References

- J. Deli, T. Lorand, D. Szabo, A. Foldesi, *Pharmazie*, **1984**, *39*, 539.
- a. A. T. Nielsen, W. Houlihan, *J. Org. React.*, **1976**, *41*, 3540.
b. R. J. Murray, N. H. Cromwell, *J. Org. Chem.*, **1976**, *41*, 3540.
c. J. V. Sinisterra, A. Garcia-Raso, *Synthesis*, **1984**, 502.
- a. R. Mhrwald, H. Schick, *Synthesis*, **1990**, 593.
b. M. Zeheng, L. Wang, J. Shao, Q. Zhong, *Synth. Commun.*, **1997**, *27*, 351.
- N. Iranpoor, F. Kazemi, *Tetrahedron*, **1998**, *54*, 9475.
- N. Irapoor, B. Zeynizadeh, A. Aghapoun, *J. Chem. Research (S)*, **1999**, 554.
- R. Nofle, G. H. Cady, *Inorg. Chem.*, **1966**, *5*, 282.
- M. Zeheng, L. Wang, J. Shao, Q. Zhong, *Synth. Commun.*, **1997**, *27*, 351.

Received 27 February, 2001