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An Efficient Synthetic Approach to Oxygenated Heterocycles

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Abstract: An efficient and reusable catalytic system allows the synthesis for Benzopyrans from Diphenylmethanol and 1, 3-dicarbonyl compounds using polymer bound pTSA catalyzed reagent provides moderate to excellent yields under mild conditions. The other oxygenated heterocycles, substituted furans have also been synthesized using the depicted methodology as the vital step.

Keywords: Polymer bound pTSA, Diphenylmethanol, Heterocycle, furan, Benzopyran.

1.0 Introduction

Polymer bound pTSA has found to be an effective catalyst for the synthesis of Benzopyrans from Diphenylmethanol substrates^[1-5], and in the synthesis of substituted furans from the alkylated compounds of 1,3-dicarbonyl compounds. In general, palladium catalyzed oxidative reactions of benzopyrans with arylboronic acids allows a direct synthesis of 4-substituent benzopyrans. Further, the employment of hydrophobic ionic liquids enhances the activity of metal triflates in Friedel-Crafts alkenylations of aromatic compounds with various alkyl- and aryl-substituted alkynes in the synthesis of benzopyrans. These approaches involve

metal reagents^[6] or the usage of expensive reagents. Hence, development of a suitable and an alternative approach is desirable.

In this context, emphasized to explore the utility of the reagent polymer bound pTSA as a mild acid catalyst for the synthesis of benzopyrans^[7-8] (scheme-1) and substituted furans (scheme-2). Further the studies have been extended, with Diphenylmethanol containing different protecting groups as the substrate. Cyclization reactions in halo solvents at ambient temperature in the presence of polymer bound pTSA were tested, which produced the benzopyrans in 85% yield in 2.5 h, substituted furans^[9-11] in 91% yield in 3 h. Explored similar reactions using different substrates.

2.0 Scheme-1:

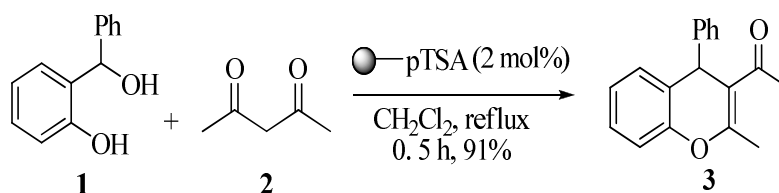


Table 1: Polymer bound pTSA Catalyzed synthesis of chromenes

| entry | alcohol | 1,3-diketone | time (min) | product | yield (%) |
|-------|---------|--------------|------------|---------|-----------|
| 1 | | | 20 | | 85 |
| 2 | | | 15 | | 86 |

^aAll the products were characterized by ¹H, ¹³C NMR and mass spectra;

^bIsolated yields

2.1 Synthesis of 4H-chromenes, 3, 5 and 7;

General procedure: To a stirred solution of 1,3-dicarbonyl compound **2** (1.0 mmol), diphenylmethanol, **1, 6** (1.0 mmol) and Polymer bound-pTSA (2 mol %) in CH₂Cl₂ (5 mL) was stirred at reflux temperature for given time (see Table 1). The reaction mixture was diluted with water (10 mL) and extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were dried over anhydrous Na₂SO₄, concentrated *in vacuo* and purified

by column chromatography on silica gel to afford pure 4H-chromenes, **3, 5** and **7**.

2.1.1 Ethyl 2-methyl-4-phenyl-4H-chromene-3-carboxylate (**5**)

Viscous liquid

IR (KBr): ν_{max} 2981, 1705, 1637, 1218, 1066 cm⁻¹

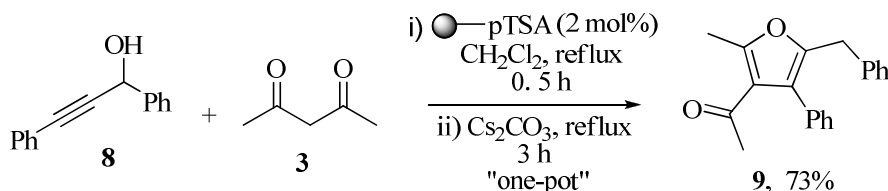
¹H NMR (300 MHz, CDCl₃): δ 7.30-7.14 (m, 6H, Ar), 7.12-6.98 (m, 3H, Ar), 5.06 (s, 1H, CH), 4.18-4.06 (m, 2H, OCH₂), 2.53 (s, 3H, CH₃), 1.21 (t, *J* = 6.9 Hz, 3H,

CH_2CH_3)¹³C NMR (75 MHz, CDCl_3): δ 167.1, 160.0, 149.2, 146.6, 129.1, 128.3, 127.7, 127.4, 126.3, 124.7, 124.4, 116.1, 106.0, 60.0, 41.4, 19.4, 14.0, MASS (ESI) (m/z): 295 [M+H]⁺

2.1.2. Ethyl 3-methyl-1-phenyl-1H-benzo [f]chromene-2-carboxylate (7)

Viscous liquid, IR (KBr): ν_{max} : 3063, 2971, 2922, 1688, 1649, 1621, 1328, 1223 cm^{-1} , ¹H NMR (300 MHz,

CDCl_3): δ 7.91 (d, J = 8.3 Hz, 1H, Ar), 7.70 (t, J = 8.1 Hz, 2H, Ar), 7.42-7.21 (m, 5H, Ar), 7.15 (t, J = 7.3 Hz, 2H, Ar), 7.077.00 (m, 1H, Ar), 5.61 (s, 1H, CH), 4.27-4.13 (m, 2H, OCH_2), 2.50 (s, 3H, CH_3), 1.34 (t, J = 6.9 Hz, 3H, CH_2CH_3), ¹³C NMR (75 MHz, CDCl_3): δ 167.2, 159.6, 147.7, 145.4, 128.7, 117.0, 107.2, 60.3, 38.2, 19.6, 14.3, 128.6, 128.3, 128.2, 126.7, 126.3, 124.5, 123.1, MASS (ESI) (m/z): 367 [M+Na]⁺



3.0 Scheme-2:

Table 2: Synthesis of tetra substituted Furans^a

| Entry | propargyl alcohol | 1,3-dicarbonyl compound | Time (h) (step-I/II) | Product ^a | Yield ^b (%) |
|-------|-------------------|-------------------------|----------------------|----------------------|------------------------|
| 1 | | | 0.5/1 | | 90 |
| 2 | | | 0.5/1.5 | | 88 |
| 3 | | | 1/2 | | 92 |

^a All products were characterized by ¹H and ¹³C NMR and MS. ^b Isolated yields.

3.1 Synthesis of tetrasubstituted furans, 9, 10, 12 and 15; General procedure: To a stirred solution of propargylic alcohol **8**, **13** (1.0 mmol) and 1,3-dicarbonyl compound, **3**, **4**, **11** and **15** (1.0 mmol) in dichloromethane (6 mL), was added polymer bound pTSA (2 mol%) and stirred at reflux for given time (see table-2, step-I) followed by the addition of caesium carbonate (2.0 mmol) and stirred at reflux temperature until the given time (see Table 2, step-II). The crude was diluted with CH_2Cl_2 (15 mL) and washed with water (2 x 10 mL). The organic layer was dried over anhydrous Na_2SO_4 , concentrated *in vacuo* and purified by column chromatography on silica gel to afford tetrasubstituted furans, **9**, **10**, **12** and **15**.

3.1.1.1-(5-Benzyl-2-methyl-4-phenylfuran-3-yl)ethanone (9)

¹H NMR (300 MHz, CDCl_3): δ 7.46-7.02 (m, 10H, Ar), 3.77 (s, 2H, CH_2), 2.53 (s, 3H, =C- CH_3), 1.87 (s, 3H, COCH_3): MASS (ESI) (m/z): 291 [M+H]⁺

3.1.2 Ethyl 5-benzyl-2-methyl-4-phenylfuran-3-carboxylate (10)

¹H NMR (300 MHz, CDCl_3): δ 7.30-7.00 (m, 10H, Ar), 4.01 (q, J = 6.7 Hz, 2H, OCH_2), 3.76 (s, 2H, CH_2Ph), 2.50 (s, 3H, =C- CH_3), 0.99 (t, J = 6.7 Hz, 3H, CH_2CH_3), MASS (ESI) (m/z): 321 [M+H]⁺

3.1.3.2-Benzyl-3-phenyl-6,7-dihydrobenzofuran-4(5H)-one (12)

Colorless solid, M.P.: 100-102 °C

FT-IR (neat): 2948, 1676, 1574, 1494, 1451 cm^{-1}

¹H NMR (300 MHz, CDCl_3): δ 7.35-7.08 (m, 10H, Ar-H), 3.90 (s, 2H, Ph-CH_2), 2.79 (t, J = 6.0 Hz, 2H, CO-CH_2), 2.41 (t, J = 6.0 Hz, 2H, = COH-CH_2), 2.10-2.04 (m, 2H, $\text{CH}_2\text{-CH}_2\text{-CO}$), ¹³C NMR (75 MHz, CDCl_3): δ 193.9, 166.,4, 150.3, 137.9, 131.4, 129.7, 128.5, 128.3, 127.9, 127.3, 126.5, 126.4, 38.5, 32.0, 3.7, 22.4, HRMS (ESI): calcd for $\text{C}_{21}\text{H}_{19}\text{O}_2$, 303.1380 [M+H]⁺; found 303.1392

3.1.4.2-Benzyl-3-(1-tosyl-1H-indol-3-yl)-4H-furo [3,2-c]chromen-4-one (15)

Colorless solid, M.P.: 80-85 °C, FT-IR (neat): 3081, 1728, 1649, 1465, 1419 cm^{-1} ¹H NMR (300 MHz, CDCl_3): δ 8.01 (d, J = 8.3 Hz, 1H, Ar-H), 7.89-7.78 (m, 3H, Ar-H), 7.53-7.12 (m, 14H, Ar-H, =C-N), 4.12 (s, 2H, Ph-CH_2), 2.35 (s, 3H, Ar- CH_3) ¹³C NMR (75 MHz, CDCl_3): δ 157.5, 157.3, 154.5, 152.5, 145.1, 136.7, 134.9, 130.7, 129.9, 128.8, 128.4, 127.1, 126.9, 126.7, 124.9, 124.4, 123.4, 120.9, 120.5, 117.2, 113.7, 112.1, 111.1, 33.1, 29.6, HRMS (ESI): calcd for $\text{C}_{33}\text{H}_{24}\text{NO}_5\text{S}$, 546.1370 [M+H]⁺; found 546.1361

4.0 Conclusion

In conclusion, we have provided the suitable method for the preparation of benzopyrans and furans using the mild reagent Polymer supported pTSA, which is economic reagent and commercially available and found as

selective in the synthesis of the targeted molecules in providing the better yields.

5.0 Acknowledgements:

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6.0 References

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