

## Ceric Ammonium Nitrate-mediated Oxidative Cycloaddition of 1,3-Dicarbonyls to $\beta$ -Aryl- $\alpha, \beta$ -unsaturated Ketones

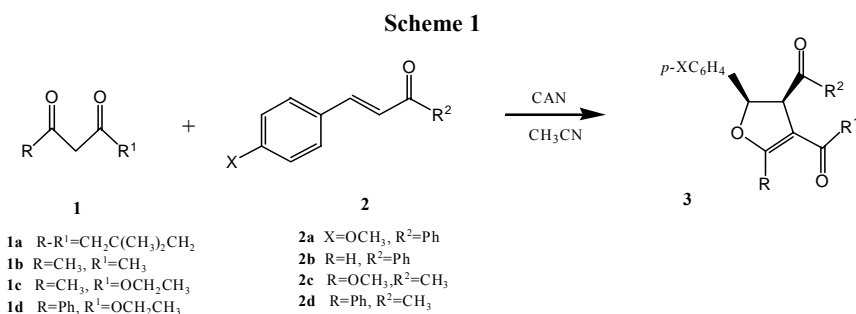
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**Abstract:** Regio and stereoselective synthesis of substituted dihydrofurans were accomplished by ceric ammonium nitrate mediated oxidative cycloaddition of 1,3-dicarbonyls to  $\beta$ -aryl- $\alpha, \beta$ -unsaturated ketones in moderate yields.

**Keywords:** ceric ammonium nitrate, cycloaddition, dihydrofurans, dicarbonyls compounds,  $\beta$ -aryl  $\alpha, \beta$ -unsaturated ketones,

The oxidative addition of carbon-centred radicals to alkenes mediated by metal salts ( $\text{Mn}^{\text{III}}$ ,  $\text{Ce}^{\text{IV}}$ ,  $\text{Hg}^{\text{II}}$ ,  $\text{Pd}^{\text{IV}}$ ,  $\text{Ag}^{\text{I}}$ , and  $\text{Cu}^{\text{II}}$ ) has received considerable attention over last decade in organic synthesis for construction of carbon-carbon bond<sup>1-5</sup>. Among these, manganese(III) acetate and ceric(IV) ammonium nitrate (CAN) have been used most efficiently. Recently, CAN-mediated oxidative cycloaddition of 1,3-dicarbonyl compounds to alkenes<sup>6</sup>, conjugated compounds<sup>7</sup>, enol silyl ethers<sup>8</sup>, and alkynes<sup>9</sup>, has been studied extensively. Although these reactions have aroused great interest, there is little information available on the CAN-mediated oxidative cycloaddition of 1,3-dicarbonyl compounds to  $\alpha, \beta$ -unsaturated ketones as radical acceptor. We describe here our recent exploitation of the CAN-mediated regioselective oxidative cycloaddition of 1,3-dicarbonyl compounds to  $\beta$ -aryl- $\alpha, \beta$ -unsaturated ketones to afford 5-aryl-3,4-diacyl-4,5-dihydrofurans stereoselectively and in moderate yields which would be used as synthetic intermediates of naturally occurring lignans.<sup>10</sup> (Scheme 1).



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**Table 1** Preparation of compounds **3a-n**

Reagents	Products <sup>a</sup>	Yield <sup>b</sup> (%)	Reagents	Products <sup>a</sup>	Yield <sup>b</sup> (%)
<b>1a/2a</b>	<b>3a</b> 	65	<b>1a/2c</b>	<b>3h</b> 	61
<b>1b/2a</b>	<b>3b</b> 	48	<b>1b/2c</b>	<b>3i</b> 	52
<b>1c/2a</b>	<b>3c</b> 	65	<b>1c/2c</b>	<b>3j</b> 	71
<b>1d/2a</b>	<b>3d</b> 	75	<b>1d/2c</b>	<b>3k</b> 	65
<b>1a/2b</b>	<b>3e</b> 	57	<b>1a/2d</b>	<b>3k</b> 	54
<b>1b/2b</b>	<b>3f</b> 	47	<b>1b/2d</b>	<b>3m</b> 	35
<b>1c/2b</b>	<b>3g</b> 	62	<b>1c/2d</b>	<b>3n</b> 	58

<sup>a</sup> Products **3a-n** all have satisfactory <sup>1</sup>H NMR, <sup>13</sup>C NMR, MS and HRMS spectra. <sup>b</sup> Isolated yields.

As shown by the results in the **Table 1**, with respect to the  $\alpha,\beta$ -unsaturated ketones, the yields of dihydrofuran from **2a** or **2c** are relatively higher than those from **2b** or **2d**. This difference may be derived from the stabilization effect of methoxy group to benzyl radical produced from the regioselective addition of dicarbonyl methylidyne radical to the  $\alpha$ -position of **2a** or **2c**. It is also observed that the yield of dihydrofurans from **1c** with **2a-d** obviously decreased. By the comparative experiments we found that it was resulted from the competitively oxidative dimerisation of **1c** which decreased the reaction proportion of **1c** with  $\alpha,\beta$ -unsaturated ketones. The yields of dihydrofurans were also influenced by reaction conditions. Comparatively, the selected procedure was favorable for increasing yield of dihydrofurans to other procedures, e.g. at room temperature or in methanol or adding CAN solid in portions. The cis-stereochemistry at C-2 and C-3 in **3a-n** was assigned by coupling constants ( $J=5.8-7.2$ ) between H-2 and H-3 and the analogy with the earlier works<sup>11</sup>, and was further supported by the NOE experiment.

### General procedure

To a stirred mixture of 1,3-dicarbonyl compounds (1.1 mmol) and  $\beta$ -aryl- $\alpha,\beta$ -unsaturated

ketones (1.0 mmol) and  $\text{NaHCO}_3$  (420 mg, 5.0 mmol) in anhydrous acetonitrile (10 mL) was added dropwise to 15 mL acetonitrile solution of CAN (1.20 g, 2.2 mmol) at  $0^\circ\text{C}$ . The reaction mixture was stirred until the disappearance of the reddish brown colour of CAN. The mixture was diluted with water (50 mL) and extracted with Ethyl acetate (50 mL). The combined organic extracts were washed with water, and dried with anhydrous  $\text{Na}_2\text{SO}_4$ . The residual obtained after removal of the solvent under reduced pressure was purified by column chromatography over silica gel (10% acetone in petroleum ether) to afford the products.

### Acknowledgments

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### References and Notes

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- Spectral data for compound **3**. **3a**: colourless oil. HR-SIMS: 377.1748 ( $\text{C}_{24}\text{H}_{24}\text{O}_4+\text{H}$ , calcd.377.1747), EIMS ( $m/z$ , %): 376 ( $\text{M}^+$ , 5), 317 (1), 271 (29), 229 (7), 135 (100), 77 (45).  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ).  $\delta$  8.16 (d, 2H,  $J=8.6$ ), 7.54 (t, 1H,  $J=7.2$ ), 7.41 (t, 2H,  $J=7.2$ ), 7.21(d, 2H,  $J=8.6$ ), 6.99 (d, 2H,  $J=8.6$ ), 5.76 (d, 1H,  $J=5.8$ , -CH-), 5.02 (d, 1H,  $J=5.8$ , -CH-), 3.81 (s, 3H, -OCH<sub>3</sub>), 2.47 (s, 2H, -CH<sub>2</sub>-), 2.27 (s, 2H, -CH<sub>2</sub>-), 1.19 (s, 3H, -CH<sub>3</sub>), 1.16 (s, 3H, -CH<sub>3</sub>).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ).  $\delta$  198.91, 193.40, 177.08, 160.14, 136.24, 133.52, 131.44, 129.04, 128.47, 114.37, 112.7, 90.04, 55.27, 54.39, 50.88, 37.85, 34.35, 28.61, 28.49. **3d** colourless oil. HR-SIMS: 446.1966 ( $\text{C}_{27}\text{H}_{24}\text{O}_4+\text{NH}_4$ , calcd. 446.1962), EIMS ( $m/z$ , %): 428 ( $\text{M}^+$ , 6), 382 (2), 323 (31), 277 (29), 105 (100), 77 (57).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ).  $\delta$  7.98 (d, 2H,  $J=8.6$ ), 7.92(d, 2H,  $J=8.4$ ), 7.55 (t, 1H,  $J=7.6$ ), 7.46-7.38 (m, 5H), 7.33(d, 2H,  $J=8.6$ ), 6.93 (d, 2H,  $J=8.4$ ), 5.66 (d, 1H,  $J=7.2$ ), 5.32 (d, 1H,  $J=7.2$ ), 3.99 (q, 2H,  $J=7.2$ , OCH<sub>2</sub>), 3.78 (s, 3H, -OCH<sub>3</sub>), 0.91 (t, 3H,  $J=7.2$ , -CH<sub>3</sub>).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ).  $\delta$  199.80, 166.74, 163.88, 159.85, 136.52, 133.20, 131.97, 130.62, 129.47, 129.11, 128.53, 128.43, 127.45, 127.14, 114.18, 85.97, 59.72, 59.11, 55.07, 13.51. **3g**. colourless oil. HR-SIMS: 337.3942 ( $\text{C}_{21}\text{H}_{20}\text{O}_4+\text{H}$ , calcd.337.3935), EIMS ( $m/z$ , %): 336 ( $\text{M}^+$ , 3), 291 (1), 249 (4), 231 (97), 203 (21), 158 (32), 115 (27), 105 (97), 77 (100).  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  7.89 (d, 2H,  $J=8.6$ ), 7.54 (t, 1H,  $J=8.6$ ), 7.44-7.27 (m, 7H), 5.61 (d, 1H,  $J=6.8$ , -CH-), 5.08 (d, 1H,  $J=6.8$ , -CH-), 4.01 (quat, 2H, -OCH<sub>2</sub>), 2.41 (s, 3H, -CH<sub>3</sub>), 0.96 (t, 3H,  $J=8.4$ , -CH<sub>3</sub>).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  200.52, 170.04, 164.75, 144.76, 140.05, 136.77, 133.34, 132.73, 128.92, 128.69, 128.57, 128.51, 124.41, 125.58, 103.91, 87.20, 57.64, 14.16. **3n**: colourless oil. HR-ESIMS: 245.1174 ( $\text{C}_{15}\text{H}_{16}\text{O}_3+\text{H}$ , calcd. 245.1172), EIMS ( $m/z$ , %): 244 ( $\text{M}^+$ , 2), 227 (3), 201 (100), 159 (30), 115 (40) 105 (85), 77 (72).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ).  $\delta$  7.45-7.21(m,5H), 5.52 (d, 1H,  $J=6.8$ , -CH-), 4.19 (d, 1H,  $J=6.8$ , -CH-), 2.35 (s, 3H, -CH<sub>3</sub>), 2.29 (s, 3H, -CH<sub>3</sub>), 2.26 (s, 3H, -CH<sub>3</sub>).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  208.68, 192.91, 168.62, 139.74, 129.07, 128.88, 125.27, 115.89, 85.61, 63.33, 30.27, 28.82, 15.39.

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