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$Fe(HSO_4)_3$: An efficient, heterogeneous and reusable catalyst for *C*-alkylation of β-dicarbonyl compounds

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Abstract. $Fe(HSO_4)_3$(FHS) was used as an efficient catalyst for the heterogeneous addition of a series of benzylic and allylic alcohols to various β-dicarbonyl compounds, which afforded moderate to excellent yields of *C*-alkylated products in 1,2-dichloroethane. In comparison with the previous methods, the present research surprisingly exhibited higher reaction yields without formation of any by-products which could be formed by self-condensation of alcohols. Moreover, the catalyst can be readily recovered and reused up to five times with almost maintained reactivity and yields.

Keywords. β-Dicarbonyl compounds; ferric hydrogen sulphate $Fe(HSO_4)_3$; *C*-alkylation; heterogeneous catalyst.

1. Introduction

Alkylation of β-dicarbonyl compounds is one of the most common methodologies for C–C bond construction as a fundamental task in generating a wide range of valuable synthetic intermediates that are utilized in the synthesis of functional materials, natural products, and pharmaceuticals in organic synthesis. In recent years, among a variety of approaches for the alkylation of β-dicarbonyl compounds, direct addition of β-dicarbonyl compounds to alcohols (affording alkylated β-dicarbonyl compounds) has attracted much interest because only H_2O is generated as the side product.[1–7] In traditional protocols, hydroxy groups usually require pre-activation through transformation into good leaving groups such as halides, carboxylates, carbonates, and phosphonates before treating with β-dicarbonyl compounds.[8] Salt wastes which were produced inevitably in such processes would set limits for the industrial application and for the scope of substrates. In the last few years, chemists have focused on some acid-catalysed intermolecular additions of β-dicarbonyl compounds to alcohols, considering them to be the most promising approaches in this field. Various Lewis acids such as $InCl_3$,[1,9] $InBr_3$,[10] $FeCl_3$,[11–15] $Fe(ClO_4)_3$,[16] $M(OTf)_3$,[17,18] Lewis acidic ruthenium complex,[19] as well as montmorillonite,[20] *p*-toluenesulphonic acid[21] have been demonstrated to facilitate dehydrative substitution of allylic and benzylic alcohols with β-dicarbonyl compounds. In comparison to the traditional synthetic procedures, application of Lewis and BrÖnsted acids which has been successful in the alkylation of 1,3-dicarbonyl compounds using alcohols as electrophiles directly,[1–5,22] offers several potential advantages, such as wide availability of starting materials and generation of H_2O as the only side product. Despite this, many of these methods have major or minor disadvantages such as low yield of products, side product formation and tedious work-up procedures. In this study, ferric hydrogen sulphate $Fe(HSO_4)_3$, was used as an efficient catalyst for alkylation of a wide variety of β-dicarbonyl compounds.

2. Experimental

2.1 *General*

The products were purified by column chromatography. Purity determinations of the products were accomplished by TLC on silica gel polygram STL G/UV 254 plates. Melting points of products were determined with an Electrothermal Type 9100 melting point apparatus. The FT-IR spectra were recorded on an Avatar 370 FT-IR Therma Nicolet spectrometer. The NMR spectra were provided on Brucker Avance 400 MHz

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instruments in $CDCl_3$. Mass spectra were recorded with a CH7A Varianmat Bremem instruments at 70 eV; in m/z (rel %). Elemental analyses were performed using a Thermofinnigan Flash EA 1112 Series instrument. The known products were characterized by IR and ^1H NMR spectra and comparison of their melting points (or those of the derivatives) with authentic samples. Catalysts were prepared and purified by the method described in literature.[23]

2.2 *General procedure for benzylation of acetylacetone catalysed by ferric hydrogen sulphate*

Ferric hydrogen sulphate (0.06 g) was added to a solution of acetylacetone (1 mmol, 0.1 g) in 1,2-dichloroethane (2 mL) at 86°C. Benzhydrol (2 mmol, 0.368 g) was dissolved in 1,2-dichloroethane (2 mL) and added to the reaction mixture dropwise during 1 h. Progress of the reaction was monitored by TLC. After completion of the reaction, the catalyst was removed by filtration. The filtrate was washed with distilled water (3 × 4) and dried over Na_2SO_4. The concentrated residue was passed through a short silica gel column chromatography using EtOAc/hexane (1:10) as an eluent. After removing the solvent under reduced pressure, 3-benzhydryl pentane-2,4-dione was obtained in 80% yield.

2.2a *3-Benzhydryl-pentane-2,4-dione (table 2, entry 1)*: Solid, yield 80%, mp 93.5–95°C (Lit. 93–95°C);[1] FT-IR (KBr) ν_{max} 3060, 3027, 2958, 2923, 2850, 1729(C=O), 1698, 1462, 1265, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 25°C) δ 7.39–7.31 (m, 8H, aryl H), 7.21–7.18 (m, 2H, aryl H), 4.81 (d, J = 12.4 Hz, 1H, CHPh), 4.74 (d, J = 12.4 Hz,1H, $\underline{CH}C{=}OCH_3$), 2.02(s, 6H, 2 × $C{=}O\underline{CH_3}$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ 201.9 (COO), 145.0 (C), 129.5(CH), 128.5 (CH), 127.9 (CH), 51.6 (CH), 30.6(CH_3), 26.7(CH) ppm; MS (EI) m/z (%) 266 [M^+, 3%], 181 [M^+-2 ($CH_3C{=}O$)], 167 [M^+-(($CH_3C{=}O)_2CH$, H), 100%], 104 [M^+-(2 ($CH_3C{=}O$), Ph), 50%].

2.2b *Ethyl 2-benzhydryl-3-oxobutanoate (table 2, entry 2)*: Solid, yield 75%, mp 84–85.5°C (Lit. 88–90°C);[24] FT-IR (KBr) ν_{max} 3084, 3060, 3031, 2990, 2953, 1736 (C=O), 1703(C=O), 1662, 1494, 1361, 1145, 752, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 25°C) δ 7.39–7.25 (m, 10H, Ph), 4.86 (d, J = 6.4 Hz, 1H, CHCO), 4.23 (q, J = 7.2 Hz, 2H,$O\underline{CH_2}CH_3$) 3.38 (d, J = 6.4 Hz 1H, CHPh), 2.40 (s, 3H, $\underline{CH_3}CO$), 1.27 (t, J = 7.2 Hz, 3H, OCH_2 $\underline{CH_3}$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ 200.8 (C=O), 167.2 (COO), 136.7 (C), 128.7 (CH), 127.6CH), 126.4 (CH), 63.5(CH), 61.4 (CH), 32.1(CH_3), 30.1(CH_2), 14.0 (CH_3) ppm; MS (EI) m/z (%) 296 [M^+, 3%], 253 [M^+– $CH_3C{=}O$], 223 [M^+- $CH_3CH_2OC{=}O$], 181 [M^+-($CH_3C{=}O$, $CH_3CH_2OC{=}O$)], 167 [M^+– 129, 100%], 105 [M^+ -($CH_3C{=}O$, $CH_3CH_2OC{=}O$, Ph), 95%], 77 [M^+– 219, 72%], 43 [M^+– 253, 60%]; Elemental analysis data for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80; Found: C, 76.95; H, 6.77.

2.2c *Diethyl 2-benzhydrylmalonate (table 2, entry 3)*: Solid, yield 87%, mp 50–51.5°C (Lit. 53°C);[25] FT-IR (KBr) ν_{max} 3080, 3062, 3028, 2925, 2859, 1736 (C=O), 1714(C=O), 1660, 1493, 1453, 1265, 1059, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 25°C) δ 7.84–7.49 (m, 10H, Ph); 4.82 (d, J = 12.4 Hz,1H, $(Ph)_2\underline{CH}$), 4.76 (d, J = 12.4 Hz, 1H, $\underline{CH}C{=}O$), 3.97 (q, J = 6.8 Hz, 4H, 2 × $O\underline{CH_2}CH_3$), 0.99 (t, J = 6.8 Hz, 6H, 2 × $OCH_2\underline{CH_3}$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ 167.2(COO), 136.7(C), 128.5(CH), 127.6(CH), 126.4 (CH), 63.5 (CH_2), 61.4(CH), 30.1(CH), 14.0(CH_3) ppm; MS (EI) m/z (%) 326 [M^+,10%], 325 [M^+-H], 324 [M^+-2H], 249 [M^+-Ph, 72%], 181 [M^+-2(CH_3CH_2O C=O), 75%], 167 [M^+-(CH_3CH_2 OC=O)$_2$ CH, 75%], 166 [M^+-(($CH_3CH_2OC{=}O)_2$ CH, H),100%], 104 [M^+-222].

2.2d *Diethyl 2-benzhydryl-2-ethylmalonate (table 2, entry 4)*: Solid, yield 85%, mp 66.5–68°C(Lit. 67–69°C);[26] FT-IR (KBr) ν_{max} 3064, 2974, 2941, 2876, 1756 (C=O), 1732 (C=O), 1658, 1450, 1277, 1232, 1153, 1037, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 25°C) δ 7.39–7.25 (m, 10H, Ph), 5.83 (s, 1H, CHPh), 4.30 (q, J = 7.2 Hz, 4H, 2 × $O\underline{CH_2}$ CH_3), 1.94 (q, J = 7.2 Hz, 2H, $\underline{CH_2}CH3$), 1.27 (t, J = 7.2 Hz, 6H, 2 × $OCH_2\underline{CH_3}$), 0.90 (t, J = 7.2 Hz, 3H, $CH_2\underline{CH_3}$) ppm;^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ169.5(COO), 145.9 (C), 128.4(CH), 127.4(CH), 125.4(CH), 70.3(C), 61.3(CH_2), 39.5(CH), 25.2(CH_2), 14.1(CH_3), 11.8 (CH_3) ppm; MS (EI) m/z (%) 354 [M^+, 3%], 309 [M^+- CH_3CH_2O, 65%], 281 [M^+- CH_3 $CH_2OC{=}O$, 60%], 187 [M^+- $(Ph)_2CH$, 85%], 104 [M^+-250, 100%], 77 [M^+-277,62%], 45 [M^+-309, 65%]; Elemental analysis data for $C_{22}H_{26}O_4$: C,74.55; H, 7.39; Found: C, 74.35; H, 7.30.

2.2e *Dimethyl 2-benzhydryl-2-chloromalonate (table 2, entry 5)*: Solid, yield 90%, mp 87–89.5°C; FT-IR (KBr) ν_{max} 3080, 3056, 3023, 2924, 2852, 1772 (C=O), 1751 (C=O), 1437, 1309, 1197, 1167, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 25°C) δ 7.84–7.49 (m, 10H,

aryl H), 5.58 (s, 1H, CH Ph), 3.63 (s, 6H, 2 × $COCH_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ 169.8 (C=O), 147.6(C), 132.4(CH), 130.1 (CH), 128.3(CH), 84.1(C), 54.6(CH_3), 44.6(CH) ppm; MS (EI) *m/z* (%) 334 [M^++2,4%], 332 [M^+, 12.5%], 297 [M^+-Cl], 179 [M^+-(Cl, 2(CH_3OC=O)), 95%], 167 [M^+-(CH_3OC=O)$_2$ CCl, 77%], 105 [M^+-(2 (CH_3OC=O), Ph, Cl), 85%]; Elemental analysis data for $C_{18}H_{17}ClO_4$: C, 64.97; H, 5.15; Found: C, 64.65; H, 5.48.

2.2f *5-benzhydryl-2,2-dimethyl-1,3-dioxane-4,6-dione (table 2, entry 6)*: Solid, yield 95%, mp 133–134°C(Lit. 134–135°C);[27] FT-IR (KBr) ν_{max} 3084, 3060, 3030,2949, 1752(C=O), 1727(C=O), 1495, 1301, 1220, 1160, 756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C) δ 7.46–7.23 (m, 10H, aryl H), 5.60 (d, *J* = 6.4Hz, 1H, CHCO), 3.97 (d, *J* = 6.4 Hz, 1H, CH Ph), 1.27 (s, 6H,2 × CH_3), ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ 171.0 (C=O), 146.0(C), 129.2(CH), 128.6 (CH), 127.7(CH), 101.7(C), 58.1(CH), 30.8(CH), 26.0(CH_3) ppm; MS (EI) *m/z* (%) 310 [M^+], 270 [M^+-C=C=C, 40%], 269 [M^+- (C=C=C,H), 43%], 267 [M^+ - OC=O,85%], 181 [M^+ -(130H), 90%], 167 [M^+ - 143, 85%]; Elemental analysis data for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85; Found: C,73.35; H, 5.80.

2.2g *2-benzhydryl-3-hydroxy-5,5-dimethylcyclohex-2-enone (table 2, entry 7)*: Solid, yield 75%, mp 120–122°C; FT-IR (KBr) ν_{max} 3456, 3060, 3031, 2962, 2925, 2872, 1737 (C=O), 1714 (C=O), 1061, 1493, 1266, 740 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C) δ 15.36 (s,1H, OH-C=C), 7.45–7.22 (m, 10H, aryl H), 4.68 (s, 1H, *CH* Ph), 2.98 (d,*J* = 6.8 Hz, 2H, CH_2C=O) 1.84 (d, *J* = 6.8 Hz, 2H, CH_2COH) 1.28 (s, 6H, 2 × CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ 196.8 (C=O), 186.5 (C), 141.1 (C), 129.3 (CH), 128.7 (CH), 126.9(CH), 110.7(C), 57.8(CH_2), 60.0 (CH_2), 36.7(CH), 34.1(C), 29.7 (CH_3) ppm; MS (EI) *m/z* (%) 306 [M^+, 10%], 305 [M^+-H], 229 [M^+-Ph, 65%], 167 [M^+-139, 85%], 139 [M^+-$(Ph)_2CH$, 60 %], 77 [M^+-229, 80%]; Elemental analysis data for $C_{21}H_{22}O_2$: C, 82.32; H, 7.24; Found: C, 82.50; H, 7.30

2.2h *3-(1-Phenylethyl)pentane-2,4-dione (table 2, entry 8)*: Solid, yield 70%, mp 43–45°C(Lit.46–47°C);[24] FT-IR (KBr) ν_{max} 3088, 3060, 3027, 2965, 2929, 2872, 1728 (C=O), 1698, 1600, 1493, 1356, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C) δ 7.31–7.26 (m, 5H, Ph), 3.89 (d,*J* = 7.2 Hz, 1H,*CH*CO), 3.21–3.16 (m, 1H, $CHCH_3$), 2.64 (s, 6H, 2 × CH_3CO), 1.50 (d, *J* = 6.4 Hz,3H, CH_3CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ 204.0 (C = O), 145.8 (C), 128.5 (CH),127.4(CH), 125.4 (CH), 70.3(CH), 32.5 (CH_3), 28.3(CH), 25.1 (CH_3) ppm; MS (EI) *m/z* (%)204 [M^+,8%], 189 [M^+-CH_3, 90%], 105 [M^+-$(CH_3C$=O)$_2$CH, 95%], 99 [M^+-105, 60%]; Elemental analysis data for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90; Found: C, 76.35; H, 7.34.

2.2i *Ethyl 2-acetyl-3-phenylbutanoate (table 2, entry 9)*: Oil,[28] yield 70%; FT-IR (neat) ν_{max} 3056, 3029, 2974, 2934, 2876, 1748 (C=O), 1715 (C=O), 1453, 1358, 1205, 1177, 1022, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C) δ 7.23–7.05 (m, 5H, Ph), 3.88 (q,*J* = 7.2 Hz, 2H, OCH_2CH_3), 3.64 (d, *J* = 10.8 Hz,1H, CHCO), 3.59–3.52 (m, 1H, $CHCH_3$), 1.85 (s, 3H, CH_3CO), 1.23 (d, *J* = 6.8 Hz,3H, CH_3CH),0.93 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ 200.2 (C=O), 165.5 (COO), 147.9 (C), 128.9 (CH), 128.0(CH), 127.8 (CH), 67.3(CH), 65.4 (CH_2), 28.1(CH_3), 27.2 (CH), 16.5(CH_3), 14.9 (CH_3) ppm; MS (EI) *m/z* (%) 234 [M^+, 12%], 219 [M^+-CH_3, 72%], 157 [M^+-Ph, 82%], 105 [M^+-129, 85%], 77 [M^+-157, 95%].

2.2j *Diethyl 2-(1-phenylethyl)malonate (table 2, entry 10)*: Oil[29] yield 70%; FT-IR (neat) ν_{max} 3060, 2984, 2941, 2908, 2872, 1752 (C=O), 1735 (C=O), 1370, 1331, 1269, 1190, 1150, 1035, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C) δ 7.39–7.26 (m, 5H, Ph), 4.68–4.62 (m, 1H, CH Ph), 4.28(q, *J* = 7.2 Hz,4H, 2 × OCH_2CH_3), 3.65 (d,*J* = 7.6 Hz, 1H, CHCOO), 1.51 (d, *J* = 7.6 Hz, 3H, CH_3CH), 1.20 (t, *J* = 7.2 Hz,6H, 2 × OCH_2CH_3) ppm;^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ 170.0 (COO), 148. 1(C), 132.4 (CH), 130.1(CH), 128.3 (CH), 64.9 (CH_2), 61.1 (CH), 27.5(CH), 20.1(CH_3), 14.8 (CH_3) ppm; MS (EI) *m/z* (%) 264 [M^+,5%], 249 [M^+-CH_3, 80%], 159 [M^+-($PhCHCH_3$), 98%], 105 [M^+-159, 85%], 77 [M^+-187, 90%].

2.2k *Diethyl 2-ethyl-2-(1-phenylethyl) malonate (table 2, entry 11)*: Oil,[30] yield 75%; FT-IR (neat) ν_{max} 3056, 2963, 2925, 2878, 2851, 1756 (C=O), 1732 (C=O), 1466, 1267, 1207, 745 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$, 25°C) δ 7.38–7.24 (m, 5H, *Ph*), 4.87 (q, *J* = 6.4 Hz, 4H, 2 × OCH_2CH_3), 4.19 (q, *J* = 6.4 Hz,1H, CHPh), 1.92 (q, *J* = 6.4 Hz,2H, CH_2CH_3), 1.48 (d, *J* = 6.4 Hz, 3H, CH_3CHPh), 1.27 (t, *J* = 6.4 Hz, 6H, 2 × OCH_2CH_3), 0.60 (t, *J* = 6.4 Hz, 3H, CH_2CH_3) ppm;^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ 169.5(COO), 139.9 (C), 128.4(CH), 127.4(CH), 125.4(CH), 70.3(C), 61.3(CH_2), 33.5(CH), 25.2(CH_2), 22.2(CH_3), 14.1(CH_3), 11.8 (CH_3) ppm;

MS (EI) *m/z* (%) 292 [M^+,10%], 277 [M^+-CH_3, 75%], 219 [M^+-($COOCH_2CH_3$), 95%], 77 [M^+-215, 90%],43 [M^+-249, 98%].

2.2l *Dimethyl 2-chloro-2-(1-phenylethyl) malonate (table 2, entry 12)*: Solid, yield 80%, mp 38–39.5°C; FT-IR (KBr) ν_{max} 3056, 3029, 2974, 2934, 2876, 1772 (C=O), 1751(C=O), 1495, 1437, 1309, 1259, 1197, 1157, 1022, 736, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 25°C) δ 7.37–7.25 (m, 5H, Ph), 4.62 (q, J = 7.2 Hz,1H, $CHCH_3$), 3.81 (s, 6H, 2 × OCH_3), 1.36 (d,J = 7.2 Hz, 3H,$CHCH_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ 169.8 (COO), 147.6(C), 132.4 (CH), 130.1(CH), 128. 3(CH), 84.1(C), 51.6(CH_3), 32.4(CH), 10.1 (CH_3) ppm; MS (EI) *m/z* (%) 272 [M^++2, 4%], 270 [M^+, 10%], 239 [M^+-CH_3O, 92%], 235 [M^+ - Cl, 80%], 193 [M^+ - ph, 70%], 179 [M^+-(Ph, CH_3), 80%], 164 [M^+-(CH_3CHPh, H), 85%], 105 [M^+ -165, 85%], 77 [M^+ -193, 60%]; Elemental analysis data for $C_{13}H_{15}ClO_4$: C, 57.68; H, 5.59; Found: C, 58.07; H, 5.62.

2.2m *2,2-Dimethyl-5-(1-phenylethyl)-1,3-dioxane-4, 6-dione (table 2, entry 13)*: Solid, yield 80%, mp 99.5–101.5°C (Lit.101°C);[31] FT-IR (KBr) ν_{max} 3064, 3031, 2959, 2930, 2872, 1727 (C=O), 1454, 1276, 1207, 1071, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 25°C) δ 7.41–7.27 (m, 5H, Ph), 4.95–4.89 (m, 1H, $CHCH_3$), 3.55 (d, J = 7.2 Hz,1H, CHCO), 1.88(s, 6H, 2 × CH_3), 1.52(d, J = 6.8 Hz,3H, $CHCH_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ 166.7 (C=O), 145.9(C), 128.4(CH), 127.4(CH), 125.4(CH), 104.3(C), 61.5(CH), 29.7(CH), 25.1(CH_3), 14.0(CH_3) ppm; MS (EI) *m/z* (%) 248 [M^+, 4%], 233 [M^+-CH_3], 208 [M^+- C=C=C], 105 [M^+-143, 100%], 77 [M^+-171, 57%], 28 [M^+-220, 66%]; Elemental analysis data for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50; Found: C, 67.35; H, 6.30

2.2n *3-hydroxy-5,5-dimethyl-2-(1-phenylethyl) cyclohex-2-enone (table 2, entry 14)*: Solid, yield 85%, mp 109.5–110.5°C; FT-IR (KBr) ν_{max} 3476, 3060, 3030, 2957, 2924, 2853, 1717 (C=O), 1620, 1496, 1453, 1265, 1115, 743, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 25°C) δ 15.00(s, 1H, *OH*-C=C), 7.41–7.27 (m, 5H, Ph), 3.56 (q, J = 7.2 Hz, 1H, $CHCH_3$), 2.49 (d, J = 7.2 Hz, 2H, CH_2C=O), 1.99 (d, J = 7.2 Hz, 2H, CH_2COH), 1.41 (d, J = 7.2 Hz, 3H, $CHCH_3$), 1.05 (s, 6H, 2 × CH_3) ppm;^{13}C NMR (100 MHz, CDCl3, 25°C) δ 196.8 (C=O), 180.0 (*C*OH), 137.6(C), 132.4(CH), 130.1(CH), 128.3(CH), 110.1 (C), 52.3 (CH_2), 46.6 (CH_2), 43.7(CH), 30.0(C), 28.9 (CH_3), 18.1 (CH_3) ppm; MS (EI) *m/z* (%) 244 [M^+, 5%], 229 [M^+-CH_3, 66%], 167 [M^+-Ph, 57%], 105 [M^+-139, 85%], 77 [M^+-167, 78%]; Elemental analysis data for $C_{16}H_{20}O_2$: C, 78.65;H, 8.25; Found: C,78.49; H, 8.59.

2.2o *Ethyl 2-acetyl-3-phenylpent-4-enoate (table 2, entry 15)*: Oil,[32] yield 85%; FT-IR (neat) ν_{max} 3081, 3059, 3025, 2923, 2854, 1740(C=O), 1711(C=O), 1600, 1493, 1452, 1029, 746, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 25°C) δ 7.41–7.18 (m, 5H, *Ph*), 6.29–6.19 (m, 1H, $CHCH$=CH_2), 4.86 (d, J= 7.6 Hz,2H, CH=CH_2), 4.59 (t, J = 7.6 Hz,1H, $CHCH$=CH_2), 4.35 (q,J = 7.2 Hz, 2H, OCH_2CH_3), 3.17 (d, J = 7.6 Hz, 1H, *CH*C=O), 2.10 (s, 3H, CH_3CO); 2.19 (t, J = 7.2 Hz,3H,OCH_2CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C) δ 196.82 (C=O), 170.0(COO), 140.1 (C), 137.6(CH), 132.4(CH), 130.1(CH), 128.3 (CH), 115.1(CH_2), 64.9(CH), 61.1(CH_2), 30.1(CH), 27.5(CH_3), 14.8(CH_3) ppm; MS (EI) *m/z* (%) 246 [M^+,12%], 201 [M^+- CH_3CH_2O, 98%], 169 [M^+- Ph,82%], 129 [M^+-117, 80%], 77 [M^+-169, 82%].

2.2p *Ethyl 2-(3-methoxybenzyl)-3-oxobutanoate (table 2, entry 16)*: Solid, yield 65%, mp 64–65.5°C (Lit.65–67°C);[33] FT-IR (KBr) ν_{max} 3056, 3029, 2974, 2954, 2876, 1744 (C=O), 1718 (C=O), 1604, 1585, 1490, 1465, 1316, 1267, 736 cm^{-1}; MS (EI) *m/z* (%) 250 [M^+, 8%], 220 [M^+- CH_3O,95%], 206 [M^+- CH_3 CH_2O], 177 [M^+- CH_3CH_2O C=O], 175 [M^+-(CH_3O, CH_3CH_2O), 90%], 121 [M^+- 129, 85%], 107[M^+-143, 80%]; Elemental analysis data for $C_{14}H_{18}O_4$: C, 67.18;H, 7.25; Found: C, 67.15;H, 7.30.

2.2q *Ethyl 2-benzyl-3-oxobutanoate (table 2, entry 17)*: Oil,[34] yield 85%; FT-IR (neat) ν_{max} 3031, 2977, 2929, 1740 (C=O), 1716 (C=O), 1650, 1450, 1367, 1317, 1245, 1152, 1040, 898, 755 cm^{-1}; MS (EI) *m/z* (%) 220 [M^+, 5%], 205 [M^+- CH_3, 75%], 175 [M^+-CH_3CH_2O, 92%], 129 [M^+-$PhCH_2$, 75%], 77 [M^+-143, 75%], 45 [M^+- 175, 88%] .

2.2r *Ethyl 2-(4-chlorobenzyl)-3-oxobutanoate (table 2, entry 18)*: Oil,[35] yield 90%; FT-IR (neat) ν_{max} 3080, 3056, 3023, 2924, 2852, 1743 (C=O), 1716 (C=O), 1648, 1410, 1367, 1318, 1252, 1041, 1014, 800 cm^{-1}; MS (EI) *m/z* (%) 256 [M^++2, 4%], 254 [M^+, 10%], 219 [M^+- Cl, 80%], 209 [M^+- CH_3CH_2O, 75%], 143 [M^+-ClPh, 75%], 77 [M^+-177, 82%], 43 [M^+-211, 80%].

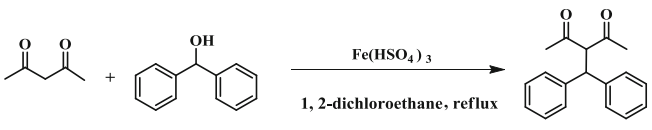
3. Results and Discussion

Optimization of reaction conditions was carried out for the reaction of acetylacetone and benzhydrol in the presence of $Fe(HSO_4)_3$ under various reaction parameters in order to achieve maximum chemical yield at the lowest reaction time and lowest reaction temperature. The general reaction is outlined in scheme 1 and the representative results are shown in table 1.

In the absence of any catalyst and solvent, there was no conversion to 3-benzhydryl pentane-2,4-dione (table 1, entries1-2). At room temperature, in the presence of 20 mol% of $Fe(HSO_4)_3$, there is no tendency between acetylacetone and benzhydrol to produce the desired product (table 1, entry 3). In refluxing 1,2-dichloroethane, $Fe(HSO_4)_3$ was identified as a catalyst for 3-benzhydryl pentane-2,4-dione formation in high yield but in prolonged reaction time (table 1, entry 4). During optimization reactions of acetylacetone with benzhydrol, we notice that the rate of addition of benzhydrol plays an important role in the yield of alkylated product. Quick addition of benzhydrol leads to the formation of excess amount of symmetric ether which was obtained from self-condensation of benzhydrol. To prevent self-condensation of benzhydrol in all of the following reactions, addition of benzhydrol should be performed dropwise, which consumes more time. In this manner, alkylated product was obtained as the chief product. In an effort to develop better reaction conditions, using 1/2 molar ratio of acetylacetone/benzhydrol in refluxing 1,2-dichloroethane produces corresponding alkylated product in short reaction time (10 min), as addition of benzhydrol should be carried out more slowly, the time of reaction was prolonged up to 2 h (table 1, entry 5). The best amount of catalyst in the formation of 3-benzhydryl pentane-2,4-dione from the reaction of acetylacetone with benzhydrol is 20 mol%. Increasing the amount of catalyst up to 30 mol% does not have any influence on the reaction rate but applying 10 mol% of $Fe(HSO_4)_3$ yields the product in longer reaction time (table 1, entries 6 and 7).

Different solvents were screened for the preparation of 3-benzhydryl pentane-2,4-dione from the reaction of acetylacetone with benzhydrol in the presence of 20 mol% of $Fe(HSO_4)_3$. The catalytic effect of $[Fe(HSO_4)_3$ was efficiently decreased in toluene, $CHCl_3$, CH_2Cl_2, 1,4-dioxane and CH_3NO_2 (table 1, entries 8–12). No product was obtained when the reaction was performed in refluxing H_2O, CH_3CN, THF and acetone (table 1, entries 13–16). As shown in table 1, when the reaction was performed in the presence of $Fe(HSO_4)_3$/silica, 3-benzhydryl pentane-2,4-dione was obtained in longer reaction time (table 1, entry 17).

Under these optimized conditions, addition of different alcohols to diverse β-dicarbonyl compounds was investigated in the presence of $Fe(HSO_4)$. The results are summarized in table 2. To prevent side product formation, addition of alcohols to the reaction mixture should be performed drop by drop and preparation of alkylated products should be prolonged. According to the results obtained from table 2, in the presence of $Fe(HSO_4)_3$, alkylation reactions of different β-dicarbonyl compounds by benzhydrol, 1-phenylethanol and cinnamyl alcohol were completed faster than alkylation with benzyl alcohol and substituted benzyl alcohols, due to higher stability of the carbocation intermediate. Reaction of acyclic and cyclic β-dicarbonyl compounds with benzhydrol was carried out in the presence of $Fe(HSO_4)_3$ and the corresponding products were produced in good to excellent yields (table 2, entries 1–7). Reaction of β-dicarbonyl compounds with 1-phenyl ethanol, cinnamyl alcohol, benzyl alcohol and substituted benzyl alcohols are also effective and yields of desired products are comparable to those of the reaction with benzhydrol (table 2, entries 8–18). Surprisingly, this method gave good yields with primary benzylic alcohols. Reaction of *ethyl acetoacetate* with benzyl alcohol and substituted benzyl alcohol affords moderate yield and much longer reaction time is needed. In comparison, presence of the electron-donating substituent in benzene ring can increase reactivity of benzylic alcohol, while the electron-withdrawing substituent in benzene ring seems to have a negative effect on benzylation reaction (table 2, entries 16–18). The catalyst is inapplicable for conversion of isopropyl alcohol (aliphatic secondary alcohol) to its corresponding product. On the basis of the proposed mechanism in scheme 2 and the experimental results obtained from table 2, alcohols with more stable carbocations are applicable for *C*-alkylation of β-dicarbonyl compounds. Also, it is seen from table 2 that more acidic β-dicarbonyl compounds were alkylated faster than the others. Lower acidic diethyl malonate and diethyl ethyl malonate react with benzhydrol in longer reaction time than dimethyl chloro malonate (e.g., compare



Scheme 1. *C*-alkylation of β -dicarbonyl compounds.

Table 1. Synthesis of 3-benzhydryl pentane-2,4-dione in the presence of $Fe(HSO_4)_3$ in various solvents, different molar ratios of reactants at different temperatures.

Entry	Molar ratio of Acetylacetone/ benzhydrol	Catalyst (mol%)	Solvent	Temperature (°C)	Time (h)	Conversion (%)
1	1/1	none	None	Room temperature	24	0
2	1/1	none	1,2-Dichloroethane	Room temperature	24	0
3	1/1	20	1,2-Dichloroethane	Room temperature	24	0
4	1/1	20	1,2-Dichloroethane	Reflux	24	100
5	1/2	20	1,2-Dichloroethane	Reflux	2	100
6	1/2	30	1,2-Dichloroethane	Reflux	2	100
7	1/2	10	1,2-Dichloroethane	Reflux	3	100
8	1/2	20	Toluene	Reflux	3	100
9	1/2	20	$CHCl_3$	Reflux	7	100
10	1/2	20	CH_2Cl_2	Reflux	12	100
11	1/2	20	1,4-Dioxane	Reflux	24	100
12	1/2	20	CH_3NO_2	Reflux	8	100
13	1/2	20	H_2O	Reflux	24	0
14	1/2	20	CH_3CN	Reflux	24	0
15	1/2	20	THF	Reflux	24	0
16	1/2	20	Acetone	Reflux	24	0
17	1/2	20	1,2-Dichloroethane	Reflux	4	100

*Reaction was performed in the presence of $Fe(HSO_4)_3$/Silica

entries 3, 4 with 5). In general, the reaction proceeded smoothly for all cases and *C*-alkylated products were obtained without formation of any side products (symmetric ethers), in very good to excellent yields. As alcohols sensitive to acid- catalyzed dehydration also tolerated this method, alkylation reaction by using 1-phenyl ethanol does not suffer from formation of styrene which can be obtained by dehydration of alcohol in acidic media (table 2, entries 8–14).

As shown in table 2, 5,5-dimethylcyclohexane-1,3-dione which is in equilibrium with its enol form 3-hydroxy-5,5-dimethylcyclohex-2-enone, was alkylated by benzhydrol and 1-phenyl ethanol to 2-benzhydryl-3-hydroxy-5,5-dimethylcyclohex-2-enone and 3-hydroxy -5,5-dimethyl-2-(1-phenylethyl)cyclohex-2-enone, respectively in the presence of $Fe(HSO_4)_3$. The FT-IR spectra of the corresponding products show absorption bands around 3600–3200 and 1737–1714 cm^{-1} due to hydroxyl and carbonyl groups of the more stable enol form of the alkylated product. Also, in ^1H NMR spectrum, a signal at 15 ppm is assigned to the OH proton of the more stable enol form of the *C*-alkylated product (table 2, entry 7, 14).

Order of addition of the reactants (β-dicarbonyl compound and alcohol) is a very important factor in alkylation reactions in the presence of $Fe(HSO_4)_3$. To minimize formation of side products (symmetric ethers), alcohol should be added drop by drop to the solution of β-dicarbonyl compound in the presence of catalyst. In our experiments, completion of the reaction was confirmed by disappearance of the β-dicarbonyl compounds or alcohols on TLC followed by disappearance of OH stretching frequency of enol or alcohol at 3400–3200 cm^{-1} in FTIR spectra. In ^{1}HNMR spectrum, CH proton of *C*-alkylated product showed (4.74–3.64 ppm) a downfield shift as compared to the CH protons of β-dicarbonyl compound. Also, in ^{13}C NMR, a signal at 110–61 ppm is assigned to the alkylated carbon which was shifted to downfield. The structure of all products was further confirmed by mass spectrometry and CHN analysis.

On the basis of these observations, we are prompted to propose the following mechanism (scheme 2) for alkylation of β-dicarbonyl compound with alcohols.

It is seen that the addition reaction is in fact a BrØnsted acid catalysed reaction. The catalytic process begins with concomitant conversion of β-dicarbonyl compound to enolic form **I** and protonation of alcohol, by hydrogen sulphate which subsequently affords stable carbocation **III** from protonated form **II** by dehydration process. Nucleophilic attack of **I** to carbocation **III** gives the *C*-alkylated product and releases the proton for the next catalytic cycle. Symmetric ether **IV** as by-product was produced by the reaction of carbocation **III** with alcohol. Also, the nucleophilic attack of alcohol to **I** leads to **V** which by losing alkoxy group produces

Table 2. Alkylation of structurally different β-dicarbonyl compounds in the presence of $Fe(HSO_4)_3$.

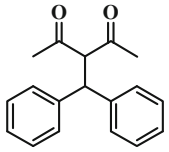
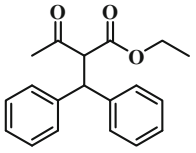
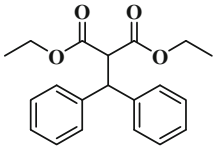
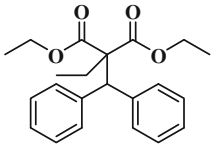
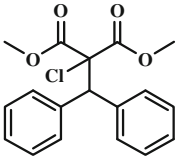
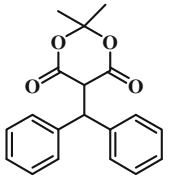
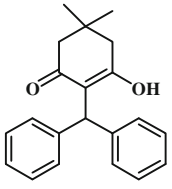
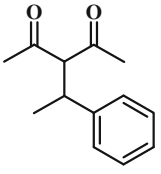
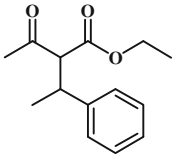
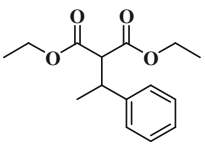
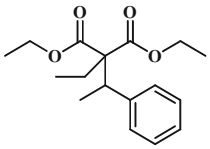
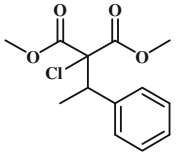
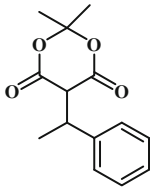
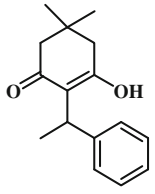
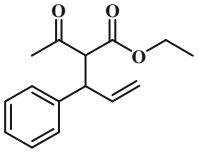
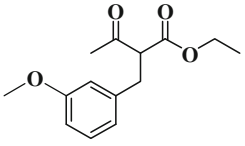
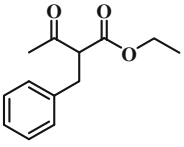
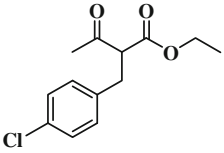
Entry	β-dicarbonyl compound	Alcohol	Molar ratio of dione/ alcohol	Product	Time (h)	Isolated Yield (%)
1	Acetylacetone	Benzhydrol	1/2		2	80
2	Ethyl acetoacetate	Benzhydrol	1/1		2	75
3	Diethyl malonate	Benzhydrol	2/1		2.5	87
4	Diethyl ethyl malonate	Benzhydrol	2/1		3	85
5	Dimethyl chloro malonate	Benzhydrol	2/1		1.5	90
6	2,2-Dimethyl-1,3-dioxane-4,6-dione	Benzhydrol	2/1		1	95
7*	5,5-Dimethylcyclohexane-1,3-dione	Benzhydrol	1/2		1	75
8	Acetylacetone	1-Phenylethanol	1/2		3	70
9	*Ethyl acetoacetate*	1-Phenylethanol	1/1		3.5	70
10	Diethyl malonate	1-Phenylethanol	2/1		3.5	70

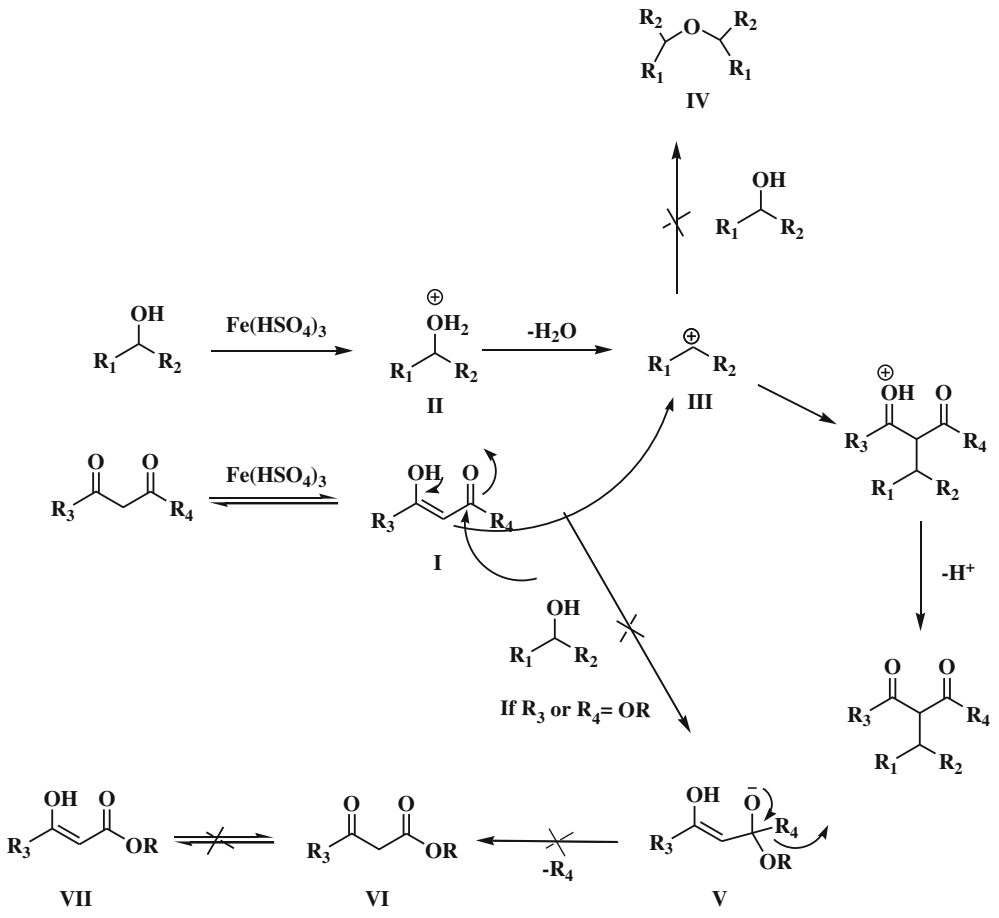
Table 2. (*contd.*)

Entry	β-dicarbonyl compound	Alcohol	Molar ratio of dione/ alcohol	Product	Time (h)	Isolated Yield (%)
11	Diethyl ethyl malonate	1-Phenylethanol	2/1		4	75
12	Dimethyl chloromalonate	1-Phenylethanol	2/1		2.5	80
13	2,2-Dimethyl-1,3-dioxane-4,6-dione	1-Phenylethanol	2/1		1.5	80
14*	5,5-Dimethylcyclohexane-1,3-dione	1-Phenylethanol	1/2		1.5	85
15	*Ethyl acetoacetate*	Cinnamyl alcohol	1/1		3	85
16	*Ethyl acetoacetate*	3-Methoxy benzyl alcohol	1/1		5	65
17	*Ethyl acetoacetate*	Benzyl alcohol	1/1		6	85
18	*Ethyl acetoacetate*	4-Chlorobenzyl alcohol	1/1		7.5	90

*Substrate is in equilibrium with its enol form (3-hydroxy-5,5-dimethylcyclohex-2-enone).
All products were identified by comparing their spectral data with those of the authentic samples

O-alkylated product **VII**. No symmetric ether and *O*-alkylated product have been formed during alkylation reaction in the presence of $Fe(HSO_4)_3$. Further investigation on the elucidation of the mechanism and scope of this reaction are currently underway in our laboratory.

$Fe(HSO_4)_3$ acts as a recyclable catalyst for alkylation of β-dicarbonyl compounds in refluxing 1,2-dichloroethane. The catalyst can be easily recovered from the reaction mixture by filtration. Solid residue was washed thoroughly with 1,2-dichloroethane and



Scheme 2. Proposed mechanism for catalytic addition of β-dicarbonyl compound to alcohol.

acetone to remove all organic compounds and then dried at 120°C. Using this treatment, recyclabilty of the catalyst was evaluated for the reaction of acetylacetone with benzhydrol (table 3). The recovered catalyst was reused at least five times without any decrease in the yield of 3-benzhydryl pentane-2,4-dione. The 6th run gave 85% conversion after 2 h, but complete conversion and similar yield were obtained after 3 h.

Table 3. Reaction of acetylacetone with benzhydrol in the presence of reused $Fe(HSO_4)_3$.

Run	Time (h)	Conversion (%)	Isolated Yield (%)
1	2	100	80
2	2	100	80
3	2	100	80
4	2	100	80
5	2	100	80
6[a]	2/3	85/100	70/80

[a]Second number in third column corresponds to conversion after 3 h

4. Conclusion

In this study, we not only investigate another catalytic activity of $Fe(HSO_4)_3$ in organic synthesis but also develop a method for a general and highly efficient $Fe(HSO_4)_3$-catalysed *C*-alkylation of a variety of β-dicarbonyl compounds (acyclic and cyclic β-diketones, β-keto esters and β-diester) using benzylic and allylic alcohols as electrophiles. It is remarkable that this methodology is attractive in comparison to the conventional methods because this method offers several advantages: (i) The catalyst is stable and reusable and offers easy handling. Moreover, isolation of the product by simple filtration of the solid acid is much easier; (ii) This method gives satisfactory yields of the *C*-alkylated products without formation of any side product.

Supplementary Information

The electronic supporting information can be seen at www.ias.ac.in/chemsci.

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