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Dry synthesis under microwave irradiation: synthesis of ferrocenylenones

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Abstract

Acetylferrocene and ferrocene carboxaldehyde were condensed with aldehydes or ketones without solvent in presence of solid KOH. Slow reactions were accelerated by microwave irradiation.

Keywords: Ferrocenylenones; Microwaves; Synthesis; Phase transfer catalysis; Group 8; Metallocene

1. Introduction

Claisen-Schmidt reactions of acetylferrocene (**1**) and ferrocene carboxaldehyde (**4**) are usually performed under classical homogeneous conditions in ethanol [1,2]. In 1990 Toma and collaborators described the synthesis of such products under phase-transfer conditions using 18-crown-6 ether as catalyst [3]. Recently, some aldol reactions were described, using pulverized KOH in the absence of solvent [4].

In our present work, we have investigated the synthesis of ferrocenylenones using powdered solid KOH as base without solvent in the presence or absence of a phase-transfer catalyst, at room temperature or under microwave irradiation [5]. As catalyst we used Aliquat 336 [6] which is generally efficient in liquid-solid phase-transfer catalysis (PTC) [7].

2. Discussion

The first part of our work has been devoted to the condensation of acetylferrocene with aromatic aldehydes (Scheme 1) using powdered solid KOH as base without solvent, in presence of Aliquat.

The reaction takes place at room temperature with benzaldehyde (**2a**), furaldehyde (**2d**) or 2-thienylcarboxaldehyde (**2e**), and condensation products are obtained in good yield (**3a** 63%, **3d** 92%, **3e** 83%) after only half an hour. Without Aliquat, partial reaction takes place with **2a** the yield after 24 h being 25%. Commercial potassium hydroxide, which contains about 15% water is used as a solid-liquid PTC.

Piperonal (**2c**) and paramethoxybenzaldehyde (**2b**) react more slowly than **2a** and after 18 h, the reaction is still incomplete. A moderate microwave irradiation (140 W at 2450 MHz, see Experimental part) accelerates the reaction and high yields (**3b** 53%, **3c** 73%) are obtained after a few minutes. Ferrocenylenones obtained in this way have the *E* configuration.

We next carried out the Claisen-Schmidt reaction of ferrocene carboxaldehyde with different ketones at room temperature, or under microwave irradiation (Scheme 2).

Only acetophenone (**5d**) reacts rapidly at room temperature. With the other ketones, we used microwave irradiation to accelerate the PTC reaction. No combustion has been observed with ferrocene carboxaldehyde, but acetylferrocene inflames in the microwave oven at a power setting of 280 W. This is probably due to the presence of iron in the acetylferrocene.

The condensation with α-tetralone (**5b**) (in the literature named as 3,4-dihydro-1-(2H)naphthalenone) and acetophenone (**5d**) leads only to the *E* isomers **6b**

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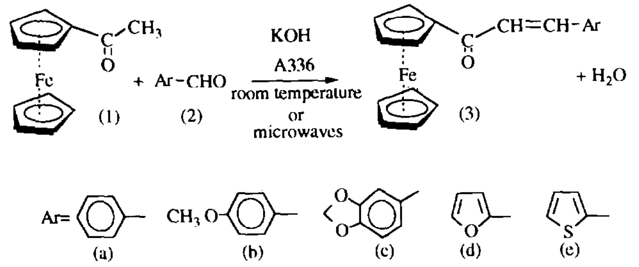
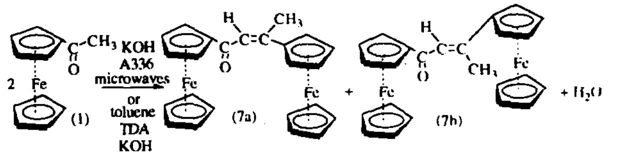


Scheme 1. Condensation of acetylferrocene (**1**).



Scheme 3. Autocondensation of acetylferrocene (**1**).

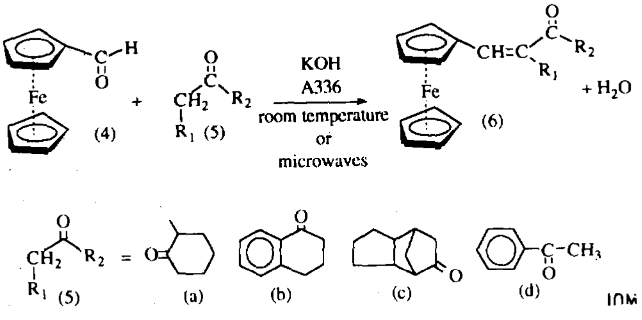
(88%) and **6d** (78%). With 2-methylcyclohexanone (**5a**) and ketone (**5c**) (tricyclo [5.2.1.0^{2,6}] decan-8-one), several by-products are formed. The main products isolated by preparative thin-layer chromatography are the *E* isomers (**6a** 63% and **6c** 55%). The by-products were not identified because of their small yields. We have also tried the condensation between ferrocene carboxaldehyde and 1-phenyl-propan-2-one but could not separate the great number of by-products.

The autocondensation of acetylferrocene to give 1,3-ferrocenyl-3-methyl-prop-2-ene-1-one (**7**) is not easy. Under homogeneous conditions, Pauson and Watts [8] obtained **7b**, using potassium tert-butoxide in refluxing benzene. Acetylferrocene with potassium hydroxide in refluxing THF under ultrasound gives no product. In refluxing toluene (4 h), with TDA-1 as phase-transfer catalyst [9], we obtained a mixture of **7a** (9%) and **7b** (14%). Reaction of acetylferrocene with potassium fluoride on alumina under microwave irradiation (490 W, 35 min) gives **7b** in 21% yield.

We describe here a simple and brief method for preparation of the *E* isomer **7b** without solvent in good yield (71%), using potassium hydroxide (Scheme 3). Preparation of the *Z*-isomer in solvent is also described, using TDA and potassium hydroxide.

All products have already been reported, except for **6a** and **6c** which are new. The yields obtained with our method are generally better than those obtained in the literature (see Experimental part).

The structures of compounds prepared were confirmed by ^{1}H and ^{13}C NMR, IR and mass spectroscopies and micro-analysis for the new compounds.



Scheme 2. Condensation of ferrocene carboxaldehyde (**4**).

3. Conclusion

Synthesis of ferrocenylenones (**3**, **6**, and **7**) from ferrocene carboxaldehyde (**4**) or acetylferrocene (**1**) without solvent in presence of solid KOH under solid-liquid PTC conditions, is rapid and efficient. When the reactions are too slow at room temperature, they may be accelerated efficiently by microwave irradiation.

4. Experimental part

Proton ^{1}H and ^{13}C NMR (reference from internal Me_4Si) were recorded on a Bruker AC 250 instrument from solutions in $CDCl_3$. Mass spectra were recorded on a Nermag R10 10H spectrometer. FT IR spectra were recorded on a Perkin-Elmer 16 PC spectrometer. Melting points. Microwave irradiations were carried out with a Toshiba microwave oven ER 7620 at 2450 MHz.

4.1. General procedure

Aldehyde (1.1 mmol) and ketone (1.0 mmol) are stirred in an Ehrlenmeyer flask, 2 mmol of powdered KOH are added and the mixture is stirred after addition of one drop of Aliquat 336. The Erlenmeyer flask is irradiated under microwave if necessary (time and power, see experimental part) and the final product is dissolved in dichloromethane. After filtration on Celite, the solvent is removed and the residue chromatographed on a preparative chromatographic layer of silica (AcOEt/cyclohexane = 20/80). The condensation product is further purified by crystallization in ether.

4.2. 1-ferrocenyl-3-phenylprop-2-ene-1-one (3a)

Obtained from acetylferrocene and benzaldehyde without irradiation, 0.5 h, yield = 63% (lit: 60% [1b], 83% [1c]); red solid; mp = 141° (139–140° [1b,c]); ^{1}H NMR ($CDCl_3$) δ: 4.19 (s, 5H, H arom), 4.57 (s, 2H, H arom), 4.9 (s, 2H, H arom), 7.1 (d, 1H, H ethyl), 7.32 to 7.6 (br, 3H, H arom), 7.6 to 7.7 (br, 2H, H arom), 7.78

(d, 1H, H ethyl); (CDCl$_3$) δ: 69.9 (C arom), ^{13}C NMR 69.95 (C arom), 70.2 (C arom), 72.85 (C arom), 123.1 (CH=*C*H–C=O), 128.35 (C arom), 129.0 (C arom), 130.2 (C arom), 140.9 (*C*H=CH–C=O), 193.1 (C=O);. MS *m/z* (%): 316 (M$^{+\cdot}$, 0.04), 251 (62.0), 223 (9.7), 185 (15.9), 178 (23.6), 165 (77.9), 157 (39.0), 129 (19.0), 121 (82.3), 114 (18.1), 94 (25.7),. 77 (46.8), 65 (15), 56 (100); IR (KBr) cm^{-1}: ν(C=O) (1650), ν(C=C) (1594).

4.3. 1-ferrocenyl-3-(4-methoxyphenyl)prop-2-ene-1-one (3b)

Obtained from acetylferrocene and p-anisaldehyde, irradiation 2 min 30 s, 140 W, yield = 53% (lit: 30% [1c]); red solid; mp = 149° (150° [1c]); ^{1}H NMR (CDCl$_3$) δ: 3.85 (s, 3H, CH$_3$O), 4.2 (s, 5H, H arom), 4.54 (br, 2H, H arom), 4.88 (br, 2H, H arom), 6.9 to 7.05 (br, 3H, H arom and H ethyl), 7.6 (d, 2H, H arom), 7.75 (d, 1H, H ethyl); (CDCl$_3$) δ: 55.5 ^{13}C NMR (CH$_3$O), 69.8 (C arom), 69.9 (C arom), 70.1 (C arom), 72.6 (C arom), 114.5 (C arom), 120.9 (CH=*C*H–C=O), 128.0 (C arom), 130.0 (C arom), 140.75 (*C*H=CH–C=O)), 161.6 (C arom), 193.4 (C=O); MS *m/z* (%): 346 (M$^{+\cdot}$, 47.9), 185 (12.2), 129 (13.6), 121 (21.8), 120 (14.1), 97 (18.9), 91 (100), 81 (27.3), 77 (14), 56 (32.9); IR (KBr) cm^{-1}: ν(C=O) (1646), ν(C=C) (1588).

4.4. 1-ferrocenyl-3-piperonylprop-2-ene-1-one (3c)

Obtained from acetylferrocene and piperonal, irradiation 3 min, 140 W, yield = 73% (lit: 37% [1b]); red solid; mp = 168° (169–170° [1b]); (CDCl$_3$) ^{1}H NMR δ: 4.2 (s, 5H, H arom), 4.56 (br, 2H, H arom), 4.88 (br, 2H, H arom), 6.0 (s, 2H, CH2), 6.82 (d, 1H, H arom), 6.95 (d, 1H, H ethyl), 7.1 to 7.3 (br, 2H, H arom), 7.7 (d, 1H, H ethyl); ^{13}C NMR (CDCl$_3$) δ: 69.77 (C arom), 69.82 (C arom), 69.97 (C arom), 72.7 (C arom), 101.6 (*C*H$_2$), 106.6 (C arom), 108.8 (C arom), 121.2 (C arom), 124.9 (CH=*C*H–C=O), 129.7 (C arom), 140.7 (*C*H=CH–C=O), 148.5 (C arom), 150.1 (C arom), 192.9 (C=O); MS *m/z* (%): 361 (M$^{+\cdot}$ + 1, 1.3), 185 (51.6), 121 (100.0), 94 (35.0), 81 (30.4), 71 (21.8); IR (KBr) cm^{-1}: ν(C=O) (1652), ν(C=C) (1584).

4.5. 1-ferrocenyl-3-(α-furyl)prop-2-ene-1-one (3d)

Obtained from acetylferrocene and 2-furaldehyde, no irradiation, 0.5 h, yield = 92% (lit: 58 [1b]); red solid; mp = 152° (154° [1b]); ^{1}H NMR (CDCl$_3$) δ: 4.21 (s, 5H, H arom), 4.58 (br, 2H, H arom), 4.91 (br, 2H, H arom), 6.50 (br, 1H, H arom), 6.69 (br, 1H, H arom), 7.0 (d, 1H, H ethyl), 7.5 (br, 1H, H arom), 7.55 (d, 1H, H ethyl); ^{13}C NMR (CDCl$_3$) δ: 69.8 (C arom), 69.9 (C arom), 70.2 (C arom), 72.8 (C arom), 112.7 (C arom), 115.5 (C arom), 120.8 (CH=*C*H–C=0), 127.2 (*C*H=CH–C=O), 142.6 (C arom), 144.4 (C arom), 190.5 (C=O); MS *m/z* (%): 306 (M$^{+\cdot}$, 1.5), 241 (3.7), 214 (8.3), 185 (10), 65 (35.2), 56 (100); IR (KBr) cm^{-1}: ν(C=O) (1652), ν(C=C) (1592).

4.6. 1-ferrocenyl-3-(α-thienyl)prop-2-ene-1-one (3e)

Obtained from acetylferrocene and 2-thiophenecarboxaldehyde, no irradiation, 0.5 h, yield = 83% lit: 75% [1c]); red solid; mp = 146° (147° [1c]); (CDCl$_3$) δ: 4.22 (s, 5H, H arom), 4.6 (br, 2H, H arom), 4.90 (br, 2H, H arom), 6.95 (d, 1H, H ethyl), 7.1 (br, 1H, H arom), 7.4 to 7.5 (br, 2H, H arom), 7.9 (d, 1H, H ethyl); ^{13}C NMR (CDCl$_3$) δ: 68.9 (C arom), 69.9 (C arom), 70.2 (C arom), 72.8 (C arom), 122.1 (*C*H=CH–C=O), 128.0 (C arom), 128.4 (C arom), 131.5 (C arom), 133.4 (CH=*C*H–C=O), 142 (C arom), 193 (C=O); MS *m/z* (%): 323 (M$^{+\cdot}$ + 1, 0.2), 121 (100.0), 114 (24.2), 108 (63.3), 94 (18.6); IR (KBr) cm^{-1}: ν(C=O) (1642), ν(C=C) (1582).

4.7. 2-ferrocenylmethylene 6-methylcyclohexanone (6a)

Obtained from 2-methylcyclohexanone and ferrocene carboxaldehyde, irradiation 2 mn, 140 W, yield = 63%; red solid; mp = 73°; C$_{18}$H$_{19}$FeO; ^{1}H NMR (CDCl$_3$) δ: 1.97 (d, 3H, CH$_3$), 1.5 to 2.6 (br, 7H, CH$_2$ and CH), 4.15 (s, 5H, H arom), 4.4 (br, 2H, H arom), 4.5 (br 2H, H arom), 7.32 (s, 1H, H ethyl); ^{13}C NMR (CDCl$_3$) δ: 16.9 (CH$_3$), 22.5 (CH$_2$), 28.9 (CH$_2$), 31.6 (CH$_2$), 43.7 (CH), 69.5 (C arom), 69.6 (C arom), 70.6 (C arom), 71.7 (C arom), 132.3 (CH=C), 136.6 (*C*H=C), 203.2 (C=O). MS *m/z* (%): 243 (33.5), 242 (18.7), 241 (13.9), 225 (12.4), 224 (16.5), 223 (9.6), 215 (29.5), 214 (9.0), 213 (33.4), 199 (34.1), 186 (16.6), 121 (35.7), 65 (10.7), 56 (100); MS *m/z*(%): 243 (33.5), 242 (18.7), 241 (13.9), 225 (12.4), 224 (16.5), 223 (9.6), 215 (29.5), 214 (9.0), 213 (33.4), 199 (34.1), 186 (16.6), 121 (35.7), 65 (10.7), 56 (100); IR (KBR: cm^{-1}: ν(C=O) (1670), ν(C=C) (1576). Found: C, 70.35; H, 6.30, C$_{18}$H$_{19}$FeO requires: C, 70.38; H, 6.23%.

4.8. 3,4-dihydro-2-ferrocenylmethylene-1-naphthalenone (6b)

Obtained from α-tetralone and ferrocene carboxaldehyde, irradiation 3 min, 210 W, yield = 88% (lit: 100% [3]); red solid; mp = 154° (lit: 153–156°^{3}); C$_{21}$H$_{18}$FeO; ^{1}H NMR (CDCl$_3$) δ: 2.97 (br, 4H, CH$_2$), 4.11 (s, 2H, H arom), 4.17 (s, 3H, H arom), 4.43 (br, 2H, H arom), 4.56 (br, 2H, H arom), 7.2 to 7.5 (br, 3H, H arom), 7.69 (s, 1H, H ethyl), 8.11 (dd, 1H, H arom); ^{13}C NMR (CDCl$_3$) δ: 27.1 (CH$_2$), 28.7 (CH$_2$), 68.9 (C arom), 69.6 (C arom), 70.1 (C arom), 70.8 (C arom), 127.0 (C arom), 128.1 (C arom), 128.2 (C arom), 131.3

(C arom), 132.9 (*C*H=C), 134.1 (C arom), 137.6 (C arom), 143.2 (CH=*C*), 187 (C=O). MS *m/z* (%): 342 (M$^{+}\cdot$, 1.75), 277 (2.3), 221 (3.9), 202 (5.2), 191 (8.5), 178 (7.0), 171 (7.7), 165 (14.3), 65 (9.6), 56 (100); MS *m/z*(%): 342 (M$^{+}\cdot$, 1.75), 277 (2.3), 221 (3.9), 202 (5.2), 191 (8.5), 178 (7.0), 171 (7.7), 165 (14.3), 65 (9.6), 56 (100); IR (KBr) cm^{-1}: ν(C=O) (1658), ν(C=C) (1600).

4.9. *9-ferrocenylmethylenetricyclo[5.2.1.0^{2,6}]decan-8-one (6c)*

Obtained from ketone **5c** and ferrocene carboxaldehyde, irradiation 2 min, 210 W, yield = 55%; red liquid; $C_{21}H_{22}FeO$; $(CDCl_3)$ δ: 1.2 to 2.5 (br, 11H, H aliph), 3.2 (s, 1H, CH=C–C–*H*), 4.12 (s, 5H, H arom), 4.4 (br, 2H, H arom), 4.55 (br, 2H, H arom), 6.95 (s, 1H, H ethyl). ^{13}C NMR $(CDCl_3)$ δ: 28.4 (C aliph), 31.7 (C aliph), 32.0 (C aliph), 32.3 (C aliph), 39.8 (C aliph), 43.2 (C aliph), 46.6 (C aliph), 53.8 (C aliph), 68.8 (C arom), 69.6 (C arom), 70.6 (C arom), 71.7 (C arom), 127.1 (*C*H=C), 138.5 (CH=*C*), 206.4 (C=O). MS *m/z* (%): 346 (M$^{+}\cdot$, 3.5), 344 (4.5), 281 (11.9), 250 (8.0), 224 (6.5), 223 (8.1), 214 (19.4), 213 (99.5), 212 (10.2), 211 (8.9), 210 (8.3), 199 (7.4), 186 (13.2), 185 (7.0), 184 (22.0), 172 (7.3), 171 (11.1); IR (KBr) cm^{-1}: ν(C=O) (1716), ν(C=C) (1638). Found: C, 72.78; H, 6.45. $C_{21}H_{20}FeO$ requires: C, 72.85; H, 6.40%.

4.10. *1-phenyl-3-ferrocenylprop-2-ene-1-one (6d)*

Obtained from acetophenone and ferrocene carboxaldehyde, no irradiation, 0.5 h, yield = 78% lit: 55% [1a], 92% [1c]); red solid; mp = 140° (136–140° [1a,1c]; ^{1}H NMR $(CDCl_3)$ δ: 4.2 (s, 5H, H arom), 4.5 (br, 2H, H arom), 4.6 (br, 2H, H arom), 7.13 (d, 1H, H ethyl), 7.4 to 7.62 (br, 3H, H arom), 7.77 (d, 1H, H ethyl), 7.95 to 8.05 (br, 2H, H arom); ^{13}C NMR $(CDCl_3)$ δ: 68.65 (C arom), 69.1 (C arom), 69.9 (C arom), 71.5 (C arom), 119.3 (CH=*C*H–C=O), 128.3 (C arom), 128.46 (C arom), 128.64 (C arom), 128.72 (C arom), 132.46 (C arom), 133.15 (C arom), 146.9 (*C*H=CH–C=O), 189.9 (C=O); MS *m/z* (%): 316 (M$^{+}\cdot$, 100.0), 252 (30.5), 251 (76.3), 215 (63.4), 214 (61.1), 186 (66.2), 121 (80.3), 105 (49.3), 95 (29.2), 56 (72.2); IR (KBr) cm^{-1}: ν(C=O) (1656), ν(C=C) (1596). The Preparation of 1,3-ferrocenyl-3-methylprop-2-ene-1-one (**7b**) followed the same general procedure, with 10 mmol of powdered KOH.

4.11. *1,3-ferrocenyl-3-methylprop-2-ene-1-one (7a)*

1 mmol of acetylferrocene and 10 mmol of KOH are heated under reflux in dry toluene with 1 ml of TDA-1 during 4 h. After filtration on Celite, the solvent is removed in vacuo and the residue is purified by preparative thin-layer chromatography (silica, Merck 7768; AcOEt/cyclohexane = 20/80). The condensation product is further purified by crystallization from ether.

4.12. *1,3-ferrocenyl-3-methylprop-2-ene-1-one (7a), E-isomer*

Obtained from autocondensation of acetylferrocene, irradiation 7 min, 210 W, yield = 41% (lit: 64% [8]); red solid; mp = 120° (118–120° [8]); ^{1}H NMR $(CDCl_3)$ δ: 2.58 (d, 3H, CH_3), 4.15 (s, 5H, H arom), 4.2 (s, 5H, H arom), 4.44 (br, 2H, H arom), 4.5 (br, 2H, H arom), 4.62 (br, 2H, H arom), 4.83 (br, 2H, H arom), 6.74 (q, 1H, H ethyl); ^{13}C NMR $(CDCl_3)$ δ: 18.2 (CH_3), 67.1 (C arom), 69.5 (C arom), 69.9 (C arom), 70.0 (C arom), 70.6 (C arom), 72.1 (C arom), 82.6 (C arom), 86.3 (C arom), 117.8 (C=*C*H–C=O), 153.6 (*C*=CH–C=O), 193.9 (C=O); MS *m/z* (%): 438 (M$^{+}\cdot$, 0.7), 373 (11.9), 228 (8.3), 185 (11.9), 121 (28.2), 56 (46.6); IR (KBr) cm^{-1}: ν(C=O) (1628), ν(C=C) (1580), 1376, 1262, 1106, 1028, 820.

4.13. *1,3-ferrocenyl-3-methylprop-2-ene-1-one (7b), Z-isomer*

Obtained from autocondensation of acetylferrocene, 4 h in refluxing toluene with TDA-1, yield = 9%; orange solid; mp = 120–122°; $C_{24}H_{22}Fe_2O$; ^{1}H NMR $(CDCl_3)$ d: 2.47 (d, 3H, CH_3), 4.0 to 4.2 (br, 10H, H arom), 4.3 to 4.5 (br, 6H, H arom), 4.79 (br, 2H, H arom), 7.8 (q, 1H, H ethyl); MS *m/z* (%): 438 (M$^{+}\cdot$, 0.6), 423 (0.89), 373 (1.9), 213 (39.0), 185 (20.7), 121 (39.3), 56 (49.3); IR (KBr) cm^{-1}: ν(C=O) (1632), ν(C=C) (1570), 1400, 1374, 1106, 1028, 880, 820, 746, 632, 602, 542.

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