Gold(III) Chloride-Catalyzed Addition Reactions of Electron-Rich Arenes to Methyl Vinyl Ketone

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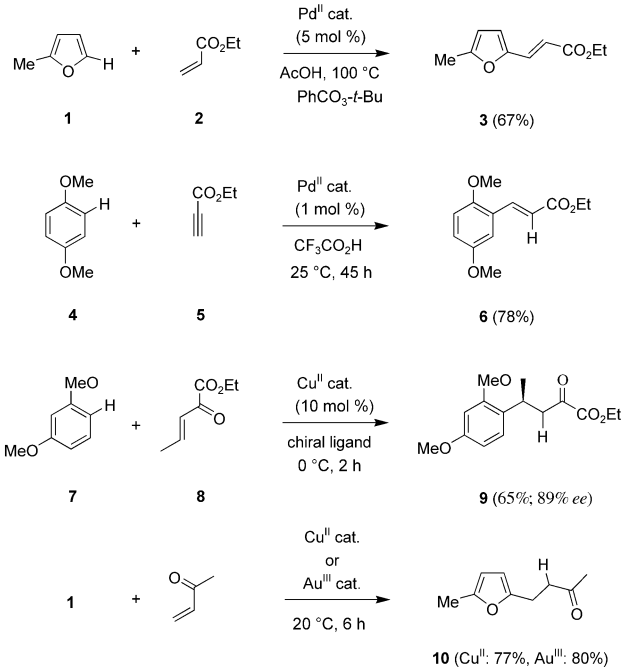
Abstract: For the reaction of α,β-unsaturated ketones with electron-rich arenes catalyzed by gold(III) chloride both, a Friedel–Crafts-type mechanism and an initial metallation, are evaluated. Gold(III) chloride has proven to be an efficient catalyst under very moderate reaction conditions, however, in the case of sterically demanding products HBF_4 turned out to be the superior catalyst.

Keywords: acids; aromatic substitution; gold; homogeneous catalysis; Lewis acids; Michael acceptors

Introduction

C/C-bond forming processes under CH-activation at arenes are of general preparative interest. Besides the classical Friedel–Crafts reactions transition metal-catalyzed methods featuring outstanding regio- or even stereoselectivities have emerged in recent years. In the case of coupling reactions with α,β-unsaturated carbonyl compounds two general mechanistic pathways can be distinguished: the transition metal either works as a Lewis acid, thus increasing the electrophilicity of the carbonyl compound (regarded as a Friedel–Crafts-type process), or a direct metallation of the arene takes place. In the latter case C/C-bond formation subsequently proceeds by a carbometallation of the α,β-unsaturated carbonyl compounds, a process that might be classified as a case of Michael addition reaction.

Typical examples are presented in Scheme 1: in the Pd-catalyzed vinylation of 2-methylfuran **1** according to Tsuji et al.[1] the heterocycle is metallated in the first reaction step; a carbopalladation followed by β-hydride elimination leads to the formation of product **3**. In this case the peracid ester is a necessary reagent for the crucial regeneration of the active Pd(II) catalyst from Pd(0). For the formation of adduct **6** the authors also favor a mechanism with an initial metallation;[2] however, in our opinion the alternative Friedel–Crafts-type mechanism under these strongly acidic conditions (trifluoroacetic acid as solvent) is not strictly ruled out by the experiments. For the enantioselective formation of **9** it is clear that the chiral Cu catalyst (with a bisoxazoline ligand) works as a Lewis acid activating the olefin **8**.[3] Related reactions of **1** with MVK used either copper[9a] or gold catalysts.[4a] Recently, gold(III) chloride became known as a very active catalyst for various C/C-bond and C/heteroatom-bond forming processes.[4]



Scheme 1. Friedel–Crafts-type and Michael-type addition reactions of electron-rich arenes to α,β-unsaturated carbonyl compounds.

Results and Discussion

We found that gold(III) chloride indeed nicely catalyzes the addition of 2-methylfuran **1** to methyl vinyl ketone

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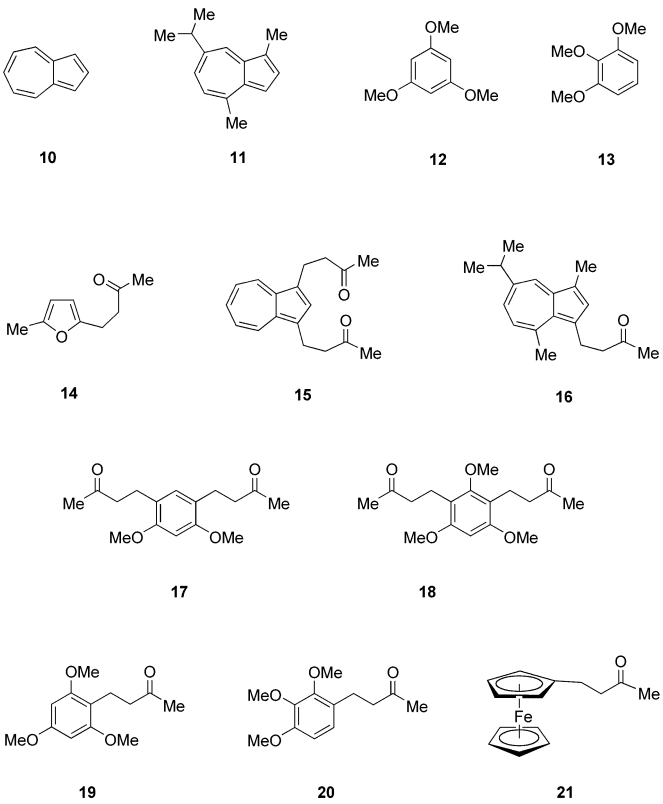
(MVK), a clean and fast reaction with a required amount of catalyst of about 1% (Table 1, entry 1). Monitoring the conversion by ^{1}H NMR proved an essentially quantitative conversion, the lower isolated yields are caused by the work-up due to the relatively high volatility of the product. NMR experiments gave hints for a direct interaction of gold(III) chloride with 2-methylfuran **1**. When one equivalent of $AuCl_3$ was added to a solution of **1** in acetonitrile, an immediate reaction took place. The resonance of the proton at the 5-position of the furan ring disappeared and for the two resonances of the hydrogen atoms at the 3- and 4-positions only broad signals were observed. Upon standing for a longer time in the absence of MVK the spectra finally only showed very broad signals of undefined material. On the other hand the addition of one equivalent of gold(III) chloride to an acetonitrile solution of MVK caused no change in the ^{1}H NMR spectrum. The gold(I) complexes PEt_3AuCl and THTAuCl (THT = tetrahydrothiophene) were initially inactive in the reaction of **1** with MVK, after the addition of one equivalent of $AgBF_4$ (the latter alone was inactive) an 80% conversion was observed in the first case and a 90% conversion in the second (entries 2 and 3). This led to the initial working hypothesis that an electrophilic CH-activation might be the crucial reaction step.

However, in the literature it was known that **14** can be prepared from **1** and MVK in SO_2 or with HCl as a catalyst.[5] Further experiments with HCl in acetonitrile prove that this clearly Brønsted acidic catalyst also formed **14** in a fast reaction, but only 50% conversion were reached and 4-chlorobutan-2-one[6] was formed as a side product (entry 4). The latter addition of HCl is a competing reaction that consumes the catalyst and thus circumvents a complete conversion. This was further supported by the reaction of MVK with a sub-stoichiometric amount of $AlCl_3$ which only led to 4-chlorobutan-2-one.[7] Since this addition should completely be suppressed by a non-nucleophilic counterion, we then tested *p*-TsOH which indeed allowed a fast and complete conversion (entry 5) similar to $AuCl_3$. The only differences were small amounts of side products visible in the crude spectra of the *p*-TsOH-catalyzed reaction.

Then various electron-rich arenes were tested for the addition reactions to MVK as model compound: $H[AuCl_4]$ and dilute hydrochloric acid were chosen for this comparison, since the hydrolysis products of $AuCl_3$ – the similar $H[AuCl_3OH]$ and of course HCl – are serious candidates for active Brønsted acidic catalysts under the reaction conditions.

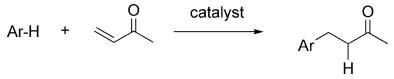
In the case of 2-methylfuran **1** both $HAuCl_4$ and HCl (entries 4 – 10) proved to be much less effective than $AuCl_3$. However, under forced reaction conditions – 1 equivalent of HCl and MVK in a large excess as solvent – a comparable yield of **14** can be achieved, although of course rather uneconomically with a significant amount of 4-chlorobutan-2-one as byproduct. Also for the coupling reaction with the somewhat acid sensitive azulenes **10** and **11** $AuCl_3$ is by far the superior catalyst: because of the moderate reaction conditions, no subsequent decomposition occurs when the work-up is delayed. In contrast, with HCl as catalyst it is crucial to interrupt the reaction after just two minutes by adsorptive filtration through a pad of silica.



Scheme 2. Substrates and products of the addition reactions of methyl vinyl ketone (MVK) to electron-rich arenes.

Starting from 1,3-dimethoxybenzene **7** an excellent yield of the double addition product **17** is obtained with 1% of $AuCl_3$ as catalyst (entry 17). Again, with a large excess of MVK and one equivalent of HCl a comparable yield of the final product can be achieved (entry 18). Most interestingly, the $AuCl_3$-catalyzed reaction with 1,3,5-trimethoxybenzene (**12**) stops at the stage of the mono addition product **19** with tremendous selectivity (entry 19). Obviously the reaction with this catalyst is rather sensitive against steric hindrance. With HCl as catalyst also the double addition product **18** is accessible (entries 20 and 21). HBF_4 – applied as 50% aqueous solution in one equivalent – turned out to be even more reactive, producing **18** in excellent yield. In addition, this catalyst is also superior to HCl because of the non-nucleophilic counterion, thus avoiding by-products. (***Warning!*** Do not apply HBF_4 in this reaction without enough additional solvent: a complete clean-up of the hood would be the least harmful consequence of the

Table 1. Results of the addition reactions of methyl vinyl ketone (MVK) to electron-rich arenes at room temperature.



Entry	Arene	Equivs. of MVK	Catalyst (mol %)[a]	Solvent[b]	Reaction Time	Products (yield)[c]
1	**1**	1	$AuCl_3$ (1%)	MeCN	40 min	**14** (80–90%)
2[d]	**1**	1	$PEt_3AuCl/AgBF_4$ (1%)	MeCN	1 d	**14** (80%)
3[d]	**1**	1	$THTAuCl/AgBF_4$ (1%)	MeCN	1 d	**14** (90%)
4[d]	**1**	1	HCl (30%)	MeCN	1 h	**14** (50%)
5[d]	**1**	1	*p*-TsOH (3%)	MeCN	1 h	**14** (90%)
6	**1**	10	$HAuCl_4$ (1%)	MeCN	40 min	**14** (10–15%)
7	**1**	100	$HAuCl_4$ (1%)	neat	40 min	**14** (10–15%)
8	**1**	10	HCl (5%)	MeCN	40 min	**14** (40–50%)
9	**1**	10	HCl (100%)	MeCN	40 min	**14** (40–50%)
10	**1**	100	HCl (100%)	neat	40 min	**14** (80–90%)
11	**10**	4	$AuCl_3$ (1%)	MeCN	2 min–3 d	**15** (50–55%)
12	**10**	4	HCl (5%)	MeCN	2 min	**15** (45–50%)
13	**10**	10	HCl (100%)	MeCN	2 min	**15** (0%)
14	**11**	2	$AuCl_3$ (1%)	MeCN	2 min	**16** (50–55%)
15	**11**	2	HCl (5%)	MeCN	2 min	**16** (45–50%)
16	**11**	10	HCl (100%)	MeCN	2 min	**16** (0%)
17	**7**	4	$AuCl_3$ (1%)	MeCN	1 d	**17** (90–95%)
18	**7**	100	HCl (100%)	MeCN	40 min	**17** (90–95%)
19	**12**	2	$AuCl_3$ (1%)	MeCN	1 d	**18** (0%), **19** (99%)
20	**12**	10	HCl (50%)	MeCN	40 min	**18** (<5%), **19** (95%)
21	**12**	100	HCl (100%)	MeCN	40 min	**18** (65%), **19** (35%)
22	**12**	100	HBF_4 (100%)	MeCN	40 min	**18** (95%), **19** (<5%)
23	**13**	4	$AuCl_3$ (1%)	MeCN	1 d	**20** (0%)
24	**13**	100	HCl (100%)	MeCN	40 min	**20** (5%)
25	**13**	100	HBF_4 (100%)	MeCN	40 min	**20** (40–50%)

[a] HCl was applied as 33% aqueous solution and HBF_4 as 60% aqueous solution.
[b] In all cases with MeCN as solvent the concentration was 0.5 mmol arene/mL solvent.
[c] in general each reaction was performed 2–4 times, therefore a range of reproducible isolated yields is given.
[d] NMR test tube experiments.
[e] Plus 25% 4-chlorobutan-2-one as by-product.

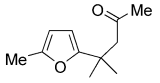
uncontrollable reaction which then starts). With 1,2,3-trimethoxybenzene **13** aqueous HBF_4 was the only catalyst tested which produced acceptable amounts of the addition product **20**. No reaction was observed with $AuCl_3$ in this case (entry 23); this result is in accord with the influence of steric hindrance pointed out above. Also the limits of HBF_4 as catalyst were tested: with ferrocene a small yield of the mono-addition product **21** was obtained (5–10%), and no reaction was observed at room temperature with 1,4-dimethoxybenzene (**4**), pyrene and tetrakis(4-methoxyphenyl)porphyrin. The latter is also true for $AuCl_3$ as the catalyst and **4** or even less electron-rich arenes like anisole, toluene and acceptor-substituted arenes like acetophenone.

In addition, some other Michael acceptors were tested: $AuCl_3$-catalysis of the addition of **1** to mesityl oxide delivered 75% of **22** in a slow but selective reaction (Table 2, entry 1). This is superior to published methods which yield only about 34% of **22**.[8] The *transoid* Michael acceptors cyclopentenone and cyclohexenone also reacted smoothly (Table 2, entries 2 and 3). The ^1H NMR spectra of the crude material proved that the reaction with cyclopentenone was also highly selective while with cyclohexenone side-products could also be detected. Again literature known methods using copper catalysts deliver only 53–55% yield.[9]

Conclusion

The experiments clearly show that not only $AuCl_3$ but under appropriate conditions also Brønsted acids with a non-nucleophilic counterion can selectively catalyze the reactions between Michael acceptors and electron-rich aromatic systems. This suggests that with the gold catalyst in the presence of water a Brønsted acid with an aurate counterion might be the active species, too. On the other hand the different selectivities observed with Brønsted acids and gold catalysts can either be explained by specific acid catalysis or by a direct participation of the metal. Thus these experiments do not rule out a CH-activation of the aromatic system by the gold catalysts, but they show how much care in the interpretation of the results obtained with transition metals in

Table 2. $AuCl_3$-catalyzed reaction of different α,β-unsaturated ketones with **1**.



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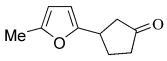

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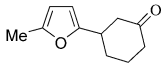

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Entry	Ketone	Catalyst (mol %)	Solvent	Reaction Time	Products (yield)
1	Mesityl oxide	$AuCl_3$ (0.5%)	MeCN	14 d	**22** (75%)
2	cyclopentenone	$AuCl_3$ (1%)	MeCN	1 d	**23** (87%)
3	cyclohexenone	$AuCl_3$ (1%)	MeCN	1 d	**24** (74%)

acidic media is necessary. The mechanism of the gold-catalyzed reaction is under further investigation, the preparation of aurated electron-rich arenes and the investigation of their reaction with MVK is the major challenge in this field.

However, $AuCl_3$ as well as aqueous HCl and HBF_4 represent a very useful set of acidic catalysts for Michael-type addition reactions, although they are not the only ones. They give a range of reactivities from moderate to very high and regularly show different selectivities.

Experimental Section

General Remarks

M.p. (uncorrected): Reichert Thermovar. IR: Perkin Elmer 841. NMR: Bruker DRX 400; ^{1}H NMR spectra (400 MHz) were recorded in $CDCl_3$ or acetonitrile-d_3 with TMS as the internal standard. ^{13}C NMR spectra (100.6 MHz) were measured by using $CDCl_3$ as the solvent and the internal standard. MS: MAT 700 ITD (70 eV) and Varian MAT 311 A. For analytical TLC precoated plastic sheets "POLYGRAM SIL G/UV254" from "Macherey-Nagel" were used. EA: Elementar/Hanau Vario EL.

1. NMR Test Tube Experiments

*a) Reaction of **1** with MVK and $AuCl_3$:* 82.1 mg (1.00 mmol) **1** and 70.0 mg (1.00 mmol) MVK in 500 μL acetonitrile-d_3 were placed in an NMR tube and 3.03 mg (10 μmol, 1 mol %) $AuCl_3$ were added. The ^{1}H NMR showed a highly selective and quantitative conversion to **14**. The spectroscopic data of 14 were known.[9]

*b) Reaction of **1** with MVK and PEt_3AuCl:* 82.1 mg (1.00 mmol) **1** and 70.0 mg (1.00 mmol) MVK in 500 μL acetonitrile-d_3 were placed in an NMR tube and 3.51 mg (10 μmol, 1 mol %) PEt_3AuCl were added. No reaction was observed after 6 hours in the ^{1}H NMR. Then 1.95 mg (10.0 μmol, 1 mol %) $AgBF_4$ were added. After 1 d the ^{1}H NMR showed a highly selective conversion to **14**, but only 80% conversion could be reached.

*c) Reaction of **1** with MVK and THTAuCl:* 82.1 mg (1.00 mmol) **1** and 70.0 mg (1.00 mmol) MVK in 500 μL acetonitrile-d_3 were placed in an NMR tube and 3.21 mg (10 μmol, 1 mol %) THTAuCl were added. No reaction was observed after 6 hours in the ^{1}H NMR. Then 1.95 mg (10.0 μmol, 1 mol %) $AgBF_4$ were added. After 1 d the ^{1}H NMR showed a highly selective conversion to **14**, but only 90% conversion could be reached.

*d) Reaction of **1** with MVK and HCl:* 82.1 mg (1.00 mmol) **1** and 70.0 mg (1.00 mmol) MVK in 500 μL acetonitrile-d_3 were placed in an NMR tube and 11.0 mg (303 μmol, 30 mol %) HCl (from 37% HCl in water) were added. After 1 h the ^{1}H NMR showed a 50% conversion to **14**, but in addition 25% of 4-chlorobutan-2-one[10] had been formed and the remaining starting material did not react any further.

*e) Reaction of **1** with MVK and $AlCl_3$:* 82.1 mg (1.00 mmol) **1** and 70.0 mg (1.00 mmol) MVK in 500 μL acetonitrile-d_3 were placed in an NMR tube and 44.4 mg (333 μmol) $AlCl_3$ were added. After 1 d the ^{1}H NMR showed starting material and a 40% conversion to 4-chlorobutan-2-one.[6] No **14** could be detected.

*f) Reaction of **1** with MVK and* p-*TsOH:* 82.1 mg (1.00 mmol) **1** and 70.0 mg (1.00 mmol) MVK in 500 μL acetonitrile-d_3 were placed in an NMR tube and 5.00 mg (28.6 μmol, 3 mol%) *p*-$TsOH \cdot H_2O$ were added. After 1 h the ^{1}H NMR showed a complete conversion to **14**, but in addition small amounts of different side-products were visible in the crude NMR.

2. Preparative Reactions

1,3-Bis(3-oxobutyl)azulene **(15):** A mixture of 211 mg (3.00 mmol) of MVK, 950 mg of acetonitrile and 300 mg (10 μmol, 0.2 mol %) of $AuCl_3$ was slowly added under argon to a vigorously stirred solution of 193 mg (1.50 mmol) of azulene (**10**) in 2 mL of acetonitrile. After 1 d at room temperature the reaction mixture was filtered through a small pad of silica (2 g) with additional 5 mL of acetonitrile as eluent. The solvent was removed under vacuum at 50 °C (from 15 mbar to 0.2 mbar) and the residue purified by flash chromatography on silica gel (petroleum ether/*tert*-butyl methyl ether, 2:1; $R_f = 0.10$). Recrystallization from CH_2Cl_2/diethyl ether afforded **15** as dark blue-green crystals; yield: 201 mg (50%), mp 63 °C; IR (KBr): $\tilde{\nu} = 3029$ (m), 2928 (m), 2889 (m), 1971 (w), 1707 (s), 1568 (s), 1529 (w), 1516 (w), 1433 (m), 1409 (s), 1361 (s), 1320 (m), 1303 (w), 1267 (w), 1228 (w), 1175 (m), 1160 (m), 1132 (w), 1052 (w), 947 (w), 851 (w), 737 (s), 717 cm^{-1} (w); UV (acetonitrile, $c = 1.04 \cdot 10^{-4}$ mol/L): λ_{max} (log ε) = 202 (3.98), 214 (3.98), 240 (4.12), 282 (4.64), 349 (3.60), 366 (3.47), 627 nm (2.19); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.12 (s, 6H), 2.87 (m, 4H), 3.31 (m, 4H), 7.00 (t, $J = 9.9$ Hz), 7.49 (t, $J = 9.9$ Hz), 7.60 (s, 1H), 8.17 (d, $J = 9.9$ Hz); ^{13}C NMR ($CDCl_3$, 125 MHz): δ =

21.17 (t), 30.11 (q), 45.16 (t), 121.12 (d), 127.12 (s), 133.07 (d), 135.92 (s), 136.47 (d), 137.73 (d), 208.42 (s); MS (EI, 70 eV, 105 °C): *m/z* (%) = 269 (7), 268 (32, M^+), 212 (15), 211 (100), 167 (17), 165 (8), 154 (29), 153 (14), 152 (11), 43 (7), 40 (6); anal. calcd. for $C_{18}H_{20}O_2$ (268.35 g/mol): C 80.57, H 7.51; found: C 80.68, H 7.49.

1,4-Dimethyl-7-(1-methylethyl)-3-(3-oxobutyl)-azulene **(16):** A mixture of 140 mg (2.00 mmol) of MVK, 950 mg of acetonitrile and 300 mg (10 μmol, 0.3 mol %) of $AuCl_3$ was slowly added under argon to a vigorously stirred solution of 198 mg (1.00 mmol) guaiazulene (**11**) in 2 mL of acetonitrile. After 1 d at room temperature the reaction mixture was filtered through a small pad of silica (2 g) with additional 5 mL of acetonitrile as eluent. The solvent was removed under vacuum at 50 °C (from 15 mbar to 0.2 mbar) and the residue purified by flash chromatography on silica gel (petroleum ether/*tert*-butyl methyl ether, 2:1; R_f = 0.50). Recrystallization from CH_2Cl_2/diethyl ether afforded **16** as dark blue crystals; yield: 148 mg (55%), mp 68 °C; IR (KBr): $\tilde{\nu}$ = 2961 (s), 2921(s), 2890 (s), 2295 (w), 1710 (s), 1601 (w), 1535 (m), 1445 (w), 1415 (m), 1400 (s), 1377 (m), 1355 (s), 1297 (w), 1264 (w), 1202 (w), 1180 (w), 1158 (s), 1091 (w), 1077 (w), 1054 (w), 1032 (w), 933 (w), 916 (w), 870 (w), 827 cm^{-1} (w); UV (acetonitrile, $c = 5.96 \cdot 10^{-5}$ mol/L): λ_{max} (log ε) = 219 (4.09), 248 (4.32), 288 (4.61), 305 (4.15, sh), 352 (3.72), 369 (3.64), 622 nm (2.56); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.32 (d, J = 6.9 Hz, 6H), 2.16 (s, 3H), 2.59 (s, 3H), 2.84 (m, 2H), 2.94 (s, 3H), 3.00 (sep, J = 6.9 Hz, 1H), 3.49 (m, 2H), 6.81 (d, J = 10.7 Hz, 1H), 7.24 (dd, J = 10.7 Hz, ^4J = 2.1 Hz, 1H), 7.42 (s, 1H), 8.04 (d, ^4J = 2.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 12.88 (q), 24.59 (t), 25.33 (q), 26.86 (q), 30.12 (q), 37.65 (d), 47.03 (t), 124.32 (s), 126.23 (d), 126.60 (s), 132.19 (s), 133.41 (d), 134.76 (d), 137.61 (s), 138.90 (s), 139.11 (d), 145.08 (s), 208.37 (s); MS (EI, 70 eV, 95 °C): *m/z* (%) = 269 (7), 268 (33, M^+), 212 (18), 211 (100), 196 (8), 195 (6), 181 (10), 165 (9); anal. calcd. for $C_{19}H_{24}O$ (268.39 g/mol): C 85.03, H 9.01; found: C 84.95, H 8.93.

1,3-Dimethoxy-4,6-bis(3-oxobutyl)benzene **(17):** A mixture of 420 mg (6.00 mmol) of MVK, 950 mg of acetonitrile and 300 mg (10 μmol, 0.3 mol %) of $AuCl_3$ was slowly added under argon to a vigorously stirred solution of 138 mg (1.00 mmol) 1,3-dimethoxybenzene (**7**) in 2 mL of acetonitrile. After 1 d at room temperature the reaction mixture was filtered through a small pad of silica (2 g) with additional 5 mL of acetonitrile as eluent. The solvent was removed under vacuum at 50 °C (from 15 mbar to 0.2 mbar) and the residue purified by flash chromatography on silica gel (petroleum ether/*tert*-butyl methyl ether, 2:1; R_f = 0.10). Recrystallization from diethyl ether afforded **17** as colorless crystals; yield: 265 mg (95%), mp 57 °C; IR (KBr): $\tilde{\nu}$ = 3001 (m), 2939 (w), 1708 (s), 1614 (m), 1588 (w), 1515 (m), 1500 (s), 1460 (m), 1440 (s), 1405 (w), 1364 (m), 1304 (s), 1287 (w), 1263 (w), 1209 (s), 1193 (w), 1159 (s), 1114 (s), 1036 (s), 1029 (s), 841 cm^{-1} (w); UV (acetonitrile, $c = 2.19 \cdot 10^{-4}$ mol/L): λ_{max} (log ε) = 201 (4.81), 230 (4.10, sh), 284 nm (3.76); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.13 (s, 6H), 2.68 (m, 4H), 2.77 (m, 4H), 3.81 (s, 6H), 6.40 (s, 1H), 6.86 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 24.30 (t), 29.87 (q), 44.15 (t), 55.54 (q), 95.30 (d), 120.76 (s), 131.11 (d), 156.72 (s), 208.78 (s); MS (EI, 70 eV, 55 °C): *m/z* (%) = 279 (8), 278 (40, M^+), 222 (14), 221 (100), 77 (19), 163 (8), 151 (7), 149 (13), 147 (6), 91 (8), 43 (27), 40 (11); anal. calcd. for $C_{16}H_{22}O_4$ (278.35 g/mol): C 69.04, H 7.97; found: C 69.01, H 7.99.

2,4-Bis(2-oxobutan-4-yl)-1,3,5-trimethoxybenzene **(18):** A mixture of 701 mg (10.0 mmol) of MVK and 420 mg (2.50 mmol) of **12** in 10 mL of acetonitrile was cooled to 0 °C under argon. A solution 1.76 g (10.0 mmol) of 50% aqueous HBF_4 in 2 mL of acetonitrile was added slowly under vigorous stirring. After 40 min at room temperature the reaction mixture was filtered through a small pad of silica (4 g) with additional 10 mL of acetonitrile as eluent. The solvent was removed under vacuum at 50 °C (from 15 mbar to 0.2 mbar) and the residue purified by flash chromatography on silica gel (petroleum ether/*tert*-butyl methyl ether, 2:1; R_f = 0.10). Recrystallization from diethyl ether afforded **18** as colorless crystals; yield: 732 mg (95%), mp 85 °C; IR (KBr): ν = 3411 (w, br), 2940 (s, sh), 2841 (m, sh), 1712 (s), 1677 (w), 1605 (s), 1587 (s), 1487 (m, sh), 1454 (s), 1410 (s), 1364 (s), 1319 (s), 1285 (w), 1257 (w), 1219 (m), 1188 (s), 1163 (s), 1127 (s), 1105 (s), 1038 (s), 1026 (m), 953 (w), 879 (w), 809 (s), 691 (w), 653 cm^{-1} (w); UV (acetonitrile, $c = 2.43 \cdot 10^{-4}$ mol/L): λ_{max} (log ε) = 281 nm (3.96); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.15 (s, 6H), 2.64 (m, 4H), 2.81 (m, 4H), 3.68 (s, 3H), 3.80 (s, 6H), 6.26 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 18.03 (t), 29.45 (q), 43.67 (t), 55.31 (q), 61.65 (q), 91.32 (d), 114.33 (s), 156.96 (s), 157.49 (s), 208.95 (s); MS (EI, 70 eV, 55 °C): *m/z* (%) = 310 (2), 309 (11), 308 (60, M^+), 251 (100), 58 (21), 43 (58).

2-(3-Oxobutyl)-1,3,5-trimethoxybenzene **(19):** A mixture of 420 mg (6.00 mmol) of MVK, 950 mg of acetonitrile and 300 mg (10 μmol, 0.3 mol %) of $AuCl_3$ was slowly added under argon to a vigorously stirred solution of 138 mg (1.00 mmol) 1,3,5-trimethoxybenzene (**12**) in 2 mL of acetonitrile. After 1 d at room temperature the reaction mixture was filtered through a small pad of silica (2 g) with additional 5 mL of acetonitrile as eluent. The solvent was removed under vacuum at 50 °C (from 15 mbar to 0.2 mbar) and the residue purified by flash chromatography on silica gel (petroleum ether/*tert*-butyl methyl ether, 2:1; R_f = 0.27) to give **19** as colorless crystals; yield: 237 mg (99.5%), mp 64 °C (Lit.[13] bp 140–142 °C/0.1 Torr); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.16 (s, 3H), 2.57 (m, 2H), 2.84 (m, 2H), 3.78 (s, 6H), 3.80 (s, 3H), 6.11 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 17.53 (t), 29.54 (q), 43.60 (t), 55.31 (q), 55.57 (q), 90.51 (d), 109.58 (s), 158.71 (s), 159.55 (s), 209.63 (s); MS (EI, 70 eV, 80 °C): *m/z* (%) = 239 (4), 238 (27, M^+), 195 (5), 182 (11), 181 (100), 168 (5), 136 (10), 121 (17), 43 (5).

1-(3-Oxobutyl)-2,3,4-trimethoxybenzene **(20):** A mixture of 701 mg (10.0 mmol) of MVK and 336 mg (2.00 mmol) of 1,2,3-trimethoxybenzene (**13**) in 10 mL of acetonitrile was cooled to 0 °C under argon. A solution of 1.76 g (10.0 mmol) of 50% aqueous HBF_4 in 2 mL of acetonitrile was added slowly under vigorous stirring. After 40 min at room temperature the reaction mixture was filtered through a small pad of silica (4 g) with additional 10 mL of acetonitrile as eluent. The solvent was removed under vacuum at 50 °C (from 15 mbar to 0.2 mbar) and the residue purified by flash chromatography on silica gel (petroleum ether/*tert*-butyl methyl ether, 2:1; R_f = 0.22). Recrystallization from diethyl ether afforded **20** as colorless crystals; yield: 229 mg (48%), mp 52 °C (Lit.[13] bp 118–120 °C/0.1 Torr); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.14 (s), 2.72 (m, 2H), 2.80 (m, 2H), 3.83 (s, 3H), 3.86 (s, 3H), 3.88 (s, 3H), 6.59 (d, J = 8.5 Hz, 1H), 6.82 (d, J = 8.5 Hz, 1H); MS (EI, 70 eV, 80 °C): *m/z* (%) = 239 (4), 238 (27, M^+), 192 (3), 181 (100), 167 (5), 134 (7), 125 (14), 43 (8).

4-Ferrocenyl-2-butanone **(21):** A mixture of 701 mg (10.0 mmol) of MVK and 372 mg (2.00 mmol) of ferrocene in 10 mL of acetonitrile was cooled to 0 °C under argon. A solution of 1.76 g (10.0 mmol) of 50% aqueous HBF_4 in 2 mL of acetonitrile was added slowly under vigorous stirring. After 40 min at room temperature the reaction mixture was filtered through a small pad of silica 4 g with additional 10 mL of acetonitrile as eluent. The solvent was removed under vacuum at 50 °C (from 15 mbar to 0.2 mbar) and the residue purified by flash chromatography on silica gel (petroleum ether/*tert*-butyl methyl ether, 2:1; $R_f = 0.25$). Recrystallization from diethyl ether afforded **21** as yellow-colored crystals; yield: 36 mg (7%), mp 41 °C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 2.15$ (s, 3H), 2.63 (m, 4H), 4.07 (s, 4H), 4.12 (s, 5H). The spectroscopic data were in accordance with the data in the literature.[14]

4-(5-Methylfuran-2-yl)penten-2-one **(22):** To 2.09 g (25.5 mmol) of **1** and 2.50 g (25.5 mmol) of mesityl oxide in 10 mL of acetonitrile were added 38 mg (0.5 mol %) of $AuCl_3$. The selective conversion was monitored by taking small aliquots and measuring ^{1}H NMR spectra. After 14 days the solvent was removed under vacuum and the crude material was purified by column chromatography on silica gel (hexanes/ethyl acetate, 3:1) to afford **22**; yield: 3.91 g (75%). The spectroscopic data were in accordance with the literature data.[8,9c,11]

3-(5-Methylfuran-2-yl)cyclopenten-1-one **(23):** To 1.18 g (14.4 mmol) of **1** and 1.18 g (14.4 mmol) of cyclopentenone in 10 mL of acetonitrile were added 43.7 mg (144 μmol, 1 mol %) of $AuCl_3$. The selective conversion was monitored by taking small aliquots and measuring ^{1}H NMR spectra. After 1 day the solvent was removed under vacuum and the crude material was purified by column chromatography on silica gel using hexanes/ethyl acetate, 4:1 to afford **23**; yield: 2.05 g (87%). The spectroscopic data were in accordance with the data in the literature.[8,9,12]

3-(5-Methylfuran-2-yl)cyclohexen-1-one **(24):** To 1.18 g (14.4 mmol) of **1** and 1.34 g (14.4 mmol) of cyclohexenone in 10 mL of acetonitrile were added 43.7 mg (144 μmol, 1 mol %) of $AuCl_3$. The selective conversion was monitored by taking small aliquots and measuring ^{1}H NMR spectra. After 1 day the solvent was removed under vacuum and the crude material was purified by column chromatography on silica gel using hexanes/ethyl acetate, 4:1 to afford **22**; yield: 1.86 g (74%). The spectroscopic data were in accordance with the data in the literature.[8,9,12]

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