Oxidative Addition of 1,3-Dicarbonyl Compounds to Conjugated Olefins

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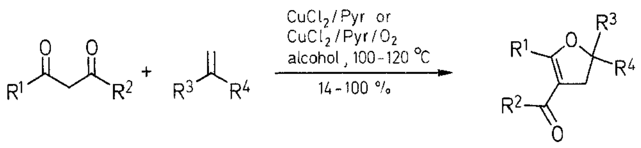
A convenient one step synthesis of the 5-aryl- or 5-(1-alkenyl)-4,5-dihydrofurans from 1,3-dicarbonyl compounds and conjugated olefins in the presence of copper(II) chloride/pyridine or copper(II) chloride/pyridine/oxygen is reported.

Oxidative addition of 1,3-dicarbonyl compounds, containing at least one ketogroup to olefins,[1-9] dienes[10-12] or enines[12,13] in the presence of manganese(III) acetate,[1-3,10-13] manganese(III) acetate/copper(II) acetate,[1,11-13] mercury(II) acetate,[5] thallium(III) acetate,[6] lead(IV) acetate,[7] palladium(II) chloride/copper(II) chloride,[8] silver(II) oxide or lead(IV) oxide[9] leads to substituted dihydrofurans. Formation of dihydrofuran in the presence of copper(II) salt alone has been observed only in the reaction of ethyl acetoacetate with styrene, the product being obtained in low yield.[4]



1 2 3

1	R¹	R²
a	CH_3	CH_3
b	$-CH_2C(CH_3)_2CH_2-$	
c	CH_3	OC_2H_5

2	R³	R⁴
a	H	C_6H_5
b	CH_3	C_6H_5
c	H	$CH{=}CH_2$
d	H	$CH{=}CHCH_3$
e	$CH{=}CH_2$	$CH_2CH_2CH{=}C(CH_3)_2$
f	H	$C({=}CH_2)CH_2CH_2CH{=}C(CH_3)_2$

Scheme A

None of the many oxidants proposed earlier for these reactions, turned out to be quite suitable for the preparative synthesis because: (i) all these oxidants are to be used in stoichiometric proportion, (ii) the reaction proceeds often with low selectivity affording the mixture of isomeric 4- and 5-substituted dihydrofurans,[5-8] and (iii) relatively high price or toxicity of some salts or oxides prevent their use in large scale experiments.

We have now found that 5-aryl- or 5-(1-alkenyl)substituted 4,5-dihydrofurans **3aa**–**3cc** are formed in the reaction of 1,3-dicarbonyl compounds (acetylacetone, dimedone, ethyl acetoacetate) with conjugated olefins (styrene, α-methylstyrene, butadiene, piperylene, myrcene) in the presence of stoichiometric amount of copper(II) chloride and excess of pyridine at 80–120°C in alcohol solution (scheme **A**). Alternatively the reaction could be carried out with copper(II) chloride/pyridine-/oxygen system. In the latter case only catalytic amount of copper(II) chloride is required. In the absence of chloride ions or pyridine the yields decrease sharply (Table 1).

Table 1. The Effect of Chloride Ions and Pyridine in the Reaction of Acetylacetone (**1a**) with Butadiene (**2c**)[a]

Cupric Salt[b]	LiCl	Pyridine	Yield[c] (%)
$CuCl_2$	–	+	92
$CuCl_2$	–	–	–
$CuCl_2/Cu(OAc)_2$ (1:1)	–	–	40
$Cu(OAc)_2$	–	–	–
$Cu(OAc)_2$	+	–	55
$Cu(NO_3)_2/Cu(OAc)_2$ (1:1)	–	–	2
$Cu(NO_3)_2$	–	+	14
$Cu(NO_3)_2$	+	+	70

[a] Reaction conditions: **1a**/**2c**/Cu/Cl/Pyr = 20 : 20 : 1 : 2 : 3; 6 h, under argon.

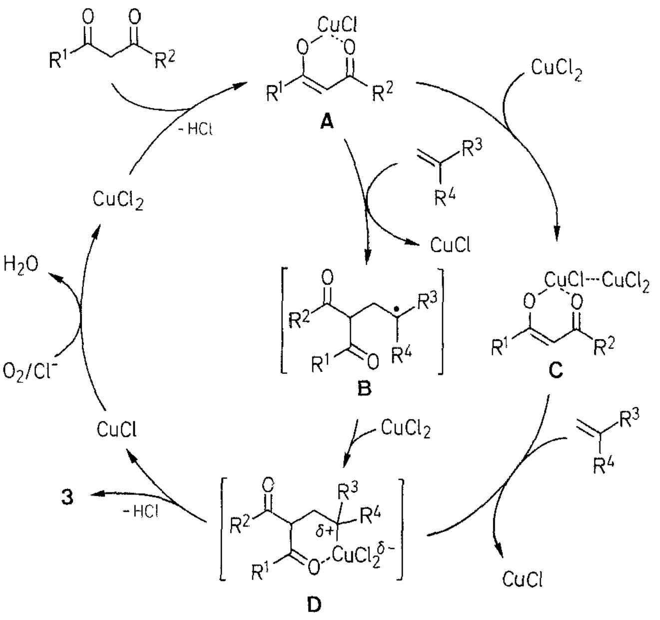
[b] Copper(II) chloride dihydrate, copper(II) acetete monohydrate and copper(II) nitrate tetrahydrate were used.

[c] GC yield based on cupric salt reacted, assuming 2 moles of cupric salt per 1 mole of dihydrofuran, in accordance with the reaction stoichiometry. Isolated yields are 5–10% lower.

The data presented in Table 2 indicate that acetylacetone reacts regioselectively with piperylene at the terminal carbon atom.

Two isomeric dihydrofurans are formed by oxidative addition of acetylacetone or dimedone to myrcene, the ratio **3af**/**3bc** and **3bf**/**3ca** being 5:1 [cf. results obtained using manganese(III) acetate/copper(II) acetate system[11]]. For the reaction with copper(II) chloride in inert atmosphere the yields of dihydrofurans **3** based on oxidant consumed were 50–100%, whereas they increased up to 4–12 moles of product per 1 mole of copper(II) chloride (that corresponds to 800–2400%), when copper salt was regenerated by bubbling air through the reaction mixture.

The proposed mechanism of the catalytic reaction of 1,3-dicarbonyl compounds with conjugated olefins is presented in Scheme **B**. One of the two reaction pathways to be assumed includes homolytic addition of enolate ligand of the complex **A** to olefin, formation of labile organometallic intermediate **D** from adduct-radical **B** with the second molecule of the salt and heterolytic decomposition of the complex **D** into products **3**.



Scheme **B**

Table 2. Synthesis of Dihydrofurans **3**[a]

Reactants 1	Reactants 2	Solvent	Product 3	Method	Yield[b] (%)	bp[c] (°C)/mbar	Molecular Formula[d] or Lit. bp (°C)/mbar
a	**a**	$C_5H_{11}OH$	**3aa**	A/C	100 (22)	133–135/1.3	126–128/0.7[20]
a	**b**	$C_5H_{11}OH$	**3ab**	A/C	60 (13)	125–127/24	–[g]
a	**c**	CH_3OH	**3ac**	A/C	92 (12)	98–100/13	108–110/25[11]
a	**d**	CH_3OH	**3ad**	A/C	45 (9)	126/20	125/15[11]
a	**e**	$C_5H_{11}OH$	**3ae**	A/C	65 (10)	109–110/1.3	110/1.3[11]
a	**f**	$C_5H_{11}OH$	**3af**	A/C	14 (2)	109–110/1.3	110/1.3[11]
b	**c**	CH_3OH	**3bc**	A/C	100 (40)	102–103/1.3	105/3[11]
b	**e**	$C_5H_{11}OH$	**3be**[e]	A/C	85 (33)	178–180/0.7	$C_{18}H_{26}O_2$ (274.4)
b	**f**	$C_5H_{11}OH$	**3bf**[f]	A/C	15 (6)	178–180/0.7	$C_{18}H_{26}O_2$ (274.4)
c	**a**	C_2H_5OH	**3ca**	A/C	60 (13)	120–122/24	–[g]
c	**c**	C_2H_5OH	**3cc**	A/C	60 (15)	104–105/13	110/19[11]

[a] All compounds were fully characterized by ^{1}H-NMR and IR data, which were in accordance with the literature data (**3aa**,[20] **3ab**,[2] **3ac**, **3ad**, **3cc**[11]).

[b] See footnote c in Table 1. Yields in parenthesis indicate yields based on the starting 1,3-dicarbonyl compound, conversion of **1** was 5–10% (Method A) and 20–50% (Methods B and C).

[c] Uncorrected.

[d] Satisfactory microanalyses obtained: C ±0.32, H ±0.15.

[e] ^{1}H-NMR (CCl_4): $\delta = 1.05$ (s, 3H); 1.06 (s, 3H); 1.50–1.65 (m, 6H); 1.85–2.73 (m, 10H); 4.98–5.92 (m, 4H).
IR ($CHCl_3$): $\nu = 1605, 1626$ (C=C–C=O) cm^{-1}.

[f] The structure proposed by analogy to literature data.[11]

[g] Ref. 2, bp not stated.

This pathway is realised *via* two successive one-electron transfer steps.[1-3,11] Another possible route of the reaction may consist in the concerted two-electron transfer in the intermediate binuclear complex **C**. The second route appears to be more plausible since dihydrofuran formation is favoured by chloride ions, which are known to be good bridging ligands capable to accelerate the electron transfer[14,15,16] (cf. the participation of similar binuclear copper(II) complexes in chlorination of carbonyl compounds,[17] oxidation of olefins,[16] phenols[17] and oxidative coupling of acetylenes[19]).

Carbonyl compounds, conjugated dienes, $CuCl_2 \cdot 2H_2O$, $Cu(OAc)_2 \cdot H_2O$, $Cu(NO_3)_2 \cdot 4H_2O$ and LiCl (all reagent grade) were distilled or recrystallized before use. All products were identified by GC, IR and ^{1}H-NMR spectral data, which were identical with the data reported.[11] GC analyses were carried out with LKhM instrument fitted with flame-ionization detector using N_2 as carrier gas. The columns used were 0.3 cm × 3 m packed with XE-60 (5%) on chromatone N-AW (0.20–0.25 mm).

2-Methyl-3-acetyl-5-vinyl-4,5-dihydrofuran (3ac); Typical Procedure:

Method A: Acetylacetone (12.0 g, 120 mmol), pyridine (1.42 g, 18 mmol) and $CuCl_2$ (1.02 g, 6 mmol) in MeOH (50 mL) are placed into a steel ampoule covered inside with teflon, and after cooling butadiene (6.49 g, 120 mmol) is added. The ampoule is shaken for 5 h at 100 °C, the mixture is filtered, poured into water (50 mL) and extracted with benzene (3 × 25 mL). The combined extract is dried (Na_2SO_4), evaporated and distilled; yield: 0.4 g (12%); bp 108–110 °C/25 mbar.

Method B: The reaction is carried out unter pressure in a special laboratory installation equiped with gas inlet and magnetic stirrer. The mixture of acetylacetone (18.0 g, 180 mmol), butadiene (9.74 g, 180 mmol), pyridine (1.42 g, 18 mmol) and copper(II) chloride (1.02 g, 6 mmol) in methanol (50 mL) is stirred for 5 h at 45 atm pressure and 100 °C, the gas (nitrogen, containing 2% of oxygen) being bubbled through the mixture at a rate 170 mL/min (at normal conditions). Work-up as described above gives the dihydrofuran **3ac**; yield: 3.15 g (12%).

2-Methyl-3-acetyl-5-phenyl-4,5-dihydrofuran (3aa); Typical Procedure:

Method C: The glass reactor, fitted with porous filter and reflux condenser, is charged with acetylacetone (9.0 g, 90 mmol), styrene (9.37 g, 90 mmol), pyridine (0.71 g, 9 mmol) and $CuCl_2$ (0.51 g, 3 mmol) in *n*-pentanol (50 mL). Air is bubbled through the mixture, and then heated to 120 °C for 5 h at a rate 40 mL/min. Work-up as described above gives dihydrofuran **3aa**; yield: 3.6 g (22%); bp 125–128 °C/0.7 mbar.

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