A Novel Copper Chelate Catalyzed Ring Closure Reaction of 1,2-Bisketenes with Alcohols To Give 5-Alkoxy-2,3-dihydrofuran-2-ones**

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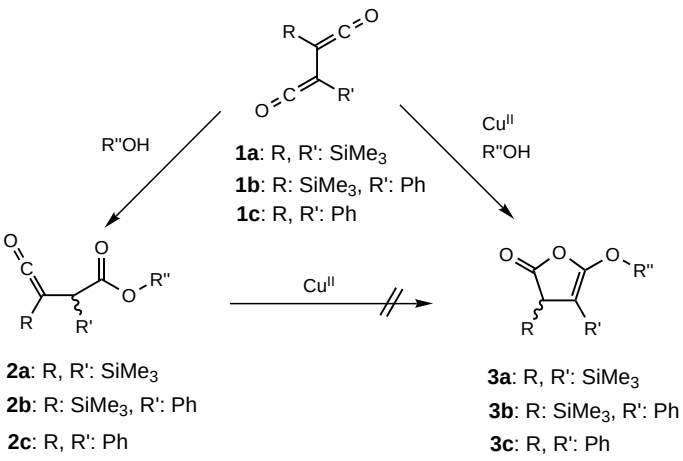
In memoriam Horst Pracejus

In the course of investigations with 1,2-bisketenes **1a–c**, which are readily accessible by a method developed by Tidwell et al.,[1] and their reaction with alcohols or phenols, respectively, we have discovered a new chelate catalyzed ring closure reaction that results in the formation of 5-alkoxy- or 5-aryloxy-2,3-dihydrofuran-2-ones **3a–c**. Up to now, only two compounds are known in which a comparable structure has been established with some certainty.[2] An efficient synthesis of this class of very reactive, β,γ-unsaturated dihydrofuran-2-ones with ketene acetal substructure is of particular interest, because numerous similarly structured, mostly α,β-unsaturated dihydrofuran-2-ones show biomimetic activity[3] for instance as antibiotics,[3a] cancerostatics,[3b,c] herbicides,[3a,d,e] or anthelmintics.[3a] Furthermore, they are also of considerable importance as part of digitalis glycosides.[3f] As the only known 5-aryloxy-substituted $\Delta^{\beta,\gamma}$-butenolide also displays antibiotic activity,[2b] interesting biological activities can also be expected from the new compounds.

One special feature of the newly discovered ring closure reaction is that until now it only succeeds catalytically and with very high selectivity. Metal complexes of ketenes as possible intermediates in catalytic reactions, such as the fixation of carbon dioxide or the CO activation, have been investigated intensively.[4] Except for a few chelate-mediated conversions of ketenes, which have mostly been stoichiometric,[5] the reaction of bisketenes mediated by complexes has not been described. Until now only interesting ring closure reactions of bisallenes, ketene allenes, and vinyl allenes, which frequently involve carbon monoxide, had been reported.[6] A bisketene complex [η^5-CpCo(η^4-bisketene)] has also been isolated.[7] Here we present the first metal complex catalyzed conversion of 1,2-bisketenes (Scheme 1).

As in an early study by Samtleben and Pracejus[8] copper(II) acetylacetonate had been employed successfully as catalyst for the alcoholysis of monoketenes, we started our investigations with this square-planar complex. However, there was no reaction between bisketene **1a** and ethanol in the presence of this catalyst. In contrast, the copper(II) complex of hydroxymethylene camphor **7**,[9] which in solution adopts a distorted tetrahedral conformation, catalyzed the conversion of the bisketene **1a** with ethanol. However, rather than the expected alcoholysis product **2a** (R″ = Et), cyclization occurred to give

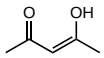
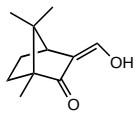
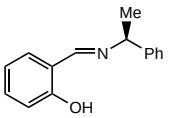
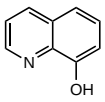
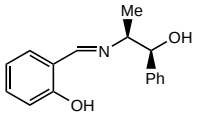
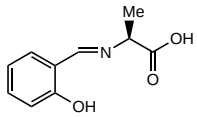


Scheme 1. Reaction of bisketenes **1** with alcohols.

the 2,3-dihydrofuran-2-one **3a** (R″ = Et) (Scheme 1). We were able to prove that this reaction does not proceed via the ketenyl ester but directly from the 1,2-bisketene to the dihydrofuran-2-one.

We achieved the highest selectivity (99 % at a conversion of 98 %) with the complex of the Schiff base **8** (Table 1).[10] The common feature of the most successful catalysts for this

Table 1. Influence of the catalyst on the reaction of **1a** with ethanol to give **3a**.[a]

	Ligand LH (or LH$_2$)	Catalyst	Conversion [%]	Selectivity [%] **3a**[13]
6		[Cu^{II}L$_2$]	< 1	–
7		[Cu^{II}L$_2$]	95	92
8		[Cu^{II}L$_2$]	98	99
9		[Cu^{II}L$_2$]	< 1	–
10		[Cu^{II}L] [Ni^{II}L] [Co^{II}L] [Pd^{II}L]	86 < 1 < 1 < 1	83 – – –
11		[Cu^{II}L]	82	78
12	L = C_8H_{12}	[Cu^{I}(cod)$_2$]BF$_4$	85	83
13	L = $Ph_2PCH_2CH_2PPh_2$	[Cu^{I}(dppe)$_2$Cl]$_2$	36	72

[a] Reaction conditions: 3 mL of a toluene solution—0.1 M of bisketene and 0.11 M of ethanol—was stirred with 3.3 mol % catalyst (prepared as a solid) for 12 h at 25 °C.

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reaction is a distorted tetrahedral structure in solution. The ring-closing reaction also took place with the tetrahedral copper(I) complexes of (*Z,Z*)-cycloocta-1,5-diene (cod) **12** or 1,2-bis(diphenylphosphanyl)ethane (dppe) **13**, whereas no conversion was observed in the presence of the square-planar bisligand complex of 1,8-hydroxyquinoline **9** or with complexes with salene or porphyrin type ligands.

Table 2. Influence of the solvent on the reaction of **1a** with ethanol; catalyst [CuL_2], LH = **8**.[a]

Solvent	Conversion [%]	Selectivity [%]
n-hexane	99	99
toluene	98	99
CH_2Cl_2	85	89
THF	23	45
DMF	< 1	–

[a] Reaction conditions see Table 1.

Since pseudo-square-planar monoligand chelates of tridentate Schiff bases derived from salicylic aldehyde and 1,2-amino alcohols **10**[11] or α-amino acids **11**[12] can be used as catalysts, we concluded that the metal center either has two free coordination sites in *cis* position or that these—as in the case of the tetrahedral complexes—can be readily created. Thus we assume the crucial step in the reaction to be the nucleophilic attack of the hydroxylic component at a copper bisketene complex that has a structure analogous to that described for a cobalt 1,2-bisketene chelate.[7] However, attempts to react this cobalt bisketene complex with alcohol to give the dihydrofuran-2-one failed; the only metal to catalyze the cyclization was copper; chelates of 14 other metals were tested (Ti, Cr, Mn, Fe, Co, Ni, Zn, Mo, Rh, Pd, Ag, Cd, Pt, Pb) but all of them turned out to be inactive.

Apolar solvents are especially suitable as reaction medium (see Table 2); with increasing coordination ability of the solvent, turnover and selectivity decrease.[13]

The structure of the component bearing the hydroxy group has no significant influence on the reaction. Thus, the ring closure was achieved with all 50 alcohols used; the conversion with tertiary alcohols is less than with primary and secondary alcohols; however, the selectivities remain higher than 95% and decrease only slightly with phenols (Table 3). The latter is presumably attributed to the higher acidity of the phenols which in turn could result in a competing acid-catalyzed reaction, leading exclusively to the ketenyl esters **2a–c**.

Use of the distinctly more reactive unsymmetrically substituted bisketene **1b** had only a minor influence on the yield

Table 3. Influence of the alcohol on the reaction with **1a** in toluene; catalyst [CuL_2], LH = **8**.[a]

R″	Conversion [%]	Selectivity [%]	B.p./*p* [°C]/[mbar]	decomp [°C]
Et	98	99	62/1.0	–
*i*Pr	97	98	67/0.5	–
adamantyl	78	96	–	87
Ph	98	91	–	94
p-nitrophenyl	93	89	–	91
p-methoxyphenyl	95	83	–	–

[a] Reaction conditions see Table 1.

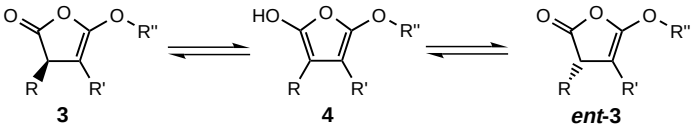
(see Table 4); the regioisomer **3b** was the only detectable product of the reaction. The further increased reactivity of the bisketene **1c** for the noncatalyzed reaction to the ketenyl ester

Table 4. Reaction of the bisketenes **1** with ethanol; catalyst [CuL_2], LH = **8**.[a]

Bisketene	R	R′	Conversion [%]	Selectivity [%]
1a	$SiMe_3$	$SiMe_3$	99	99
1b	Ph	$SiMe_3$	99	91
1c	Ph	Ph	92	65

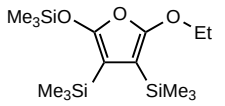
[a] Reaction conditions see Table 1; compound **1a** was generated thermally as a solid, **1b**,**c** by irradiation at 350 nm in situ.[1b]

2c led to a decrease in selectivity so that only 65% of the desired 2,3-dihydrofuranone **3c** could be obtained. It was not possible to conduct the reaction enantioselectively by using chiral catalysts. The reason for this could be a racemization, in which the 2,3-dihydrofuran-2-ones **3a–c** interconvert through the furanes **4** (Scheme 2). We were able to trap furane **4a** as isolable trimethylsilyl ether **5a**.



Scheme 2. Racemization of the 2,3-dihydrofuranones **3**.

These new findings that copper complexes open up specifically a formerly unknown reaction pathway for the reaction of 1,2-bisketenes with alcohols should stimulate future research in the long-neglected field of metal complex catalyzed reactions with ketenes.



5a

Experimental Section

3a: A solution of **1a** (5.0 g, 22 mmol),[1] ethanol (1.1 g, 23 mmol), and catalyst **8** (0.3 g, 3 mol%)[10] in toluene (70 mL) was stirred for 12 h at room temperature. The solvent was removed and the residue was fractionally distilled under vacuum to give **3a** as a colorless fraction with a boiling point of 62 °C (1 mbar). Yield: 5.8 g (95%). ^{1}H NMR (400 MHz, C_6D_6, 25 °C): δ = 4.06 (q, ^3J(H,H) = 7.1 Hz, 1H; CH_2), 3.96 (q, ^3J(H,H) = 7.1 Hz, 1H; CH_2), 2.94 (s, 1H), 1.25 (t, ^3J(H,H) = 7.13 Hz, 3H; CH_3), 0.11 (s, 9H; $SiMe_3$), 0.09 (s, 9H; $SiMe_3$); ^{13}C NMR (400 MHz, C_6D_6, 25 °C): δ = 176.9 (C2), 159.0 (C5), 84.3 (C4), 66.9 (CH_2), 43.7 (C3), 14.7 (CH_3), –0.3 (C4-Si(CH_3)$_3$), –2.7 (C3-Si(CH_3)$_3$). IR (toluene, CaF_2, 0.1 mm, 25 °C): $\tilde{\nu}$ = 1796 cm^{-1} (C=O), 1638 cm^{-1} (C=C).

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[13] The turnovers are related to the disappearance of the bisketenes **1a – c** and the selectivities to the formation of the dihydrofuranones **3a – c**. The values were obtained by IR spectroscopy after 12 h; the standard deviation is about ±1%. The ketenyl esters **2a – c** were the only observable by-products.

Rhodium and Iridium Pyrazolato Blues**

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Since the first report in 1908, great progress[1] has been made concerning the knowledge of the fascinating "platinum blues". These cationic complexes generally exhibit a chain of four platinum atoms of mixed valencies, and metal-metal interactions. They also show antitumor activity.[2] The tetranuclear chain is held together by an unsupported metal – metal bond between two dinuclear complexes. These invariably display a face-to-face structure bridged by two ligands of the type N-C-O (such as 2-pyridonate and related ligands; N represents an endocyclic nitrogen) in a head-to-head arrangement. This configuration contains two different platinum centers; one of which is O,O-coordinated and the other N,N-coordinated. Noticeably, the unsupported metal – metal bond is always formed between the O,O-coordinated platinum atoms, which are the less hindered centers. Interdimer bond formation between the N,N-coordinated platinum atoms has never been observed. Furthermore, as already pointed out by Matsumoto et al.,[2] the synthetic methods for some antitumor active blue compounds are not reproducible.

In contrast, related cationic compounds of the neighboring metals are rare for gold[3] and unknown for iridium. On the other hand, a range of oligomeric mixed-valence rhodium complexes has been reported,[4a] based on electronic spectroscopy solution studies, but full characterization has been carried out in only a few cases.[5] Closely related to this work is an intensely colored $[Rh_4]^{6+}$ species proposed by Gray et al.,[4b] and shown to be a mixed-valence compound by Mann et al.[5b] In all cases, the coordination planes in the metal chain are almost parallel, which is the most sterically favorable situation for the formation of oligomers. Once again, the parent species are dinuclear complexes with face-to-face arrangement or, alternatively, mononuclear compounds. Here we describe a straightforward and reproducible reaction from open-book dinuclear pyrazolato complexes, to form novel tetranuclear iridium and rhodium blue compounds.

Beautiful blue, EPR-silent solutions are obtained by mixing equimolecular amounts of the recently reported[6] yellow complexes $[\{Rh(\mu\text{-pz})(CN\textit{t}Bu)_2\}_2]$ (**1**) and $[\{Rh(\mu\text{-pz})(CN\textit{t}Bu)_2(NCMe)\}_2](PF_6)_2$ (**2**), from which crystals of the new tetranuclear "rhodium blue" complex $[\{Rh(\mu\text{-pz})(CN\textit{t}Bu)_2\}_4](PF_6)_2$ (**3**) were isolated (Figure 1; pz = pyrazolato). Alternatively, complex **3** can be obtained by oxidation of **1** with $[FeCp_2]PF_6$ (in a 1:1 molar ratio) in acetonitrile, and recrystallization of the crude solid from acetone/diethyl ether.

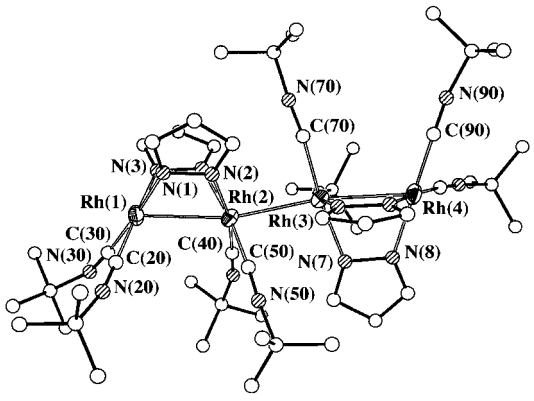

Figure 1. Molecular representation of the cation in the tetranuclear complex $[\{Rh(\mu\text{-pz})(CN\textit{t}Bu)_2\}_4](PF_6)_2$ (**3**). Only one group of atoms has been drawn for the disordered ligands. Selected bond lengths [Å] and angles [°]: Rh(1)–Rh(2) 2.721(4), Rh(2)–Rh(3) 2.713(4), Rh(3)–Rh(4) 2.723(4), Rh–N 1.99(3) – 2.13(3), Rh–C 1.84(3) – 1.97(4); Rh(1)-Rh(2)-Rh(3) 165.51(14), Rh(2)-Rh(3)-Rh(4) 167.17(15), Rh-C-N 172(3) – 179(3), C-N-C 159(4) – 176(4).

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