Synthetic and mechanistic aspects of α-alkylation and α-arylation of β-dicarbonyl compounds *via* their transition metal complexes

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Some transition metal complexes of β-dicarbonyl compounds react with electrophiles at α-C. These reactions, carried out under neutral conditions, offer a broader scope than their conventional counterparts, and are generally performed in the presence of stoichiometric or catalytic amounts of strong bases. Mechanistic observations using different reaction conditions are also relevant from a synthetic point of view.

Key words: β-dicarbonyl compounds, transition metal complex; α-alkylation; α-arylation; mechanisms.

1. Introduction

The α-alkylation of β-dicarbonyl compounds is an important C—C bond-forming reaction.[1] With the aid of a stoichiometric amount of a strong base the β-dicarbonyl compound is converted into an enolate, which undergoes S_N2 reactions with appropriate alkyl halides or tosylates. Unfortunately only methyl, allyl, benzyl and some other primary halides afford reasonable yields. Some of the problems usually found are the lack of regiospecificity (C *vs.* O alkylation), dialkylation processes, and the limitation to starting material or final products not sensitive to the basis media.[2]

However, some transition metal complexes of β-dicarbonyl compounds react with carbon electrophiles in essentially neutral media compatible with a vast array of reagents and final products. This report covers our contributions to the use of transition metal complexes of β-dicarbonyl compounds in synthetic organic methodology (for C—C bond formation) including some interesting mechanistic aspects.

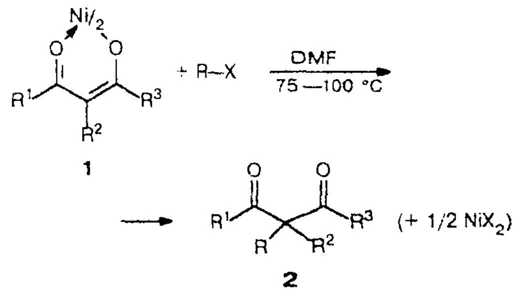
2. α-Alkylation

2.1. Alkylations stoichiometric in metal

Transition metal complexes of β-dicarbonyl compounds and their solutions are neutral in the Brønsted sense, their solubility in organic solvents being significant. This provides the required conditions for alkylations with sensitive alkyl halides.

2.1.1. The use of Ni, Co, Cu, and Zn complexes. A dual mechanistic pathway. The Ni^{II} complexes of some β-dicarbonyl compounds (**1**) react with alkyl halides to afford α-alkylation products (**2**).[3–5] The reactions are carried out in hot DMF which gives better results than $CHCl_3$, CH_3CN or DMSO. As shown in Table 1 benzylic (entries 1—7), allylic (entries 9—11) and α-carbonylic halides (entries 12, 13) are active and give moderate to good yields of condensation products. Even using chloroacetone (entry 13), an alkyl halide very sensitive to basic media, the reaction proceeds with moderate yield.

Scheme 1



1a: $R^1 = R^3 = Me$; $R^2 = H$
1b: $R^1 = R^2 = R^3 = Me$
1c: $R^1 = Me$; $R^2 = H$; $R^3 = OMe$
1d: $R^1 = Me$; $R^2 = H$; $R^3 = Ph$
1e: $R^1 = R^3 = Ph$; $R^2 = H$

We postulated[4] a mechanism in which metal—halogen coordination helps both oxygen—metal and carbon—halogen cleavage to occur (Scheme 2).

Scheme 2

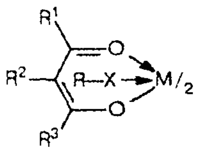


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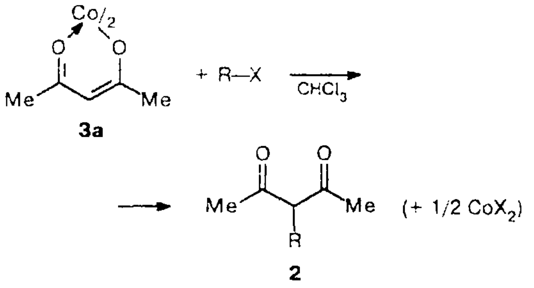
Table 1. Reactions of Ni^{II} complexes of β-dicarbonyl compounds with alkyl halides (**1**) (see Scheme 1)

Entry	Compound	R—X	Yield of **2** (%)	Ref.
1	**1a**	$PhCH_2Br$	69	3, 4
2	**1b**	$PhCH_2Br$	17	4
3	**1c**	$PhCH_2Br$	35	4
4	**1d**	$PhCH_2Br$	61	4
5	**1e**	$PhCH_2Br$	—	4
6	**1a**	$PhCH_2Cl$	32	3, 4
7	**1a**	$4\text{-}O_2NPhCH_2Cl$	18	4
8	**1a**	PhCH(Me)Br	3	4
9	**1a**	$MeOCOCH=CHCH_2Br$	65	3, 4
10	**1a**	$MeOCOCH=C(Me)CH_2Br$	54	4
11	**1a**	$(MeCOO)_2CH=CHCH_2Br$	53	4, 5
12	**1a**	$MeOCOCH_2Br$	53	3, 4
13	**1a**	$MeCOCH_2Cl$	30	3, 4
14	**1a**	$HC\equiv CCH_2Br$	22	4
15	**1a**	$n\text{-}C_3H_7I$	8	3, 4
16	**1a**	$n\text{-}C_4H_9Br$	17	3, 4
17	**1a**	$n\text{-}C_8H_{17}Br$	8	4
18	**1a**	$n\text{-}C_{16}H_{33}Br$	4	4
19	**1a**	Me_2CHBr	—	4

Pentane-2,4-dione can be C-alkylated with a large number of alkyl halides through its Co^{II} complex (**3a**) (Scheme 3).[5–10]

Scheme 3

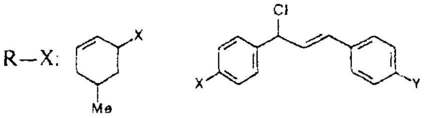


The use of $CHCl_3$ as solvent avoids all side reactions caused by DMF (nucleophilic solvent) with a corresponding improvement in reaction yields (Table 2). In our initial studies we realized that almost all the successfully tested alkyl halides have the common feature of being precursors of stabilized carbenium ions. Thus, our method introduces clear advantages over the classical methods for S_N1 active halides. *p*-Methoxybenzyl bromide (precursor of a stabilized carbenium ion) reacts easily with $Co(acac)_2$ (Table 2, entry 2), whereas *p*-nitrobenzyl bromide is nearly inert (entry 3). Entry 7 deserves particular mentioning since although 2-bromo-2-phenylpropane spontaneously looses hydrogen bromide, the yield of the final product is still significant.

Table 2. Reactions $Co(acac)_2$ (**3a**) with alkyl halides (see Scheme 3)

Entry	R—X	Conditions	Yield of **2** (%)	Ref.
1	$PhCH_2Br$	[a]	53	5
2	$4\text{-}MeOPhCH_2Br$	[a]	88	6
3	$4\text{-}O_2NPhCH_2Br$	[a]	6	6
4	Ph_2CHBr	[a]	97	5
5	Ph_3CCl	[a]	29	5
6	PhCH(Me)Br	[a]	94	5
7	$PhC(Me)_2Br$	-20 °C	14	5
8	$Me_2C=CCH_2Cl$	[a]	76	5
9	$(MeCOO)_2CHCH=CHCH_2Br$	90 °C	8	5
10	3-Bromocyclohexene	100 °C	75	9
11	MeCH(Br)CH=CHMe	100 °C	58	9
12	1-Bromoadamantane (**4**)	[b]	81	6, 7
13	2-Bromoadamantane	[c]	21	9
14	Me_3CBr	[a]	4	5
15	Me_3CI	100 °C	15	9
16	9-Bromofluorene (**5**)	[a]	[d]	8
17	**6**[e]	80 °C	90[f]	10
18	**7**[g]	120 °C	71[h]	10
19	**8**[i]	100 °C	88[j]	10

[a] Refluxing. [b] In refluxing chlorobenzene. [c] In 1,1,2,2-tetrachloroethane at 185 °C. [d] Not disclosed. [e] *Cis/trans* = 25 : 75; [f] *cis/trans* = 15 : 85; [g] *cis/trans* = 46 : 54; [h] *cis/trans* = 18 : 82; [i] **8a**/**8b** = 40 : 60; [j] **a**/**b** = 56 : 44.



6: X = Br
7: X = Cl

8a: X = Cl, Y = NO_2
8b: X = Cl, Y = Cl

The same procedure (Scheme 4) can be applied to Co^{III} and Zn^{II} acetylacetonates, which show a reactivity similar to that of Co^{II} (Table 3).[5–7]

This suggests a similar mechanistic pathway for the three complexes. Coordinatively saturated complexes $Co(acac)_3$ and $Zn(acac)_2$ can act as Lewis acids activating the halide, if they previously lose at least one ligand.

Scheme 4

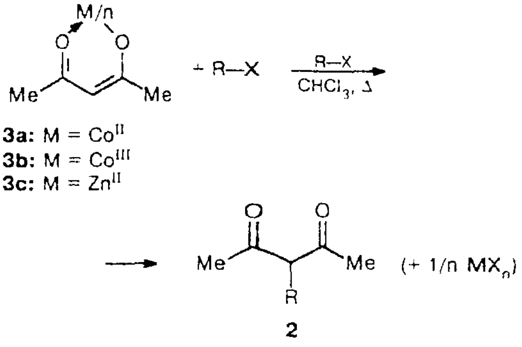


Table 3. Yields of alkylation products (**2**) using different metal complexes **3a—c** (see Scheme 4)

Entry	R—X	Yield of **2** (%)			Ref.
		$Co(acac)_2$	$Co(acac)_3$	$Zn(acac)_2$	
1	$PhCH_2Br$	53	59	65	5, 6
2	$4\text{-}MeOPhCH_2Br$	88	77	[a]	6
3	$4\text{-}O_2NPhCH_2Br$	6	0	0	6
4	Ph_2CHBr	97	96	87	6
5	Ph_3CCl	29	[a]	18	5, 6
6	PhCH(Me)Br	75	58	61	6
7	**4**	81[b]	[a]	75[b]	6, 7

[a] Not performed. [b] In refluxing chlorobenzene.

The extension of the Co^{II}-based alkylation method to the complexes of several diketones is described in Table 4 and Scheme 5.

Scheme 5

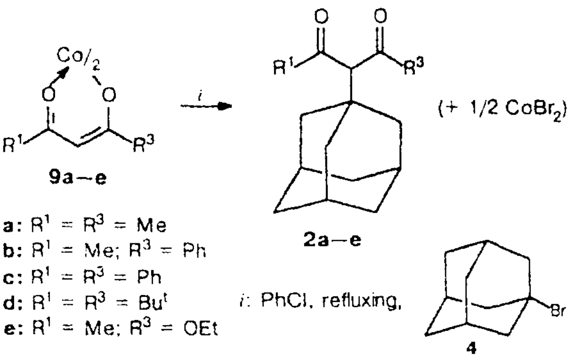


Table 4. Reactions of Co^{II} complexes of β-dicarbonyl compounds (**9a—e**) with 1-bromoadamantane (see Scheme 5)

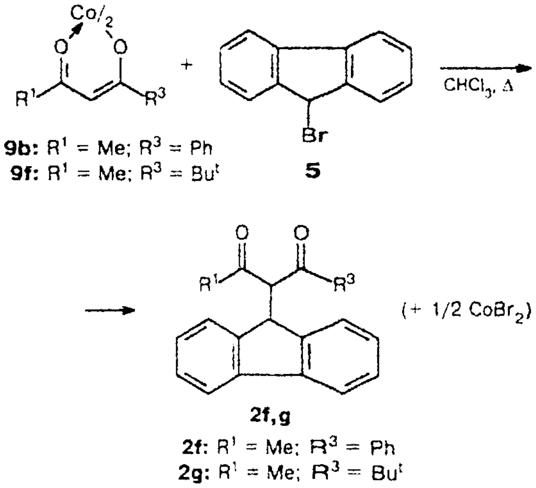
Entry	Compound	Product	Yield of **2** (%)	Ref.
1	**9a** = **3a**	**2a**	81	6, 7
2	**9b**	**2b**	89	6, 7
3	**9c**	**2c**	80	6, 7
4	**9d**	**2d**	31	7
5	**9e**	**2e**	38	6, 7

In spite of the low reactivity of 1-bromoadamantane (**4**) in substitution reactions, the alkylation reaction gives excellent results (Table 4).[6,7]

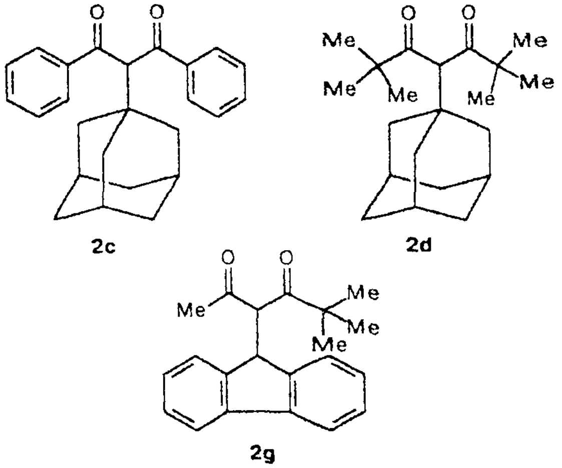
Preparative useful yields are also obtained with 9-bromofluorene **5** (Scheme 6).[8]

It should be noted that some of the β-diketones so prepared are sterically hindered (Scheme 7).[6—8]

Scheme 6



Scheme 7



It is clear that this methodology offers clear advantages over the classical methods for active S_N1 halides and for others such as **4** and **5**. These reactions carried out in relatively dilute solutions do not show any sensitivity to the presence of radical scavengers,[6] and their general features as well as the halides involved suggest a non-radical pathway with activation by the cobalt species as Lewis acid.

An improvement of the original method is related to the elucidation of an alternative mechanism triggered under certain experimental conditions. The procedure consists in carrying out the reactions under high concentration conditions or simply evaporating the solvent at 120 °C (Scheme 8).[9] This gives very fast reactions[11] and some halides, unreactive under the conditions previously reported, gave now good condensation yields (entry 1 of Table 5 as compared with entry 3 of Table 2).

The kinetic behavior of these reactions at high concentration conditions show, for different alkylating agents,

Scheme 8

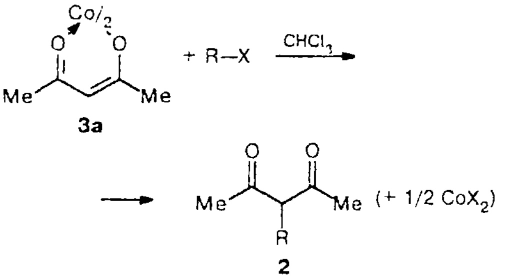


Table 5. Reactions of alkyl halides (**3a**) with $Co(acac)_2$ using high concentration conditions (see Scheme 8)

Entry	R—X	τ/min*	Yield of **2** (%)
1	$4\text{-}O_2NPhCH_2Br$	90	72
2	$4\text{-}O_2NPhCH_2Cl$	60	0
3	$PhCH_2Br$	1.5	89
4	$4\text{-}MeOPhCH_2Br$	12	87
5	$Me_2C{=}CH_2Br$	2	66
6	$PhCH(CH_3)Br$	6	65
7	**4**	240	68

* τ is the duration of the reaction.

Note. Standard conditions: A round-bottomed flask, without reflux condenser, containing $Co(acac)_2$ (1 mmol), alkyl halide (2 mmol), and chloroform (2 mL) was introduced in an oil bath at 120 °C.

an induction period that is reduced at higher concentrations. Once the reaction starts, they are almost instantaneous, at least up to 50% conversion, suggesting a chain reaction. The induction period is reduced in the presence of $CoCl_2$ (autocatalyzed reaction), and free radicals are only present at the initiation steps (galvinoxyl increases the induction period but the process is almost instantaneous once elicited). The isolation of radical dimers supports the conclusion that free radicals are present. Our experiments indicate that the reaction rate is very sensitive to the leaving group (I > Br > Cl > OAc > OH). All data referred to the initiation steps[12] can be accommodated to Scheme 9. It includes a slow first step (perhaps responsible for the induction period) that would produce $Co^{II}X_2$ species, which induces an inner sphere electron transfer only possible with halides as leaving groups. These initiation steps produce an alkylcobalt(III) complex that would start the chain.

Scheme 9

$$(acac)_2Co^{II} + 2\,RX \rightarrow 2\,acacR + Co^{II}X_2 \qquad (1)$$

(induction period)

$$Co^{II}X_2 + RX \rightarrow R^{\bullet} + Co^{III}X_3 \qquad (2)$$

(inner sphere electron transfer)

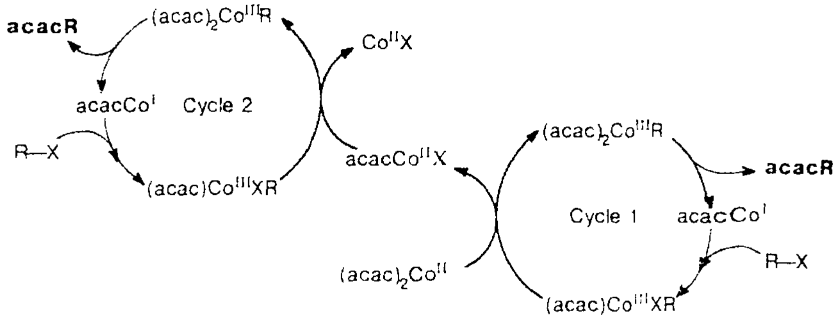
$$R^{\bullet} + (acac)_2Co^{II} \rightarrow (acac)_2Co^{III}R \qquad (3)$$

As we have commented, experiments with galvinoxyl indicate that no alkyl free radicals are present in the propagation cycle. The absence of cyclized alkylation products in experiments with cyclizable probes (radical clocks) also suggest the same hypothesis. Therefore, we have proposed[12] a chain process based on cobalt's ability to undergo redox processes between the Co^{I} and Co^{III} states, including oxidative addition and reductive elimination steps. The chain propagation sequence is shown in Scheme 10.

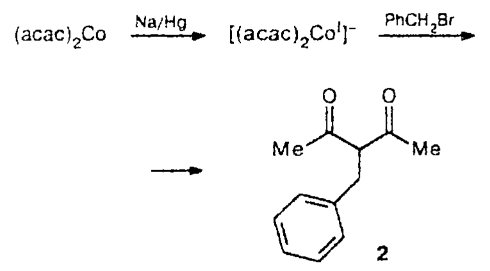
Scheme 10

$$\left\{\begin{array}{l} (acac)_2Co^{III}R \longrightarrow \mathbf{acacR} + acacCo^{I} \\ acacCo^{I} + R{-}X \longrightarrow acacCo^{III}XR \\ acacCo^{III}XR + (acac)_2Co^{II} \longrightarrow (acac)_2Co^{III}R + acacCo^{II}X \end{array}\right\} \text{Cycle 1}$$

$$\left\{\begin{array}{l} acacCo^{III}XR + acacCo^{II}X \longrightarrow (acac)_2Co^{III}R + Co^{II}X_2 \\ (acac)_2Co^{III}R \longrightarrow \mathbf{acacR} + acacCo^{I} \\ acacCo^{I} + R{-}X \longrightarrow acacCo^{III}XR \end{array}\right\} \text{Cycle 2}$$



Scheme 11



$[(\mathrm{acac})_2\mathrm{Co^I}]^- + \mathrm{R{-}X} \longrightarrow (\mathrm{acac})_2\mathrm{Co^{III}R} + \mathrm{X}^-$

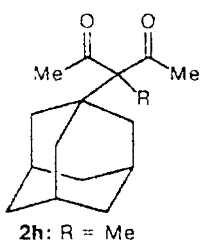
$(\mathrm{acac})_2\mathrm{Co^{III}R} \longrightarrow \mathrm{acacCo^I} + \mathrm{acacR}$

$\mathrm{acacCo^I} + \mathrm{R{-}X} \longrightarrow \mathrm{acacCo^{III}XR}$

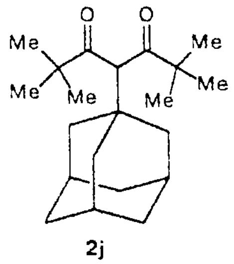
Our experiments show that these reactions can be carried out using anionic Co$^{\mathrm{I}}$ complexes independently generated. These results confirm the operation of Co$^{\mathrm{I}}$ species as intermediates. Thus, Co(acac)$_2$ is reduced with sodium amalgam and the resulting [Co(acac)$_2$]$^-$ reacts with benzyl bromide to afford 3-benzylpentane-2,4-dione (Scheme 11).[12]

The yield obtained in this experiment (32%) suggests that only the (acac) unit was consumed. Following our model (Scheme 11) is seems that the cobalt ends as (acac)CoXR, a complex relatively inert to reductive elimination. This could explain the fact that in some cases the first (acac) unit is consumed faster (1st Cycle, Scheme 10) than the second (2nd Cycle, Scheme 10).

2.1.2. The use of Cu complexes. Preparation of severely hindered **β*-diketones.*** We propose that Co$^{\mathrm{III}}$ species are intermediates in the mechanism of cobalt mediated C-alkylations. Since Co$^{\mathrm{III}}$ species are also known[13] and Cu is two places away from Co in the periodic table, of β-diketones we could expect similar behavior for both metals. Cu$^{\mathrm{II}}$ complexes are easily accessible, but more stable and quite inert toward alkylating agents so they have been rather used to protect intercarbonyl positions.[14,15] Nevertheless, Cu$^{\mathrm{II}}$ β-diketonates are also excellent alkylation substrates (Scheme 12, Table 6) and react with alkyl bromides under high concentration conditions[14,16–18] (by radical-initiated mechanism) to give highly congested β-diketones such as **2h** and **2i**, which have two contiguous quaternary centers, and hindered β-diketone **2j**.

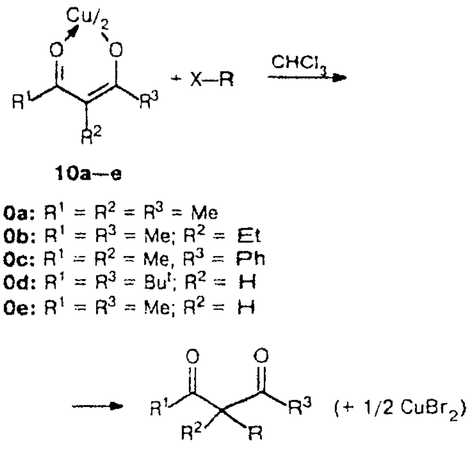


2h: R = Me
2i: R = Et



2j

Scheme 12



10a–e

10a: R^1 = R^2 = R^3 = Me
10b: R^1 = R^3 = Me; R^2 = Et
10c: R^1 = R^2 = Me, R^3 = Ph
10d: R^1 = R^3 = Bu^t; R^2 = H
10e: R^1 = R^3 = Me; R^2 = H

2

Table 6. Reactions of Cu$^{\mathrm{II}}$ complexes of β-dicarbonyl compounds (**10a–e**) with alkyl halides (see Scheme 12)

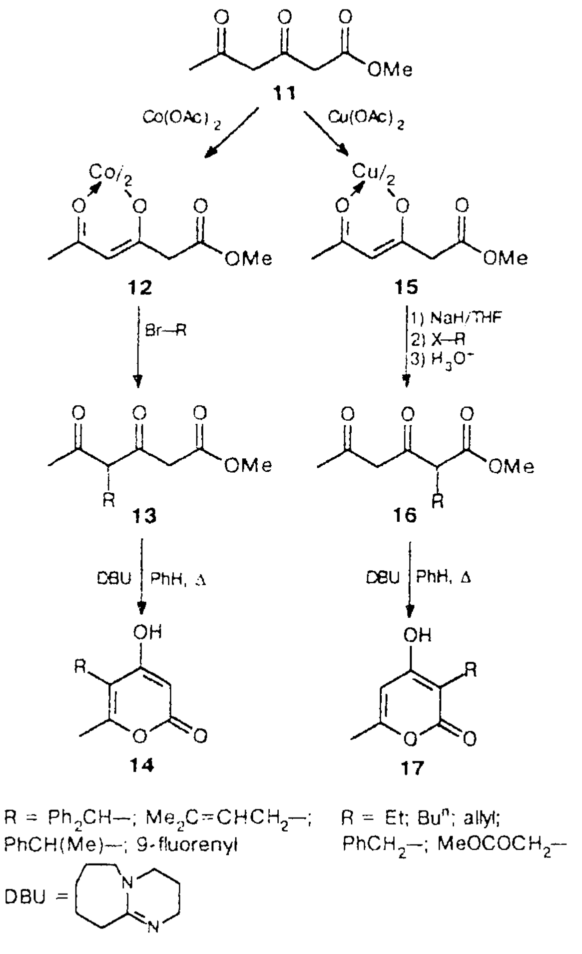
Entry	Compound	X–R	T/°C	Yield 2 (%)	Ref.
1	**10a**	BrCH$_2$Ph	100–115	80	16, 17
2	**10a**	BrCHPh$_2$	100–115	44	16, 17
3	**10a**	BrCH$_2$CH=CH$_2$	100–115	88	16, 17
4	**10a**	3-Bromocyclohexene	50	56	18
5	**10a**	**4**	100–115	25 (**2h**)	16, 17
6	**10b**	**4**	100	31 (**2i**)	16
7	**10a**	**5**	100–115	65	16, 17
8	**10c**	BrCH$_2$Ph	100–115	43	16, 17
9	**10c**	BrCHPh$_2$	100–115	76	16, 17
10	**10c**	BrCH$_2$CH=CH$_2$	100–115	30	16, 17
11	**10c**	**4**	100–115	1	16, 17
12	**10c**	**5**	100–115	30	16, 17
13	**10d**	**4**	160	31 (**2j**)	17
14	**10e**	BrCHPh$_2$	*	77	14

* Refluxing.

Copper(II) bromide, the other product of the reaction (Scheme 12), is itself a brominating agent for activated positions such as intercarbonylic methine groups. This imposes a limitation when using Cu$^{\mathrm{II}}$ β-diketonates **10** in alkylation reactions (entries 13, 14 in Table 6). No such limitation exists for the Co$^{\mathrm{II}}$ complexes since cobalt(II) halides are not halogenating agents.

2.1.3. Regioselective alkylation of polyketide model through activation and protection by Co and by Cu. Regioselective useful alkylations of poly-β-carbonyl compounds are still a synthetic challenge. The presence of more than one activated position with protons of similar

Scheme 13



R = Ph$_2$CH—; Me$_2$C=CHCH$_2$—; PhCH(Me)—; 9-fluorenyl

R = Et; Bu^n; allyl; PhCH$_2$—; MeOCOCH$_2$—

acidity renders the synthetic goal really difficult. Regioselective C-alkylations at the intercarbonylic positions C-4 and C-2 of the polyketide model methyl 3,5-dioxohexanoate (**11**) have been accomplished through reactions of its Co^{II} and Cu^{II} complexes, respectively (Scheme 13).[14] Regioselective alkylation on Co^{II} complex **12** (activation by Co of position C-4) affords methyl 4-alkyl-3,5-dioxohexanoates (**13**) which can be cyclized to 5-alkyl-4-hydroxy-6-methyl-2-pyrones (**14**). In sharp contrast, copper protects the diketone moiety in complex **15** (more stable than the cobalt one), and alkylations under conventional conditions produce diketoesters **16** which can be cyclized to 3-alkyl-4-hydroxy-6-methyl-pyrones (**17**).

Apparently, the Co^{II} and Cu^{II} complexes of β-diketonates look very different in reactivity. However, an active alkyl halide such as benzhydryl bromide can react with both metal complexes (Schemes 13 and 14).[14] Double alkylations at C-2 and C-4 are accomplished by initial reaction at C-2 of the copper complex **15** (protection of the diketone), avoiding the hydrolysis step, and continuing by a second reaction with benzhydryl bromide at C-4 due to activation of this position by the metal (Scheme 14). In fact, Cu protects the intercarbonylic C-4 position in S_N2 type reactions and both Co and Cu activate the same C-4 toward radical-organometallic type alkylations.

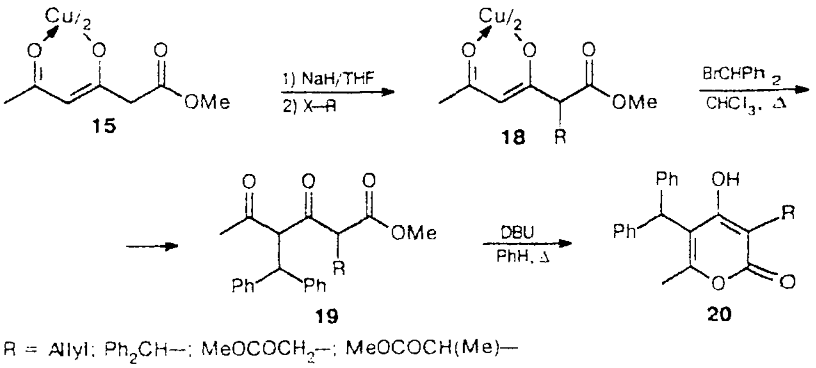
Allylations of active positions under palladium catalysis constitute a powerful carbon—carbon bond formation method. Thus, we applied combined cobalt—palladium and copper—palladium methodologies to achieve regioselective allylation of the model polyketide

Table 7. Palladium catalyzed allylation of Cu complexes of methyl 3,5-dioxohexanoate (**15**) (see Scheme 15)[15]

Entry	R—OAc (or R—OCOOEt)	T/°C	τ/h	Yield (%)	
				16	**21**
1	(E)-PhCH=CHCH$_2$—	75	19	17	50
2	2-Cyclohexen-1-yl	80	17	89	0
3	(E)-MeCH=CHCH(Me)—	75—79	17	72	0
4	Me$_2$C=CHCH(Me)—	80—95	27	8	33
5	Me$_2$C=CHCH$_2$—	70	5	25	33

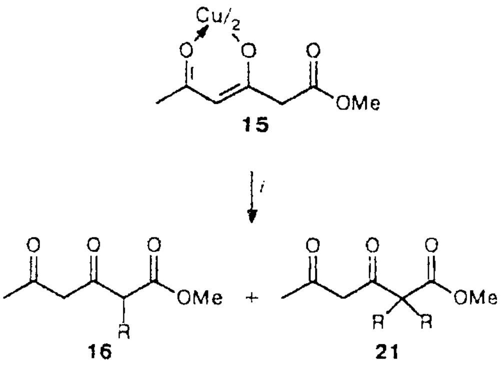
Note. Standard conditions: To a mixture of NaH and **15** is added a solution of R—OAc, Pd(dba)$_2$, and PPh$_3$. Molar ratio of reagents: **15** : NaH : R—OAc : Pd : PPh$_3$ = 1 : 2 : 2 : 0.02 : 0.2.

Scheme 14



R = Allyl; Ph$_2$CH—; MeOCOCH$_2$—; MeOCOCH(Me)—

Scheme 15

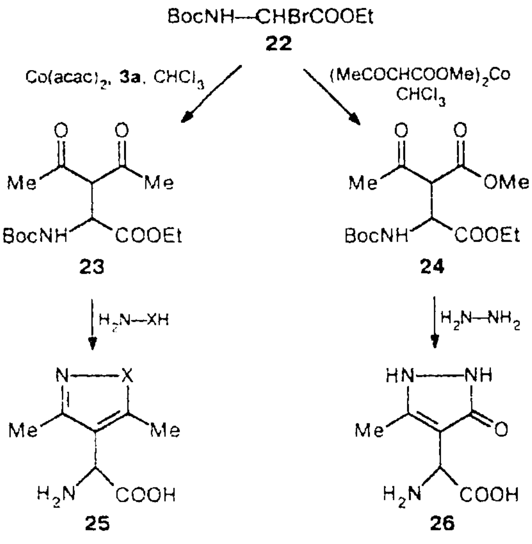


i. 1) NaH; 2) R—OAc (or R—OCOOEt), Pd(dba)$_2$/PPh$_3$.

system methyl 3,5-dioxohexanoate (**11**).[15] Copper(II) complex **15** is sequentially treated with sodium hydride and with the corresponding allylic acetate under palladium catalysis to give good yields of allylation products **16** and **21** from regioselective allylation at C-2 (Scheme 15, Table 7). The reactions are successful with primary (entries 1 and 5) as well as with secondary acetates or carbonates (entries 2—4). Initial results indicate that cobalt(II) complex can be also useful.

2.1.4. Induction of enantioselectivity at the electrophile. The preparation of homochiral five-membered heterocyclic α-amino acids. As mentioned before, we have developed a method based on an initiation in which a carbon radical, R•, is formed and a propagation in which organometallic intermediates play a key role. Therefore, alkyl halides forming stabilized captodative radicals ought to be good alkylating agents.

Scheme 16



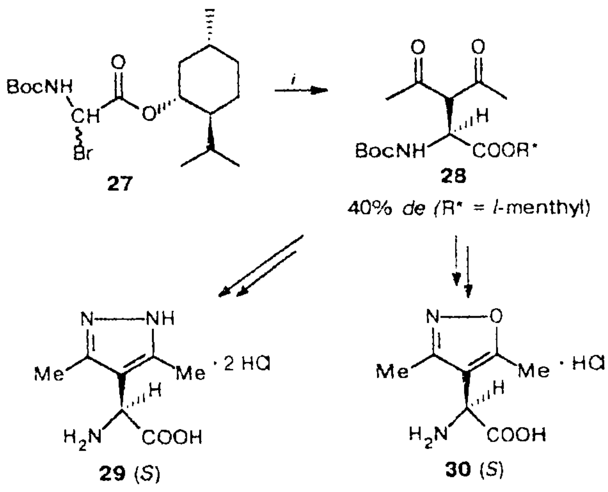
X = N, O; Boc = ^{t}BuOC(=O)—

Glycine derivatives, both electrophilic and nucleophilic at the central carbon atom, are broadly used for amino acids preparation.[19] However, radical synthons of glycine derivatives have been seldom used.[20,21]

The *N*-Boc-2-bromoglycine derivative **22** reacts with Co^{II} complexes of β-dicarbonyl compounds to afford compounds **23** and **24** which are further converted into five-membered heterocyclic amino acids (Scheme 16). We proposed the formation of a radical-organometallic glycine synthon, using 2-bromoglycine derivatives as a source of the stabilized captodative radical.[22]

The chiral version is shown in Scheme 17. Thus, (1*R*, 3*R*, 4*S*)-menthyl 2-bromo-*N*-*t*-Boc-glycinate (**27**) reacts with cobalt(II) bis(pentane-2,4-dithionate) (**3a**) to afford both diastereoisomers of **28** (70 : 30). The major one is isolated by crystallization. Reactions of **28** with hydrazine and with hydroxylamine afford the enantiomerically pure amino acids after deprotection.[22]

Scheme 17



i: Co(acac)$_2$/CHCl$_3$, 18—25 °C

2.2. Catalytic alkylations

The effect of Co^{II} chloride reducing the induction period of radical-initiated reactions has been previously mentioned in this review (see Section 2.1.1). In our continuing effort to improve the methodology we have studied the direct alkylation of β-dicarbonyl compounds using catalytic amounts of cobalt without previous formation of cobalt chelates.[23,24] As seen in Table 8 the corresponding α-substituted products are efficiently obtained through catalysis by cobalt(II) chloride bis(triphenylphosphine) in chloroform and in the presence of potassium carbonate (Scheme 18).[23] The active alkyl halides are of the same type as those active in radical initiated alkylations. By analogy we suggest an electron transfer initiation step due to the radical character and

Table 8. Cobalt(II) catalyzed alkylation of β-dicarbonyl compounds (see Scheme 18)[23]

Entry	R^1	R^3	R^2	τ/h	Yield of **2** (%)
1	Me	Me	Ph_2CH	1	75
2	Me	Me	$Ph(CH_3)CH$	8	78
3	Me	Me	1-(2-Naphtyl)ethyl	3	83
4	Me	Me	$4\text{-}O_2NPh(CH_3)CH$	12	40
5	Me	Me	$PhCH_2$	4	62
6	Me	Me	$4\text{-}O_2NPhCH_2$	3	61
7	Ph	Me	Ph_2CH	3	89
8	Ph	Ph	Ph_2CH	3	83
9	Ph	Me	$Ph(CH_3)CH$	3	88
10	Ph	Ph	$Ph(CH_3)CH$	4	61
11	Me	EtO	$Ph(CH_3)CH$	12	52

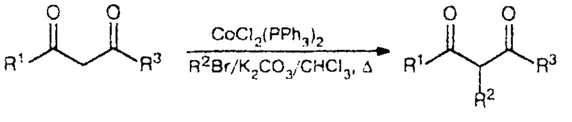
Table 9. Comparison between the Co^{II} catalyzed and the uncatalyzed alkylations[23]

Entry	R^1	R^3	R^2	τ/h	Conversion[a]	
					Catalyzed[b]	Uncatalyzed
1	Me	Me	$Ph(CH_3)CH$	5	14/82	76/12
2	Me	EtO	$Ph(CH_3)CH$	6	6/66	55/9
3	Me	Me	$CH_2{=}CHCH_2$	5	23/63	49/51
4	Me	Me	$PhCH_2$	4	3/97	80/20
5	Me	Me	Ph_2CH	2	15/70	81/13
6	Me	Me	$4\text{-}O_2NPhCH_2$	5	0/99	41/57

[a] Ratios of starting bromide to final product chromatographic areas. [b] In the presence of 0.1 equivalent of $CoCl_2(PPh_3)_2$.

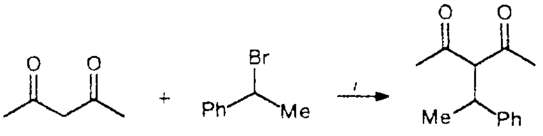
redox ability of Co^{II} to elicit a chain mechanism. The results in Table 9 indicate that the alkylation of β-diketones and ethyl acetoacetates under these conditions is remarkably accelerated by the presence of cobalt(II) chloride bistriphenylphosphine.[23]

Scheme 18



2

Other results that confirm the operation of Co^{I} species as intermediates in the radical-initiated mechanism are shown below. Thus, the reaction of pentane-2,4-dione with 1-bromo-1-phenylethane (**31**) can be catalyzed by $CoCl(PPh_3)_3$ as efficiently as the Co^{II} complex does.



31 **2**

i. K_2CO_3, $CHCl_3$, 80 °C, 5 h.

Catalyst	**31**/**2***
—	88/12
$CoCl_2(PPh_3)_2$	1.42/81
$CoCl(PPh_3)_3$	0.52/81

* Relative chromatographic areas of the peaks corresponding to the starting product **31** and the final product **2**.

3. α-Arylation

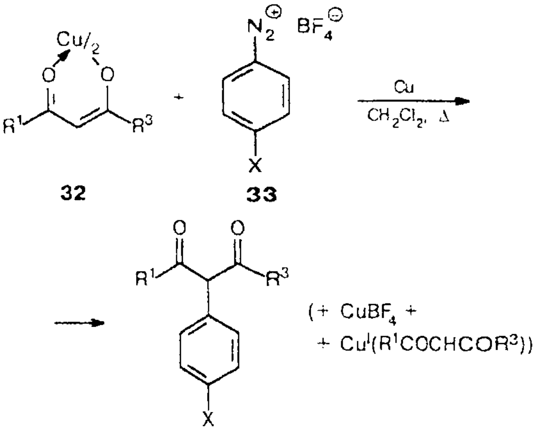
Arylation of organic compounds is an important synthetic goal that attracts considerable attention. Most of the methods described for arylating active methylene compounds are based on halides as leaving groups, the use of diazonium salts in arylation of β-diketones at α-C being limited in scope.[25]

3.1. The use of Cu complexes

No direct reaction is observed between transition metal complexes of β-diketones and arylhalides. Thus, according to the radical-initiated cyclic mechanism we have proposed, we decided to examine the possibility of arylating by generating the aryl radical from arenediazonium salts and copper powder.

Copper complexes of 2,2,6,6-tetramethylheptane-3,5-dione and other β-diketones afford α-aryl-β-diketones (**34**) when treated with arenediazonium tetrafluoroborates (**33**) and copper powder in dichloromethane as solvent (Scheme 19).[26] Our results are summarized in Table 10. $CuBF_4$ and Cu^{I} complexes, the other suspected reaction products, were not isolated; their formation is assumed on the basis of the recovery of half the starting diketone upon work-up.

Scheme 19



34

Table 10. Reactions of Cu^{II} complexes (**32**) with diazonium salts (**33**) and Cu powder (Scheme 19)[25]

Entry	R^1	R^3	X	Yield of **34** (%)
1	Me	Me	MeO	21
2	Me	Me	H	41
3	Me	Me	Cl	21
4	Me	Me	NO_2	38
5	Me	Ph	H	21
6	Ph	Ph	H	35
7	Bu^t	Bu^t	H	34
8	Bu^t	Bu^t	F	31
9	Bu^t	Bu^t	Cl	25
10	Bu^t	Bu^t	Br	34
11	Bu^t	Bu^t	NO_2	10

A review covering other synthetic applications of transition metal complexes of β-dicarbonyl compounds has been recently published by us.[26]

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