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Metal catalysed reactions of β,β′-tricarbonyl derivatives with isocyanates

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ABSTRACT

The reactions of β,β′-tricarbonyl derivatives with isocyanates are catalysed by 2 mol % transition metal acetylacetonates (e.g., [Co(acac)$_2$] and [Zn(acac)$_2$]) at room temperature. 3-Oxo-1,5-pentanedioic acid dimethylester (**1**) reacts with RNCO (R=Et, $CH_2CH{=}CH_2$, CH_2Ph, Ph, 4-Cl–Ph) to give 1:1 adducts involving the formation of a new C–C bond between the intercarbonylic methylene and the isocyanato group. Under similar conditions 2,4,6-heptanetrione (**2**) reacts with the same isocyanates to afford pyridinone and pyranone derivatives resulting from the cyclisation of unstable 1:1 and 1:2 adducts.

1. Introduction

Polyketides represent a class of natural products, which cyclise to a great number of aromatic and heteroaromatic derivatives or are transformed in fatty acids.[1]

Tricarbonyl derivatives, such as dialkyl 3-oxopentane-dionates, have been studied as simple polyketide models. In particular the regioselective alkylation of Cu(II) and Co(II) complexes of ethyl 3,5-dioxohexanoate has been reported.[2]

It is well known that β-dicarbonyls derivatives react in the presence of metal catalysts with carbon electrophiles,[3] such as isocyanates,[4] Michael acceptors[5] and nitriles,[6] in the presence of metal catalysts to give adducts derived from the formation of new C–C bonds between the methylene group of dicarbonyls and the reactive atom of the electrophile.

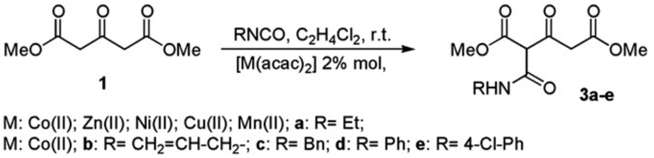
In an interesting recent extension new chiral bifunctional ruthenium-based catalysts are very efficiently used in Michael reactions involving a series of dicarbonyls and activated olefins.[7] In all cases deprotonation of 1,3-dicarbonyl compounds to give coordination to the metal of C- or O-bonded enolates is the key step of the catalytic process.

In this context, it is surprising that, to the best of our knowledge, no catalytic reactions of β,β′-tricarbonyl derivatives with electrophiles have been up to now reported. In fact, on the basis of the previously reported results on the metal catalysed reactions of β-dicarbonyls with electrophiles,[3–7] and on the alkylation of Cu(II) and Co(III) metal complexes of diethyl 3-oxopentane-dionate,[2] it is expected that also β,β′-tricarbonyl derivatives should give similar interesting C–C bond formations.

In this paper we report the reactions of 3-oxo-1,5-pentanedioic acid dimethylester (**1**) and of 2,4,6-heptanetrione (**2**), chosen as model compounds, with isocyanates in the presence of catalytic amounts of metal acetylacetonates.

2. Results and discussion

The reactions of the two tricarbonyl substrates **1** and **2** with the various isocyanates were performed in dichloroethane in the presence of 2 mol % transition metal acetylacetonates, at room temperature and times changing from 1 day for **1** to 3 days for **2**. Under these conditions 3-oxo-1,5-pentanedioic acid dimethylester (**1**) was allowed to react with ethyl isocyanate: high yields of the 1:1 adduct **3a** (Scheme 1) were obtained using as catalyst [Co(acac)$_2$] (yield 98%), [Zn(acac)$_2$] (97%), [Ni(acac)$_2$] (95%), [Cu(acac)$_2$]



Scheme 1.

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(91%) and [Mn(acac)$_2$] (95%). No product was obtained in a test reaction of **1** with ethyl isocyanate in the absence of catalyst.

The formation of compound **3a** clearly indicates that the presence of a metal catalyst is able to promote C–C bond formation between one intercarbonylic and one isocyanato carbon atom, thus closely resembling the behaviour observed with β-dicarbonyls substrates.

[Co(acac)$_2$] was employed in the reactions of β,β′-ketodiester **1** with different R substituted isocyanates. The results were very similar: higher yields (ca. 90%) were obtained in the reactions with R=ethyl, vinyl and benzyl, whereas with aryl isocyanates (R=Ph, 4-Cl–Ph) (Scheme 1) yields dropped to ca. 65%.

Although compound **3** series could present more than one species in solution, the ^{1}H NMR spectra in CDCl$_3$ show the presence of only one tautomer characterised by two resonances at ca. 9.0 and ca. 18.5 ppm, attributable, respectively, to an NH and an OH involved in hydrogen bonds. Moreover the ^{13}C NMR spectrum shows an absorption at 186.9 ppm attributable to the enolic carbon atom.

On the basis of these data the more probable species present in solution is the enolic tautomer depicted in Figure 1.

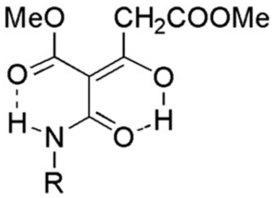


Figure 1.

X-ray diffraction analysis of the crystalline compound **3e** derived from the reaction of **1** with 4-chlorophenylisocyanate demonstrated that in the solid-state this compound has the structure depicted in Figure 2. The presence of two strong hydrogen bonds explains the ^{1}H NMR absorptions of OH and of NH hydrogens at very high frequency.

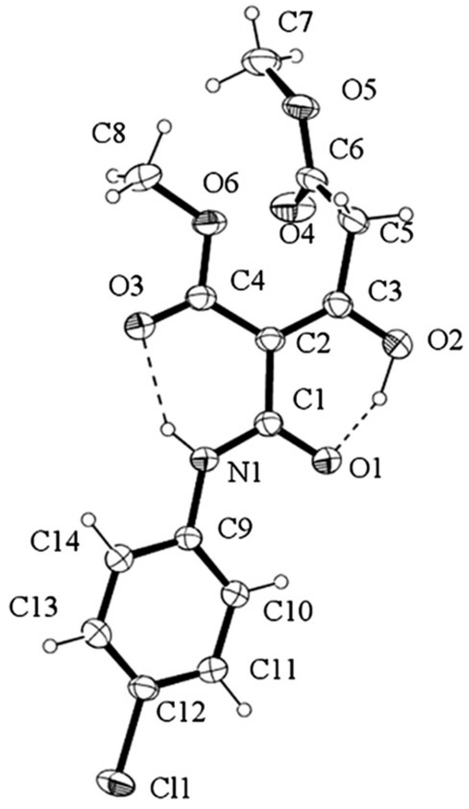
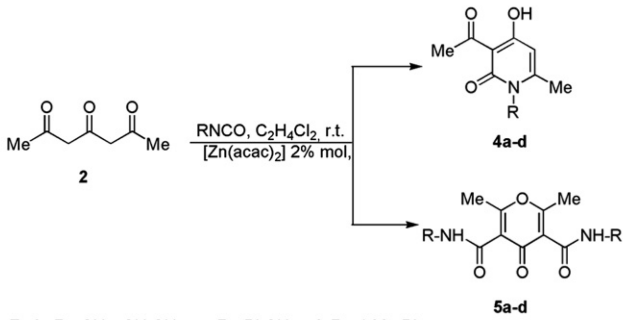


Figure 2. An ORTEP view of compound **3e** displaying the thermal ellipsoids at 30% probability.

By contrast with the reactions of the β,β′-ketodiester **1**, the triketone 2,4,6-heptanetrione (**2**) reacts with isocyanates (R=Et, CH$_2$=CH–CH$_2$, PhCH$_2$, 4-Me–Ph) in the presence of [Zn(acac)$_2$] (2 mol %) to give two types of products, the pyridinones **4** and the 4-pyranones **5** (Scheme 2).



a: R= Et; **b**: R= CH$_2$=CH-CH$_2$-; **c**: R= PhCH$_2$-; **d**: R= 4-Me-Ph

Scheme 2.

The pyridinone **4** can simply be derived from an 1:1 adduct analogous to compound **3**, which cyclises to give **4** with elimination of a molecule of water, whereas the formation of the 4-pyranone **5** requires the addition/insertion of two molecules of isocyanate to triketone **2**. One can envisage the formation of an unstable 1:2 adduct followed by its cyclisation involving also in this case elimination of a water molecule. As expected the reactions carried out with a higher RNCO/(**2**) molar ratio (Table 1) afford the double insertion product **5** in higher yields.

Table 1
Reaction of 2,4,6-heptanetrione (**2**) with isocyanates catalysed by [Zn(acac)$_2$] with varying reagents ratios

R	RNCO/(**2**) molar ratio	Yield (%)	
Et	1.1/1	35 (**4a**)	8 (**5a**)
Et	4/1	6 (**4a**)	41 (**5a**)
CH$_2$=CHCH$_2$	1.1/1	45 (**4b**)	14 (**5b**)
CH$_2$=CHCH$_2$	4/1	20 (**4b**)	40 (**5b**)
PhCH$_2$	1.1/1	35 (**4c**)	15 (**5c**)
PhCH$_2$	4/1	10 (**4c**)	65 (**5c**)
4-MeC$_6$H$_5$	1.1/1	35 (**4d**)	14 (**5d**)
4-MeC$_6$H$_5$	4/1	10 (**4d**)	42 (**5d**)

The different behaviour exhibited by the two types of tricarbonyls requires a few comments. The reaction mechanism implies the formation of the real catalyst via ligand exchange of the tricarbonyl substrate with the acetylacetonato metal complex. This reaction involves the deprotonation of the intercarbonylic methylene group. Metal(II) complexes of this type (M=Mg,[8] Ca,[8] Mn,[9] Co,[9] Ni,[9] Cu,[8,9] Zn[8,9]) are well known, and this exchange reaction represents a reported synthetic procedure to give triketonato complexes.[10] With β,β′-ketodiesters only one of the methylene groups can be deprotonated, giving a monoanionic ligand coordinated to only one metal center (Fig. 3, form A). The situation drastically changes with the 1,3,5-triketones, in fact here deprotonation of one or both methylene groups can occur, giving rise to coordination of one or two metal centers for each triketonato ligand (Fig. 3, forms A and B).[11–13]

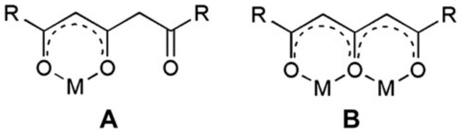


Figure 3. Possible coordination modes of tricarbonyl compounds.