Letter

Metal-catalysed reactions of β-dicarbonyl compounds with fumaronitrile

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Abstract

β-Dicarbonyl derivatives **1a–f** react with fumaronitrile in the presence of catalytic amounts of [Ni(acac)$_2$] or Ni(OAc)$_2$ to give 7-oxa-bicyclo[2,2,1]heptene derivatives **3a–f**, while in similar experimental conditions, methyl malonate **1g** affords the enaminodiester **5**. © 1999 Elsevier Science B.V. All rights reserved.

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1. Introduction

β-Dicarbonyl compounds react with nitriles in the presence of metal catalysts to afford β-enaminodicarbonyl derivatives arising from the formation of a new C–C bond between the methylene group of dicarbonyls and the cyano group of nitriles. The reactions of β-dicarbonyls with electrophylically activated nitriles (cyanogen [1], trichloroacetonitrile [2], acylcyanides [3,4], alkylcyanoformates [5], and malononitrile [6,7]) were carried out in the presence of catalytic amounts of metal acetylacetonates, while the reactions with non-electrophylically activated nitriles (such as benzylcyanide and ben-zonitrile) were carried out in the presence of stoichiometric amounts of tin (IV) chloride [8,9].

In most of these reactions, the metal catalyst was able to modify the reaction course giving different products from the corresponding ones obtained in the presence of a base [10].

It is well-known that α,β-unsaturated nitriles react under basic conditions giving compounds derived from a Michael addition of the β-dicarbonyl anion to the C–C double bond of the nitrile [11].

Taking into account the difference between base and metal-promoted reactions, we are investigating the effect of metal catalysis on the reactions of β-dicarbonyls with α,β-unsaturated nitriles and in this communication we report on the reactions of β-diketones **1a–c**, ketoester **1d**, ketoamides **1e,f** and diester **1g** with fumaronitrile **2**.

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2. Results and discussion

The reactions of β-dicarbonyl derivatives **1** with fumaronitrile **2** were carried out under four different experimental conditions.

(i) In the presence of [Ni(acac)$_2$] as catalyst (5% mol) in chlorinated solvents. Under these conditions, acetylacetone **1a** and methylacetoacetate **1d** reacted with **2** in chloroform or dichloroethane (DCE) to give the 7-oxa-bicyclo[2,2,1]hept-2-ene derivatives **3a** [1] and **3d**, respectively (Scheme 1, entries 1 and 7).

(ii) In the presence of metal acetylacetonates as catalysts (5% mol) and BF$_3$·Et$_2$O as co-catalyst (5% mol) in dichloromethane at room temperature for 24 h. Under these conditions, the bicyclo derivatives **3a** and **3d** were obtained in good yields using [Ni(acac)$_2$] as catalyst (entries 2 and 8), while compound **3a** was obtained in lower yield using [Co(acac)$_2$] (entry 3). Also bicyclo derivatives **3e** and **3f**, not formed under conditions (i), were obtained starting from the pertinent *N*-acetoacetamides **1e** and **1f** (entries 9 and 10). No product was obtained in the reaction of acetylacetone **1a** with fumaronitrile using Cu(II), Zn(II) and Mn(II) acetylacetonates as catalysts also in the presence of BF$_3$·Et$_2$O.

(iii) In the presence of Ni(OAc)$_2$ 5 mol% in dichloromethane; a drop of acetic acid was added in order to obtain a homogeneous solution and this was heated under reflux for 24 h. Under these conditions, benzoylacetone **1b** and dibenzoylmethane **1c** gave the bicyclo derivatives **3b** and **3c**, respectively (entries 5 and 6). These derivatives were not obtained in the reactions of **1b** and **1c**, carried out under conditions (i) and (ii). Methyl malonate **1g** reacts with **2** in the presence of Ni(OAc)$_2$ 5%mol in MeOH to afford the enaminodiester **5** (R=R′=OMe, entry 11).

(iv) In the presence of stoichiometric amounts of Ni(OAc)$_2$ in MeOH: the reaction of acetylacetone **1a** with fumaronitrile under these stoichiometric conditions gave the unexpected deacetylated derivatives **4** (R=Me, entry 4).

The formation of the obtained compounds can be explained by the mechanism depicted in Scheme 2. The key step of all these reactions is the formation, catalysed by the metal center, of a new C–C bond between the methylene group of dicarbonyls and one of the cyano groups of malononitrile with the formation of β-en-aminodicarbonyls **5**.

In the reaction of dimethyl malonate **1g** with **2**, the reaction stops at this stage giving the β-enaminodiester **5** (R=R′=OMe). In all the other reactions, intermediates **5** were not isolated and different final products were obtained.

In the majority of the reactions studied, the intermediates **5** cyclise into furane derivatives **6**, which derive from the intramolecular nucleophilic attack of the acetyl oxygen atom on to the C–C double bond of the unsaturated nitrile moiety. The so formed furane derivatives were not isolated in that they react further with fumaronitrile in a Diels Alder cycloaddition reaction to give the bicyclo derivatives **3**. Two diastereomers of **3** could be formed, both having the cyano groups in a *trans* configuration, but in our reactions, always one diastereomer was isolated. The spectroscopic data of these compounds are consistent with the proposed general structure **3**, but they do not allow to determine

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[1] To a solution of acetylacetone **1a** (3.08 g, 30 mmol) and fumaronitrile (4.0 g, 51 mmol) in chloroform (6 ml) [Ni(acac)$_2$] (0.154 g, 0.6 mmol) was added. The reaction mixture was heated under reflux for 5 h and cooled. The separated solid was treated with Et$_2$O to give brown crystals, 5.7 g (yield 87%), which were dissolved in hot ethyl acetate. The obtained suspension was filtered to eliminate the insoluble metal complexes and the resulting solution was allowed to stand at room temperature for 12 h to give colourless crystals of **3a**, 3.4 g (yield 52%), m.p. 172–175°C. IR (KBr): 3390, 3310, 3275, 3220, 3180, 2260, 2250, 1660, 1610, 1510 cm^{-1}. ^{1}H-NMR (DMSO-d$_6$): δ 1.86 (s, 3H, Me), 2.14 (s, 3H, Me), 3.55 and 3.76 (2H, AB system, $J = 17.6$ Hz, CH$_2$), 3.88 and 4.03 (2H, AB system, $J = 4.0$ Hz, CH–CH), 4.16 (br, 2H, NH$_2$). ^{13}C-NMR (DMSO-d$_6$): δ 17.94 (q, $J = 137$ Hz, Me), 18.19 (t, $J = 129$ Hz, CH$_2$), 29.24 (q, $J = 126$ Hz, Me), 41.01 (d, $J = 139$ Hz, CH), 43.87 (d, $J = 150$ Hz, CH), 85.39 (s, C–O), 87.97 (s, C–O), 109.86 (s, C=C–COMe), 116.02 (s, CN), 116.23 (s, CN), 118.36 (s, CN), 161.14 (s, NH$_2$–C=C), 190.39 (s, C=O).
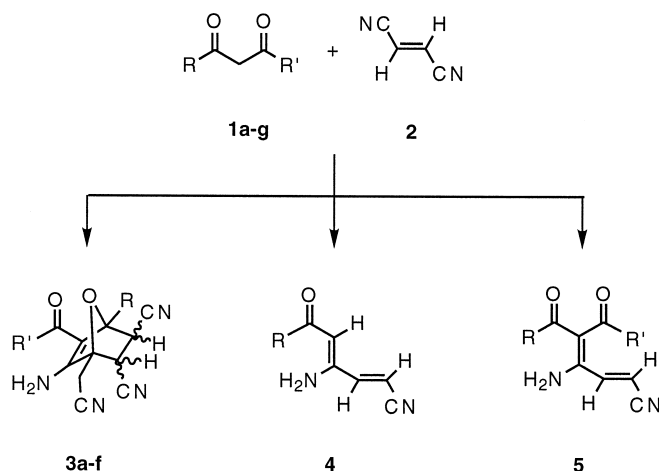
Scheme 1.

entry		R	R'	molar ratio **1:2**	cata-lyst[a]	experimental conditions	product (yield)
1	**1a**	Me	Me	1:1.5	A	$CHCl_3$, reflux, 5 h	**3a** (52%[b])
2	**1a**			1:2	B	DCE, r.t., 24 h	**3a** (63%[b])
3	**1a**			1:2	C	DCE, r.t., 24 h	**3a** (30%[b])
4	**1a**			1:1	D	MeOH, r.t., 48 h	**4a** (40%)
5	**1b**	Me	Ph	1:1	E	CH_2Cl_2+AcOH, reflux, 24 h	**3b** (39%)
6	**1c**	Ph	Ph	1:1	E	CH_2Cl_2+AcOH, reflux, 24 h	**3c** (24%)
7	**1d**	Me	OMe	1:1	A	DCE, reflux, 12 h	**3d** (20%)
8	**1d**			1:1	B	DCE, reflux, 1h; r.t., 24h	**3d** (70%)
9	**1e**	Me	$NH-CH_2Ph$	1:1	B	DCE, r.t., 24 h	**3e** (43%)
10	**1f**	Me	$NH-CH_2pClPh$	1:1	B	DCE, r.t., 24 h	**3f** (21%)
11	**1g**	OMe	OMe	1:1	E	MeOH, reflux, 24 h	**5** (35%)

a) catalyst: A: [Ni(acac)$_2$] 5% mol; B:[Ni(acac)$_2$] 5% mol, BF$_3$·Et$_2$O 5% mol; C: [Co(acac)$_2$] 5% mol, BF$_3$·Et$_2$O 5% mol; D: Ni(OAc)$_2$ stoichiometric; E: Ni(OAc)$_2$ 5%mol.
b) yields calculated on fumaronitrile.

the actual configuration and several attempts to obtain crystals suitable for an X-ray analysis till now failed.

The best catalyst for these reactions is [Ni(acac)$_2$]; the co-catalyst BF$_3$ · Et$_2$O is useful, in some cases necessary, and it allows milder experimental conditions improving the yields of the bicyclo derivatives **3**. It is possible that the Lewis acid co-catalyst increases the electrophilicity of the cyano carbon atom, by forming a RCN–BF$_3$ adduct.

Ni(OAc)$_2$ can also be used and it catalyses the formation of compounds **3b**, **3c** and **5** (R,R′ =OMe); however, the reaction of acetyl-
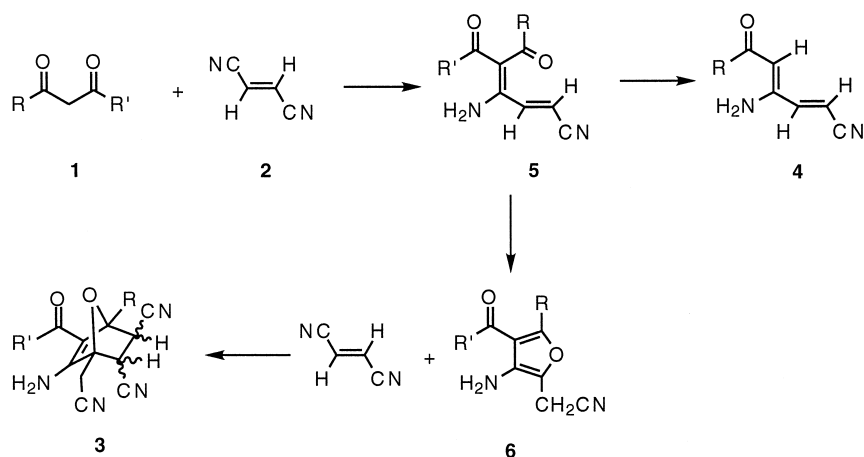
Scheme 2.

acetone **1a** with fumaronitrile, carried out in the presence of stoichiometric amounts of $Ni(OAc)_2$ in methanol, affords only the deacetylated adduct **4a** (R=Me), resulting from a retro-Claisen reaction of the intermediate **5** (R=R'=Me).

The most relevant point of these reactions is that metal catalysis is able to promote the formation of a new C–C bond between the methylene and the cyano groups, thus reversing the reactivity of β-dicarbonyls with fumaronitrile observed in basic conditions [12]. This allows the formation of a series of bicyclic derivatives via a selective cascade of intra- and intermolecular steps.

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