

## Metal-catalysed synthesis of nitroenaminones from $\alpha$ -nitroketones or -esters and nitriles

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### Abstract

Transition metal(II) carbonylnitronates or acetates selectively catalyse the carbon–carbon bond formation reaction between benzoylnitromethane and methyl (or ethyl) nitroacetate with electrophilically activated nitriles to form the nitroenaminones  $O_2N(RCO)C=C(R')NH_2$  **3a–d** in high to medium yields (73–50%; **a**: R = Ph, R' = CCl<sub>3</sub>; **b**: R = MeO, R' = CCl<sub>3</sub>; **c**: R = EtO, R' = CCl<sub>3</sub>; **d**: R = MeO, R' = EtOCO). The use of metal catalysts permits of avoiding the basic conditions in which compounds **3** are unstable. The proposed mechanism, which implies coordination of the  $O_2NCHCOR^-$  moiety and nucleophilic attack of the metal-chelate to the nitrile carbon atom, is supported by the successful synthesis of the intermediate complex  $[Ni\{O_2N(MeOCO)CC(CCl_3)NH\}_2(H_2O)_2]$ . © 1999 Elsevier Science B.V. All rights reserved.

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### 1. Introduction

Organic nitro compounds exhibit a rather variegated reactivity; the electron-withdrawing property of the nitro group makes the adjacent carbon atom a good electrophile, but, at the same time, increases its acidity, facilitating the formation of a nucleophilic anion. Furthermore, the NO<sub>2</sub> group itself can be a leaving group [1,2] or be transformed in several functional groups, thus making these compounds very useful synthetic intermediates [3–7]. In particular,  $\alpha$ -nitroketones and -esters are widely used in the synthesis of amino acids, of numerous heterocyclic compounds and of carbohydrates containing the nitro or amino group [8]. Most reactions involve carbon–carbon bond formation as in: (i) alkylation reactions, generally in the presence of alkoxides; (ii) reactions with aldehydes to give  $\alpha$ -nitro- $\beta$ -hydroxy esters, which can be converted via dehydration to nitro acrylates; (iii) Michael additions, in the presence of bases, to nitroolefins and to  $\alpha,\beta$ -unsaturated aldehydes, ketones, esters and nitriles. The ambident nature of the involved alkane nitronate  $O_2NCHR^-$  makes

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these reactions under basic conditions scarcely selective, being possible the nucleophilic attack either of the C or the O atom [9]. A great improvement on the regio- and stereoselectivity has been achieved with the use of homogeneous metal catalysts in neutral media [10–13].

We have already shown that many C–H acid compounds as  $\beta$ -dicarbonyls,  $\beta$ -ketoamides,  $\beta$ -ketophosphonates or phosphonoacetates can be added to nitriles, in the presence of metal acetylacetonates or tin tetrachloride, to give selective C–C bond formation between the methylene and cyano carbon atoms [14–16]. Thus it seemed interesting to explore the potentiality of this metal-based synthetic approach in the reaction of trichloroacetonitrile and ethyl cyanofornate with an  $\alpha$ -nitroketone as benzoylnitromethane or with the  $\alpha$ -nitro esters methyl and ethyl nitroacetate, by employing as catalysts known metal salts and properly designed new nitro complexes [17].

## 2. Experimental

Infrared spectra were recorded on a Bruker IFS 66 FT;  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra on a Jeol FX 90Q FT or a Bruker AC (200 MHz) spectrometer. The high-resolution solid-state  $^{13}\text{C}$  measurements were performed on a Bruker AM 250 with the setting conditions described in Ref. [18]. Thermal analyses employed the Perkin-Elmer TGS-2 equipment; mass spectra utilised a single focus mass spectrometer VG MM16 operating in electron ionisation mode at 70 eV. The reagents were high purity products and used as received. The metal complexes were prepared under argon in anhydriated solvents and carefully deoxygenated reaction apparatus. Catalytic syntheses of organic compounds were performed under an uncontrolled atmosphere.

### 2.1. Synthesis of complexes

#### 2.1.1. $[M(\text{O}_2\text{NCHC}(\text{O})\text{Ph})_2(\text{EtOH})_n] \mathbf{1}$ ( $M = \text{Mn(II)}, \text{Fe(II)}, \text{Co(II)}, \text{Ni(II)}, \text{Cu(II)}, \text{Zn(II)}, \text{Pd(II)}$ )

The complexes were prepared by reaction of the metal acetate with benzoylnitromethane in ethanol or acetone, according to a reported procedure [17,19]. The new complex  $[\text{Fe}(\text{O}_2\text{NCHC}(\text{O})\text{Ph})_2(\text{EtOH})_2] \mathbf{1}\text{-Fe}$  was prepared in ethanol with good yield (80%) and satisfactory elemental analysis (Found: C, 50.26; H, 4.10; N, 6.29.  $\text{C}_{18}\text{H}_{18}\text{FeN}_2\text{O}_7$  requires: C, 50.26; H, 4.21; N, 6.51%). Paramagnetic,  $\mu = 5.3$  BM;  $\tilde{\nu}_{\text{max}}(\text{cm}^{-1})$  (KBr, most representative bands) 1596 m and 1587 m [ $\nu(\text{C}=\text{O})$ ], 1396 m and 1263 s [ $\nu(\text{NO}_2)$ ]. It loses the two molecules of ethanol below 50°C and it decomposes at 191°C. The deuterated complex  $[\text{Cu}(\text{O}_2\text{NCD}(\text{O})\text{Ph})_2] \mathbf{1}\text{-Cu-}d$  was synthesised in EtOD;  $\tilde{\nu}_{\text{max}}(\text{cm}^{-1})$  (KBr, most representative bands) 1593 w [ $\nu(\text{C}=\text{O})$ ], 1377 s and 1288 s [ $\nu(\text{NO}_2)$ ]. These bands were found unchanged with respect to those of the non-deuterated  $\mathbf{1}\text{-Cu}$ . Caution: all, but  $\mathbf{1}\text{-Pd}$ , complexes explode violently for temperatures above 185–245°C.

#### 2.1.2. $[\text{Ni}(\text{O}_2\text{NCHC}(\text{O})\text{R})_2(\text{EtOH})_2] \mathbf{2}$ ( $R = \text{OMe}, \text{OEt}$ )

Both complexes  $\mathbf{2}\text{-OMe}$  and  $\mathbf{2}\text{-OEt}$  were prepared from  $\text{NiCl}_2$  and  $\text{O}_2\text{NCH}_2\text{C}(\text{O})\text{R}$  in the presence of  $\text{Et}_3\text{N}$  in anhydrous ethanol [17].

#### 2.1.3. $[\text{Ni}(\text{O}_2\text{N}(\text{MeOCO})\text{CC}(\text{CCl}_3)\text{NH})_2(\text{H}_2\text{O})_2]$

$\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$  (0.125 g, 0.50 mmol) and  $\text{O}_2\text{N}(\text{MeOCO})\text{C} = \text{C}(\text{CCl}_3)\text{NH}_2$  (0.264 g, 1.0 mmol) were dissolved in ethanol (20  $\text{cm}^3$ ) and left at 40°C under stirring for 20 h, periodically renewing the atmosphere by pumping out the vapours. The complex precipitated as a pale blue solid at room temperature, yield 46%, m.p. (dec.) 190°C (Found: C, 19.93; H, 1.80; N, 8.98.  $\text{C}_{10}\text{H}_{12}\text{Cl}_6\text{N}_4\text{NiO}_{10}$  requires: C, 19.38; H, 1.95; N, 9.04%);  $\tilde{\nu}_{\text{max}}(\text{cm}^{-1})$  (KBr, most representative bands) 3256 vw, 1667

m and 1646 s [ $\nu(\text{C}=\text{O})$ ], 1454 m, 1420 s, 1359 m, 1330 m and 1213 m. It loses the two molecules of water below 130°C and it decomposes violently at 190°C.

## 2.2. Synthesis of the nitroenaminones $\text{O}_2\text{N}(\text{RCO})\text{C}=\text{C}(\text{CR}')\text{NH}_2$ **3a–d**

### 2.2.1. $\text{O}_2\text{N}(\text{PhCO})\text{C}=\text{C}(\text{CCl}_3)\text{NH}_2$ , 3-Amino-4,4,4-trichloro-2-nitro-1-phenyl-2-buten-1-one, **3a**

Benzoylnitromethane (0.330 g, 2.0 mmol), trichloroacetonitrile (0.205 cm<sup>3</sup>, 2.0 mmol) and complex **1-Co** (19 mg, 0.04 mmol) were suspended in chloroform (2 cm<sup>3</sup>) in a small glass reactor (4 cm<sup>3</sup>). The reaction mixture was left under stirring at 50°C for 50 h, after which the solvent was removed and the residue treated with ethanol. The unaltered metal catalyst was filtered off and the unreacted benzoylnitromethane was precipitated from the resulting yellow solution by addition of hexane. Reduction of volume afforded white microcrystals of **3a** in various fractions, some of which were purified by preparative TLC (acetone/dichloromethane 1/2 v/v;  $R_F(\mathbf{3a}) = 0.9$ ). Yield 73%, m.p. 129°C (Found: C, 38.89; H, 2.16; N, 8.81.  $\text{C}_{10}\text{H}_7\text{Cl}_3\text{N}_2\text{O}_3$  requires: C, 38.80; H, 2.28; N, 9.05%);  $\tilde{\nu}_{\text{max}}(\text{cm}^{-1})$  (KBr, most representative bands) 3413 s and 3231 m [ $\nu(\text{N-H})$ ], 1663 s [ $\nu(\text{C}=\text{O})$ ], 1610 s, 1597 s and 1585 s [ $\nu(\text{C}=\text{C})$ ], 1532 m, 1450 w, 1425 m, 1371 s, 1240 vs;  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 7.2–8.1 (m, 5H, Ph), 8.60 (s, br, 2H,  $\text{NH}_2$ );  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) 91.0 ( $\text{CCl}_3$ ), 120.9 ( $\text{C}-\text{NO}_2$ ), 128.8, 133.6 and 137.0 (Ph), 155.5 ( $\text{C}-\text{NH}_2$ ), 185.9 ( $\text{C}=\text{O}$ );  $m/z$  307(1) ( $M-H$ ), 273(1) ( $M-Cl$ ), 262(2) ( $M-\text{NO}_2$ ), 238(1) ( $M-2Cl$ ), 226 (15) ( $M-H-Cl-\text{NO}_2$ ), 187(8) ( $M-\text{NH}_2-\text{PhCO}$ ), 145(7) ( $M-\text{NO}_2-\text{CCl}_3$ ), 121(2) ( $\text{PhCONH}_2$ ), 105(100) ( $\text{PhCO}$ ), 77(76) ( $\text{Ph}$ ).

Lower yields were obtained varying reaction times and type of catalyst **1**.

### 2.2.2. $\text{O}_2\text{N}(\text{MeOCO})\text{C}=\text{C}(\text{CCl}_3)\text{NH}_2$ , 3-Amino-4,4,4-trichloro-2-nitro-2-butenic acid methyl ester, **3b**

Methyl nitroacetate (0.50 cm<sup>3</sup>, 4.2 mmol), trichloroacetonitrile (0.50 cm<sup>3</sup>, 4.9 mmol) and zinc acetate (18 mg, 0.08 mmol) were suspended in chloroform (1 cm<sup>3</sup>) in a small glass reactor (4 cm<sup>3</sup>). The reaction mixture was heated at reflux for 2 h, after which the solvent was partly removed to give yellow crystals. These were treated with diethyl ether and the insoluble inorganic part filtered off. The resulting solution gave on addition of hexane white crystals of **3b**, yield 75%, m.p. 119°C (Found: C, 22.42; H, 1.68; N, 10.54.  $\text{C}_5\text{H}_5\text{Cl}_3\text{N}_2\text{O}_4$  requires: C, 22.79; H, 1.91; N, 10.63%);  $\tilde{\nu}_{\text{max}}(\text{cm}^{-1})$  (KBr, most representative bands) 3422 s and 3230 m [ $\nu(\text{N-H})$ ], 1728 s [ $\nu(\text{C}=\text{O})$ ], 1620 s, 1601 s [ $\nu(\text{C}=\text{C})$ ], 1521 w, 1431 s, 1384 s, 1295 m, 1238 vs;  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 3.89 (s, 3H,  $\text{CH}_3\text{O}$ ), 8.2 (s, br, 2H,  $\text{NH}_2$ );  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) 55.5 ( $\text{CH}_3\text{O}$ ), 90.9 ( $\text{CCl}_3$ ), 119.1 ( $\text{C}-\text{NO}_2$ ), 154.3 ( $\text{C}-\text{NH}_2$ ), 161.9 ( $\text{C}=\text{O}$ );  $m/z$  262(5) ( $M^+$ ), 181(2) ( $M-Cl-\text{NO}_2$ ), 157(2) ( $M-3Cl$ ), 145(70) ( $M-\text{CCl}_3$ ), 117(10) ( $M-2Cl-\text{NH}_2-\text{COOMe}$ ), 99(100) ( $M-\text{NO}_2-\text{CCl}_3$ ), 68(70) ( $M-\text{NO}_2-\text{CCl}_3-\text{Me}$ ).

Lower yields of **3b** were obtained using as catalyst (2 mol%): complex **2-OMe** (63%, chloroform, 5 d at r.t.), nickel acetate (42%, dichloromethane, 10 d at r.t.), zinc or nickel acetylacetonate (< 10%), copper, cobalt or palladium acetates (~ 0%). Rapid decomposition of the forming **3b** was observed in the presence of equimolar sodium acetate in 1/1 methanol–water.

### 2.2.3. $\text{O}_2\text{N}(\text{EtOCO})\text{C}=\text{C}(\text{CCl}_3)\text{NH}_2$ , 3-Amino-4,4,4-trichloro-2-nitro-2-butenic acid ethyl ester, **3c**

Ethyl nitroacetate (0.23 cm<sup>3</sup>, 2.0 mmol), trichloroacetonitrile (0.20 cm<sup>3</sup>, 2.0 mmol) and **2-OEt** (17 mg, 0.04 mmol) were suspended in chloroform (0.5 cm<sup>3</sup>) in a small glass reactor (2 cm<sup>3</sup>). The reaction mixture was kept under stirring for 6 d, after which the solvent was removed under reduced pressure. The oil was treated with diethyl ether and the insoluble inorganic part filtered off. The resulting solution gave on fractional addition of hexane an oil, which on cooling with liquid nitrogen

afforded **3c** as a yellowish solid, yield 50%, m.p. 57°C (Found: C, 25.82; H, 2.35; N, 9.81.  $C_6H_7Cl_3N_2O_4$  requires: C, 25.97; H, 2.54; N, 10.10%);  $\tilde{\nu}_{\max}$  ( $cm^{-1}$ ) (KBr, most representative bands) 3429 m, 3346 m and 3255 s [ $\nu(N-H)$ ], 1735 s [ $\nu(C=O)$ ], 1621 s, 1603 s [ $\nu(C=C)$ ], 1521 w, 1383 s, 1283 m, 1238 vs;  $\delta_H$  ( $CDCl_3$ ) 1.27 (t, 3H,  $CH_3$ ), 4.25 (q, 2H,  $CH_2O$ ), 8.2 (s, br, 2H,  $NH_2$ );  $\delta_C$  ( $CDCl_3$ ) 13.6 ( $CH_3$ ), 62.7 ( $CH_2O$ ), 90.9 ( $CCl_3$ ), 119.3 ( $C-NO_2$ ), 153.8 ( $C-NH_2$ ), 161.8 ( $C=O$ );  $m/z$  276(3) ( $M^+$ ), 231(3) ( $M-Cl$ ), 195(1) ( $M-Cl-NO_2$ ), 159(50) ( $M-CCl_3$ ), 117(10) ( $M-2Cl-NH_2-COOEt$ ), 113(40) ( $M-NO_2-CCl_3$ ), 68(60) ( $M-NO_2-CCl_3-Et$ ), 29(100) ( $Et$ ).

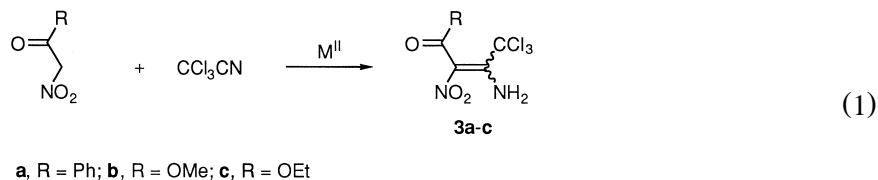
#### 2.2.4. $O_2N(MeOCO)C=C(COOEt)NH_2$ , 3-Amino-2-nitro-2-butenedioic acid 1-methyl 4-ethyl ester, **3d**

Methyl nitroacetate (0.77  $cm^3$ , 8.4 mmol), ethyl cyanoformate (0.97  $cm^3$ , 9.8 mmol) and nickel acetate (41 mg, 0.17 mmol) were suspended in chloroform (1  $cm^3$ ) in a small glass reactor (4  $cm^3$ ). The reaction mixture was heated at reflux for 4 h, after which it was chromatographed on a silica gel column (eluent ethyl acetate/petroleum ether 3/7 v/v). Compound **3d** was obtained as a yellow oil, yield 54% (Found: C, 38.27; H, 4.70; N, 13.21.  $C_7H_{10}N_2O_6$  requires: C, 38.54; H, 4.62; N, 12.84%);  $\tilde{\nu}_{\max}$  ( $cm^{-1}$ ) (neat, most representative bands) 3400 s and 3300 m [ $\nu(N-H)$ ], 1750 s [ $\nu(C=O)$ ], 1630 s [ $\nu(C=C)$ ], 1560 m, 1460 s, 1260 m; two species (ratio 7/3) are detectable in the NMR spectra,  $\delta_H$  ( $CDCl_3$ ) 1.26 and 1.40 (2t, 3H,  $CH_3CH_2O$ ), 3.86 (s, 3H,  $CH_3O$ ), 4.33 and 4.44 (2q, 2H,  $CH_3CH_2O$ ), 6.8 and 8.9 [2s, 1.4H,  $NH_2$  (main species)], 6.4 and 8.6 [2s, 0.6H,  $NH_2$  (minor species)];  $\delta_C$  ( $CDCl_3$ ) (main species) 13.6 ( $CH_3CH_2O$ ), 53.2 ( $CH_3O$ ), 64.4 ( $CH_3CH_2O$ ), 120.1 ( $C-NO_2$ ), 146.7 ( $C-NH_2$ ), 161.2 ( $C=O$ ), 162.3 ( $C=O$ );  $\delta_C$  ( $CDCl_3$ ) (minor species) 13.6 ( $CH_3CH_2O$ ), 52.6 ( $CH_3O$ ), 64.2 ( $CH_3CH_2O$ ), 118.0 ( $C-NO_2$ ), 154.1 ( $C-NH_2$ ), 162.1 ( $C=O$ ), 163.0 ( $C=O$ ).

A lower yield (28%) of **3d** was obtained in the same experimental conditions using as catalyst zinc acetate.

### 3. Results and discussion

The reaction of benzoynitromethane and of methyl (or ethyl) nitroacetate with trichloroacetonitrile gives in the presence of catalytic quantities of metal(II) catalysts selective formation of nitro-enaminones (Eq. (1)).



The syntheses are performed in chloroform with times varying from 2–4 h to days in function of the temperatures (from 20°C to reflux). The yields on compounds **3a–c** markedly depend on the nature of the catalysts and are in the range 73(**a**)–50(**c**) %.

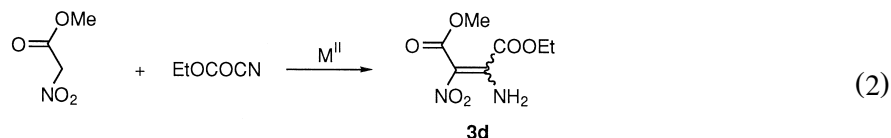
Their  $^1H$  NMR spectra in  $CDCl_3$  solution show, in particular, the resonance of the amino protons as a broad singlet near 8.3 ppm, thus indicating an almost free rotation around the  $C-NH_2$  bond, at room temperature. Furthermore, the presence of strong EWD groups like  $CCl_3$  and  $NO_2$  has a great effect on the  $^{13}C$  resonance of the various carbon nuclei: the value of 90.9–91.0 ppm for  $CCl_3$  is higher than in  $CHCl_3$  (77.7) and close to that found in  $CCl_4$  (96.7); the signals of the alkene carbons

[119.1–120.9 (C–NO<sub>2</sub>) and 153.8–155.5 (C–NH<sub>2</sub>)] span the large chemical shift range expected in the presence of polar substituents; the carbonyl resonances [185.9 (**a**) and 161.8–161.9 (**b,c**)] are at the lower limit of  $\alpha,\beta$ -unsaturated systems, showing a great reduction of the C=O double bond character [20].

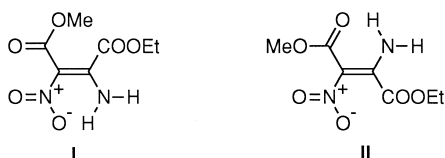
The infrared spectra of **3** in KBr show two bands in the N–H stretching region for **3a** (3413 and 3232 cm<sup>-1</sup>) and **3b** (3422 and 3230 cm<sup>-1</sup>), and three for **3c** (3429, 3346 and 3255 cm<sup>-1</sup>). The large difference in the wavenumber between the two bands at ca. 3420 and 3240 cm<sup>-1</sup> is clearly indicative of an intramolecular hydrogen bonding for all three compounds, whereas the additional band at 3346 cm<sup>-1</sup> [ $\nu_s$  (N–H)] in **3c** suggests the presence also of a free amino group [21]. The C=O stretching value [1663 (**3a**), 1728 (**3b**), 1734 (**3c**)] is characteristic of  $\alpha,\beta$ -unsaturated keto and ester carbonyls, thus excluding a C=O  $\cdots$  HN interaction, which should produce a shift to lower energies. At the same time the strong  $\nu_s$ (N–O) band of the starting  $\alpha$ -nitro derivative at 1565–1555 cm<sup>-1</sup> is absent in compounds **3** and has surely moved to lower values. The attribution is complicated by the presence of various adsorptions; if we exclude the weak peak at 1532–1521 cm<sup>-1</sup>, the first strong band in all three compounds is at 1433–1425 cm<sup>-1</sup>, with a downshift of ca. 130 cm<sup>-1</sup>, well in accord with a reduction of NO bond order as a consequence of intramolecular hydrogen bonding.

The fragmentation pattern of the keto and ester derivatives are rather different; in general the mass spectra of the last ones are more intense and clean, showing the peaks of the molecular ion and of the fragments resulting from the successive removal of CCl<sub>3</sub>, NO<sub>2</sub> and OMe (or OEt).

The extension of this metal-catalysed C–C bond formation to different nitriles has been checked by reacting methyl nitroacetate with ethyl cyanoformate in the presence of nickel acetate (2 mol%) (Eq. (2)).



Compound **3d** is obtained, after 4 h at reflux in chloroform, as a yellow oil in 54% yield. Its <sup>1</sup>H and <sup>13</sup>C NMR spectra in CDCl<sub>3</sub> show the presence of two species in approximate 7/3 ratio; both are characterised by two distinct resonances (at 6.8, 8.9 and 6.4, 8.6) for the amino protons, thus indicating intramolecular hydrogen bonding. The spectra of the two forms are on the whole rather similar, albeit with important differences on the chemical shift of the C–NO<sub>2</sub> (120.1 vs. 118.0) and C–NH<sub>2</sub> (146.7 vs. 154.1 ppm) carbon nuclei. These data support the formation of the two isomers **I** and **II**, in which the rotation around the C–NH<sub>2</sub> bond is inhibited by the presence of a strong hydrogen bond with the nitro (**I**) or carbonyl (**II**) oxygen atom.



As discussed above, an enaminone structure of type **I**, with a weaker hydrogen bond is likely also for compounds **3a–c**.

The effect of the nature of the metal centre has been fully exploited in the synthesis of the keto derivative **3a**. This was allowed by the existence of a series of benzoylnitromethane complexes of the type  $[M(O_2CHC(O)Ph)_2(EtOH)_n]$  **1** ( $M = Mn, Fe, Co, Ni, Cu, Zn, Pd$ ) [17,19], one of which (**1-Fe**) prepared for the first time. The results obtained, at 50°C in  $CHCl_3$ , are illustrated in Fig. 1, as yield of isolated compound **3a** in function of metal catalyst (**1**, 2 mol%). The best value (73%) is obtained with **1-Co** after 50 h, longer reaction times afford great amounts of by-products.

A simple stoichiometric mechanism, which takes into account the catalytic effect exhibited by the metal centre is shown in Scheme 1 ( $R = Ph$ ).

The partial negative charge on the methine carbon [17] favours its nucleophilic attack on the cyano carbon of the electrophile activated by the EWG  $CCl_3$  group (i). The metal intermediate so obtained can exchange with the free benzoylnitromethane to reform the starting complex and liberate in solution the product **3a** (ii).

Regarding the intimate mechanism, it was already demonstrated, in the case of  $\beta$ -carbonylenolates [22], that preliminary nitrile coordination to the metal is needed before carbon–carbon bond formation. This interpretation was supported by kinetic studies and by the great dependence of the catalytic efficiency on the nature of the metal centre; for example, in the reaction of methyl acetoacetate with trichloroacetonitrile catalysed by metal(II) acetylacetonates the TN numbers range from more than 1000 with Co(II) and Zn(II) to 1 with Fe(II) [22]. These differences are much less marked in our case, albeit the Co(II) complex appears definitely more efficient. It is interesting to note that also **1-Pd** is moderately active in this catalysis; this behaviour contrasts with that observed in

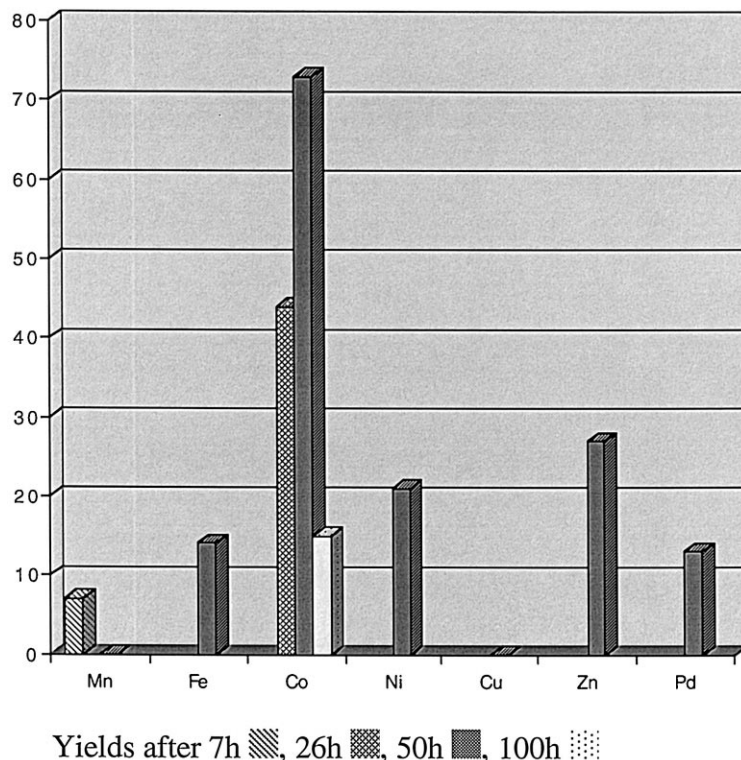
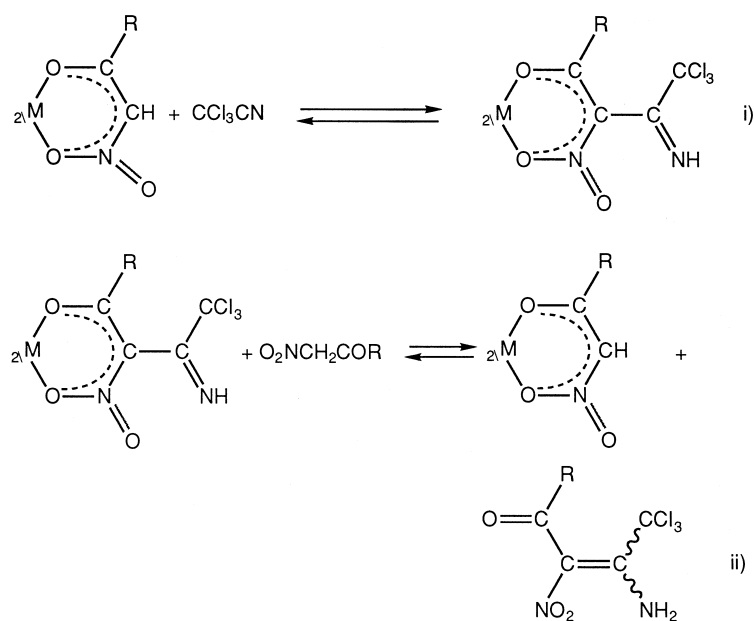
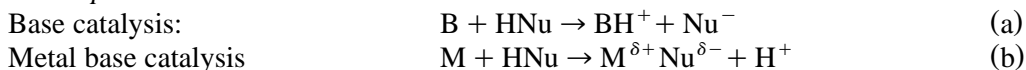


Fig. 1. Effect of the nature of the metal centre on the catalytic synthesis of **3a** ( $CHCl_3$ , 50°C,  $[PhCOCH_2NO_2]=[CCl_3CN] = 1 \text{ mol dm}^{-3}$ ,  $[1] = 2 \text{ mol}\%$ ).

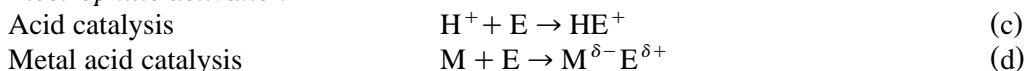


the synthesis of  $\beta$ -enaminodiones from  $\beta$ -dicarbonyls and nitriles, where the lack of catalytic effect by the palladium centre was attributed to the scarce tendency of Pd(II) to liberate a free coordination site necessary to coordinate the nitrile. The two observations [scarce differences on catalytic efficiency between various metals(II) and reactivity of Pd(II)] are consistent with the hypothesis that the intimate reaction mechanism does not involve nitrile coordination. The type of activation by the metal catalyst is better discussed by taking in mind the following concepts:

*Nucleophilic activation*



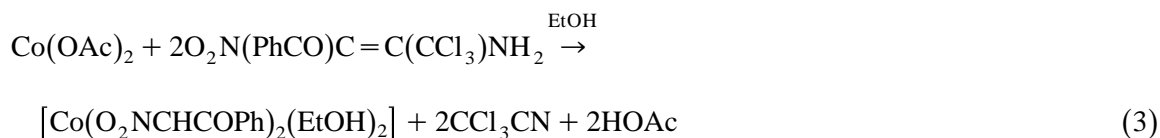
*Electrophilic activation*



It results that a metal centre can activate a pronucleophile by replacing the proton and coordinating the anion (b) and at the same time it can activate the electrophile (d). If we consider only these effects, the same metal behaves in (b) as a base (albeit the real base, needed to stabilise  $\text{H}^+$ , is the anion of the metal or the solvent) and in (d) as an acid and we can speak of a metal acid–base catalysis. This type of double activation (metal centred reaction) has been proposed in the reaction of nitriles with  $\beta$ -dicarbonyls and it should be underlined in this context that also a very good Lewis acid as  $\text{Yb}^{3+}$  can display base catalysis [11]. In the reaction of  $\alpha$ -nitroketones and -esters with trichloroacetonitrile we can propose that the metal simply activates nucleophilically the methine carbon atom (b) making it capable of direct attack to the cyano carbon of the nitrile (ligand centred reaction). This does not understate the role of the metal which can behave, via coordination, also as a protecting group towards the nitro and the keto functions, so enhancing the selectivity of the process.

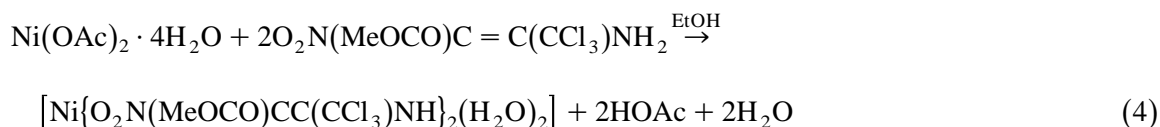
We have attempted to find a measure of the degree of negative charge on CH and to correlate it with the observed catalytic efficiency of the various metal centres. NMR data can be obtained only for **1**-Pd and **1**-Zn; the zinc complex shows the CH resonances at 6.35 ppm (in deuterioacetone) for the proton and at 113.4 ppm (solid state) for the carbon. These values are similar to those found in the palladium complex [6.54 (in deuterated dimethyl sulphoxide) and 116.3 ppm] [17] and are simply indicative of metal-chelate rings with a substantial degree of double carbon–carbon bond [18]. The electronic delocalisation on the system is confirmed by the shift to 183.9 ppm of the carbonyl resonance. Also infrared data do not help much for our purposes; it was shown with acetylacetonate complexes that the position of the carbonyl stretching band depends on the degree of negative charge on the chelate ligand, so that higher wavenumbers and higher reactivities are expected for complexes with more ionic metal–ligand bonds. No trend is observed in the CO stretching value in complexes **1**, being in the narrow range 1596–1587 cm<sup>-1</sup>. The attribution for the two NO stretchings has been made on the basis of a deuteration experiment on **1**-Cu; the spectrum of **1**-Cu-*d*, synthesised in deuterated ethanol in order to exchange the methylene hydrogens, shows important variations in the range 1460–1430 cm<sup>-1</sup>, whereas the other bands in the region 1600–1200 cm<sup>-1</sup> remain practically unchanged. The higher ones at 1593, 1532 and 1500 cm<sup>-1</sup> are attributable to the coordinated carbonyl, to a combination band C=O + C=C of the chelate, and to the aromatic ring, respectively [18,23], so that the remaining bands at 1377 and 1288 cm<sup>-1</sup> should result from the NO stretching of the uncoordinated and coordinated oxygen atoms, in accord also with literature data on similar Cr(III), Fe(III) and Al(III) complexes [24]. The values determined by analogy for all **1** are as follows: 1347 and 1299 (Mn), 1396 and 1264 (Fe), 1351 and 1302 (Co), 1353 and 1302 (Ni), 1352 and 1300 (Zn), 1393 and 1264 (Pd) cm<sup>-1</sup>. No evident correlation can be found between these data and the observed catalytic efficiency of the various catalysts, so that the specific role of the nature of the metal centre remains to be cleared.

The involved equilibria are very complex, as demonstrated by the necessity of controlling carefully the experimental conditions to prevent an evolution of the primary product. The reaction of **1**-Co (or **1**-Ni) with CCl<sub>3</sub>CN in 1/2 molar ratio, in chloroform at reflux, gives only the unreacted starting complex, showing that the equilibrium of stage (i) is very unfavourable. Thus only the presence of free benzoylnitromethane allows the reaction to proceed via substitution of the functionalised ligand (ii). As a matter of fact, the catalyst **1** is always recovered unchanged from the reaction mixtures, before the product **3a** begins to evolve. The instability of the reactive metal intermediate resulting from C–C bond formation is supported by the reaction of cobalt (or nickel) acetate hydrate with O<sub>2</sub>N(PhCO)C=C(CCl<sub>3</sub>)NH<sub>2</sub> in ethanol, in which is formed **1**-Co (or **1**-Ni) according a stoichiometry of the type described in Eq. (3).



Thus, the metal centre can promote the C–C bond breaking in a retrosynthetic process, which is the reverse of stage (i).

The reaction has a different course with the α-nitroester methyl nitroacetate (Eq. (4)).





The isolation of the metal intermediate proposed in stage (i) supports the mechanism and points out the important role played by the substituents in this type of chemistry. The great differences between  $\alpha$ -nitroketones and -esters has been already noted in the study of their coordinating ability towards various metal centres [17]. The infrared data of the octahedral nickel intermediate are consistent with coordination of the nitro and carbonyl oxygen atoms, as the carbonyl stretching shifts to 1667 and 1646  $\text{cm}^{-1}$  and no bands are present near 1550  $\text{cm}^{-1}$  in the range characteristic of the asymmetric stretching of free  $\text{NO}_2$ . On the other hand  $\beta$ -iminocarbonylenolato nickel complexes (N,O coordination), which are catalytic metal intermediates in the reaction of  $\beta$ -dicarbonyls with nitriles, are generally square planar and show an intense stretching band of the metal-bonded N–H group [17,18]. This is not the case with the carbonylnitronato intermediate, so the O,O coordination is reasonably stated and the scarce affinity of the metal centre towards the imino nitrogen is of further support to the hypothesis of direct CH attack to external nitrile.

Passing to the  $\alpha$ -nitroesters, only the metal-catalysed reaction of methyl nitroacetate with trichloroacetonitrile has been optimised by carefully checking the best experimental conditions. The impossibility of synthesising complexes of type **1** for metal different from nickel [17] has forced to use acetate salts or acetylacetonato complexes. The approximate catalytic efficiency order for the various metal(II) acetates is  $\text{Zn} > \text{Ni} \gg \text{Co}, \text{Cu}, \text{Pd}$ ; lower yields are obtained with zinc or nickel acetylacetonates with respect to their acetates. Clearly, the procatalyst is involved in an exchange equilibrium, which produces the catalytically active species:



This equilibrium is generally to the left with acetates, as shown by the fact that complexes **2** can not be obtained with this route [17], and apparently the situation is even worse with acetylacetonates. The nickel complex **2**-OMe is however obtained with a different procedure and shows a catalytic efficiency better of its acetate and close to that of zinc acetate. The inefficiency of Cu(II) and Pd(II) is well explained by the observation that they induce hydrolysis of the ester group [17].

In conclusion, metal catalysis offers a unique convenient procedure to the direct synthesis of new nitroenaminones from  $\alpha$ -nitroketones or -esters and electrophilically activated nitriles. The use of a metal(II) centre enhances the selectivity of the reaction and makes not necessary basic conditions in which the products and/or the products may be unstable. The proposed mechanism is supported by the different catalytic efficiency of the various metals(II), by the isolation of the reactive intermediate and by a parallel study on the coordinating properties of the anion of the nitro derivatives.

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