



Advanced Synthesis & Catalysis

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Journal:	<i>Advanced Synthesis & Catalysis</i>
Manuscript ID:	adsc.201400207.R2
Wiley - Manuscript type:	Full Paper
Date Submitted by the Author:	n/a
Complete List of Authors:	Ramon, Diego J.; Universidad de Alicante, Quimica Organica Pérez, Juana; Universidad de Alicante, Departamento de Química Orgánica
Keywords:	Aldehydes, Azo compounds, Cobalt, Heterogeneous catalysis
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DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

Cobalt-Impregnated Magnetite as General Heterogeneous Catalyst for the Hydroacylation Reaction of Azodicarboxylates

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Received: ((will be filled in by the editorial staff))

 Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/adsc.201#####>. ((Please delete if not appropriate))

Abstract. Cobalt and nickel impregnated on magnetite catalysts have been prepared, characterized and used for the hydroacylation reaction of different azodicarboxylate compounds with aldehydes, using nearly stoichiometric amounts of both reagents in only 3 h. Furthermore, this reaction has been conducted with the smallest amount of catalyst. The cobalt catalyst is stable enough to be removed by a magnetic decantation and recycled ten-fold without detrimental effect on the results.

Keywords: Aldehydes, Azo compounds, Cobalt, Heterogeneous catalysis

Introduction

The C-N bond formation is one of the most important reactions in organic synthesis, which has found a wide application in the synthesis of many organic substances including natural products.^[1] This type of bonds has been constructed using polar, radical and transition metal-catalyzed reactions,^[2] with dialkyl azodicarboxylate compounds being used during the last few decades to perform this type of transformation. These reagents contain a vacant orbital and a strong electron-withdrawing group which contributes to make them good nucleophilic acceptors, favouring their reaction. Several types of reactions, such as the zwitterion intermediate reaction, the electrophilic α -amination of carbonyl compounds, the C-H activation at the α -position of amines and ethers, and the ene-type reaction with olefins have been extensively studied using azodicarboxylate compounds.^[3] However, the hydroacylation reaction with aldehydes has been less considered.^[4]

The first example of the hydroacylation of azodicarboxylate derivatives using an excess of formaldehyde^[5] was introduced in 1914 and after that, the scope of the aliphatic aldehydes for the reaction was increased, affording in all cases moderate yields after several days of reaction time.^[6] Recently, the use of unusual solvents, such as ionic liquids^[7] or water^[8] has been introduced in order to increase the reaction scope as well as to overcome other previous drawbacks. However, the reaction using arenecarbaldehydes still is very challenging and unsuccessful.

The first metal catalyzed process was introduced in 2004 using $[\text{Rh}(\text{OAc})_2]_2$ (2 mol%), with the aforementioned arenecarbaldehyde limitation not being overcome.^[9] The use of copper(II) acetate,^[10] as well as zinc^[11] catalyst, allowed to carry out the reaction with aliphatic and aromatic aldehydes with similar yields for both substrates, but increasing the reaction time from 10 h for aliphatic aldehydes to several days for arenecarbaldehydes. It should be pointed out that there is only one example of heterogeneous catalyst performing the hydroacylation of azodicarboxylate derivatives.^[12] The reaction using CuO nanoparticles supported on silica (10 mol%), as catalyst, gave similar results, in terms of yields and reaction times (12-30 h) independently on the nature of aldehyde.

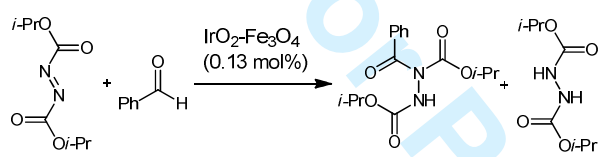
We have recently developed a new, simple and robust method to immobilize different metal oxides^[13] on the surface of the magnetite.^[14] Here we show the application of this new cobalt catalyst^[15] for the hydroacylation reaction of azodicarboxylates compounds.

Results and Discussion

The hydroacylation reaction of diisopropyl azodicarboxylate (DIAD, **1a**) and benzaldehyde (**2a**) catalyzed by iridium impregnated on magnetite was selected as the model for the optimization of the reaction conditions (Table 1). Benzaldehyde was chosen for its limited success in previous protocols, and the iridium catalyst for its tendency to have an easy electronic state change. Initially, the effect of

temperature on the results was examined (entries 1-6), achieving the best result at 60 °C (entry 4). Then, different solvents were tested (entries 4 and 7-15), with the reaction proceeding with similar results in water and dichloroethane and reaching the best results in trichloroethylene. It should be pointed out that the hydrazine byproduct (**4a**) was obtained as the main compound in THF. In order to establish the hydrogen-donor for the process, the reaction was repeated using tetrahydrofuran-d₈. After quenching the reaction by addition of toluene and magnetic decantation, the GC-MS of crude mixture showed the corresponding deuterated by-product **4a**, with the incorporation of the second deuterium being lower than 25%. Then, the reaction was conducted with α -deuterobenzaldehyde and THF, with the mono-incorporation of deuterium to the byproduct **4a** being negligible.

Table 1. Optimization of the Reaction Conditions^{a)}



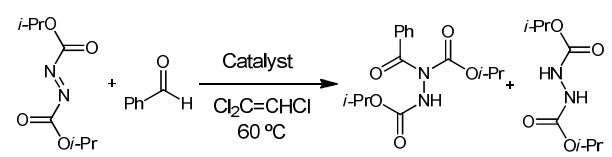
Entry	T (°C)	Solvent	t (h)	Yield 3a (%) ^{b)}	Yield 4a (%) ^{b)}
1	25	CH ₃ CN	72	2	0
2	40	CH ₃ CN	72	18	0
3	50	CH ₃ CN	72	32	0
4	60	CH ₃ CN	72	65	5
5	70	CH ₃ CN	72	15	0
6	100	CH ₃ CN	72	9	0
7	60	-	72	54	7
8	60	THF	72	7	92
9	60	H ₂ O	72	70	21
10	60	PhMe	72	30	4
11	60	(ClCH ₂) ₂	72	69	2
12	60	CHCl ₃	72	24	9
13	60	CCl ₄	72	25	4
14	60	Cl ₃ CCH ₃	72	12	5
15	60	Cl ₂ C=CHCl	24	80	10

^{a)} Reaction carried out using compounds **1a** (1mmol), **2a** (1.2 mmol), in 1 mL of solvent. ^{b)} Isolated yield after column chromatography.

Once the optimal conditions were determined, the reaction was submitted to a variety of catalyst prepared by simple impregnation protocol (Table 2). The reaction without catalyst gave a poor yield (entry 1). Then, the activity of the support was evaluated using magnetite as the unique catalyst. Nanoparticles or microparticles of magnetite (entry 2 and 3) were used with the results showing the inactivity of the support, reaching the same yield to that without catalyst. Once the activity of magnetite was tested, different metal oxides impregnated on magnetite (entries 4, 7, 10-18) were evaluated as catalyst,

achieving surprisingly the best result with the cobalt catalyst in only 3h (entry 4). To the best of our knowledge, this is the first time that a cobalt catalyst showed its great activity for the hydroacylation reaction. This reaction time is the shortest time ever reported for this type of reaction. The molecular oxygen seems to have an important role in the initial radical acyl formation in non-catalyzed processes.^[8c] In order to clarify this aspect, the reaction was repeated but in inert atmosphere, obtaining similar result (entry 4, footnote d). Then, the reaction was carried out with different bimetallic catalysts (entries 19 and 20), obtaining worse results. Different amounts of catalyst were tested (entries 5, 6, 8 and 9) finding that increasing the amount of nickel or cobalt, the amount of byproduct **4a** was increased, whereas the decrease of the catalyst amount, decreased the yield of **3a**.

Table 2. Optimization of the Catalyst^{a)}



Entry	Catalyst (mol%)	t (h)	Yield 3a (%) ^{b)}	Yield 4a (%) ^{b)}
1	-	5	42	7
2	Fe ₃ O ₄ (21.6)	3	45	7
3	Fe ₃ O ₄ (21.6) ^{c)}	3	52	8
4	CoO-Fe ₃ O ₄ (1.42)	3	90 (93) ^{d)}	6
5	CoO-Fe ₃ O ₄ (2.8)	3	78	18
6	CoO-Fe ₃ O ₄ (0.28)	3	60	8
7	NiO-Fe ₃ O ₄ (1.03)	3	83	6
8	NiO-Fe ₃ O ₄ (2.06)	3	70	27
9	NiO-Fe ₃ O ₄ (0.21)	3	66	6
10	CuO-Fe ₃ O ₄ (0.91)	3	40	10
11	Ru ₂ O ₃ -Fe ₃ O ₄ (1.03)	3	51	7
12	Rh ₂ O ₃ -Fe ₃ O ₄ (0.42)	3	50	7
13	PdO-Fe ₃ O ₄ (1.22)	3	69	8
14	Ag ₂ O/Ag-Fe ₃ O ₄ (1.25)	3	49	8
15	WO _x -Fe ₃ O ₄ (0.57)	3	51	7
16	OsO-Fe ₃ O ₄ (0.51)	3	38	9
17	PtO/PtO ₂ -Fe ₃ O ₄ (0.54)	3	49	8
18	Au ₂ O ₃ /Au-Fe ₃ O ₄ (0.14)	3	43	9
19	NiO/Cu-Fe ₃ O ₄ (0.91/0.88)	3	43	12
20	PdO/Cu-Fe ₃ O ₄ (1.53/0.90)	3	4	11
21	CoO(1.42)	3	46	9
22	NiO(1.03)	3	46	8

^{a)} Reaction carried out using compounds **1a** (1mmol) and **2a** (1.2 mmol) and 1 mL of solvent. ^{b)} Isolated yield after column chromatography. ^{c)} Reaction performed with nanoparticulate magnetite (<50 nm). ^{d)} Reaction performed in argon atmosphere.

Reactions using cobalt oxide or nickel oxide alone gave moderate yields (entries 21 and 22), with these results pointing out the high activity of these nanostructured catalysts. It should be highlighted that the optimal amount of catalyst is the lowest one ever reported.

Having established the similar catalytic activity for cobalt and nickel derivatives, the problem of recycling was faced (Figure 1). When the catalyst was recovered from the reaction mixture by magnetic decantation, washed with toluene, and reused under the same reaction conditions, the expected product **3a** was obtained in good yields with both catalysts. These catalysts could be recycled up to 10 times with a slight loss of their activity for the case of NiO-Fe₃O₄, in which the yield decreased to 53%. However, the CoO-Fe₃O₄ catalyst kept its activity practically constant and only in the last reaction cycle the yield decreased slightly.

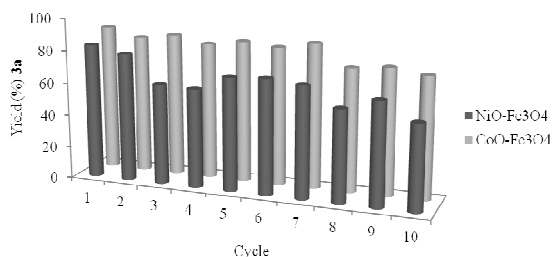


Figure 1. Recycling of the NiO-Fe₃O₄ and CoO-Fe₃O₄ catalyst.

In order to study the effect of the reaction conditions on the cobalt catalyst, the nanosize distribution of the cobalt catalyst was measured after only one reaction process, and after ten-times, observing a small sinterization of the nanoparticles. Before the reaction, the size of 77% of the cobalt oxide particles on the surface of the catalyst was between 1 and 4 nm. After the first recycling of the catalyst, the average of the cobalt oxide particles was practically the same, as the fresh one. However, after ten reactions, the recycled catalyst suffered a small sinterization process, with the 73% of cobalt oxide particles measuring between 2 and 6 nm (Figure 2).

The XPS study of catalyst^[16] showed the transformation of cobalt(II) oxide onto the corresponding cobalt(II) hydroxide. These small changes in particle size as well as the initial cobalt species seemed not to affect the activity of the catalyst, since it could be reused ten times with similar results. To know if the reaction took place by the leached cobalt species to the organic medium, we performed the standard reaction (Table 3, entry 1). After that, the catalyst was removed carefully by a magnet at high temperature, and washed with trichloroethylene. The solvents of the above solution, without catalyst, were removed under low pressure

and DIAD (**1a**) and 3-methylbenzaldehyde, as well as 1 mL of Cl₂CCHCl, were added to the above residue. The resulting solution was heated again at 60 °C for 3 h. The analysis of crude mixture, after hydrolysis, revealed the formation of compound **3a** in 93% (catalyzed process) and product **3c** in 72% yield by GC-analysis (compare with entry 3 in Table 3). It seems that the reaction takes place under homogeneous conditions. Finally ICP-MS analysis of the crude reaction solution showed the leaching of a small amount of cobalt (1.4% of the initial amount) and iron (0.17% of the initial amount).

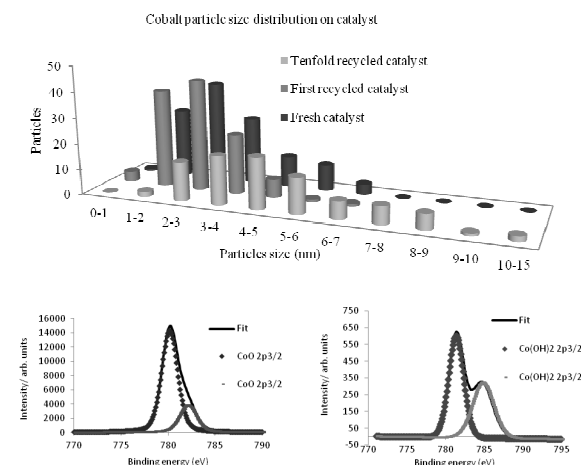


Figure 2. a) Cobalt particle size distribution on catalyst. b) XPS of cobalt catalyst before reaction. c) XPS of cobalt catalyst after ten reactions.

All these data seem to point into the direction that the initial cobalt-impregnated magnetite catalyst is only a reservoir for homogeneous cobalt species, and after the reaction has taken place in the homogeneous solvent phase, the cobalt species is efficiently re-adsorbed by the magnetite surface, keeping its activity.

The evolution of yield for compound **3a** with the time at different catalyst and reactive loadings is depicted in Figure 3. Assuming that the equation rate is simple and that the reaction conditions permit a pseudo-first order approximation for all reagents, the equation rate could be expressed as $\ln r_{oi} = \alpha \ln [A]_{oi} + \text{constant}$, being $[A]$ the initial concentration of catalyst or reagents. The estimation of the initial reaction rate for each trial and their representation allowed us to estimate the value of the reaction order for the catalyst and for both reagents, with the obtained value being very close to $\frac{1}{2}$ for both reagents and $\frac{3}{4}$ for cobalt catalyst. These results pointed out that the mechanism is not very simple and

could be an indirect indication of a previously reported radical mechanism. To verify this fact, a radical scavenger (TEMPO) was added to the initial reaction solution, recovering the starting reagents unchanged after 6 h. In order to know if the sun light had some impact on the possible radical reaction pathway, the reaction was performed in a light protected tube, affording a similar result (88%) to that presented in Table 2, entry 4.

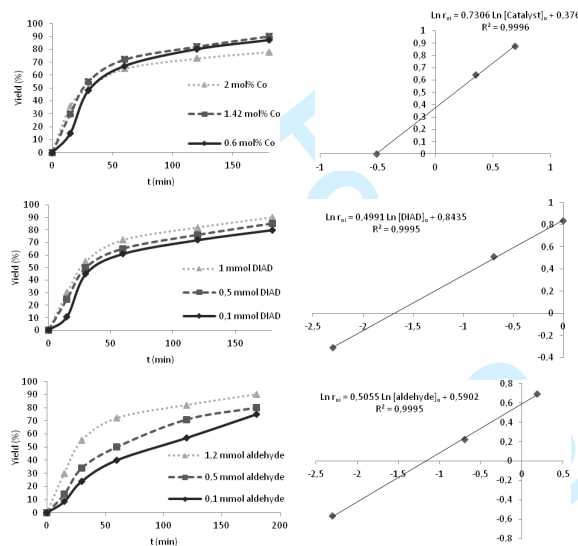


Figure 3. Plot-time yield, and correlation between initial rates and the corresponding catalyst and reagents.

With the best conditions in hand, the scope of the reaction was evaluated using cobalt as well as nickel catalyst (Table 3). The reaction gave excellent and consistent results when diisopropyl azodicarboxylate reagent was employed using different arenecarbaldehydes bearing electron withdrawing groups (Table 3, entries 7-10). However, the presence of electron donating groups at the aryl moiety decreased somehow the yield, with the reaction using 3,4,5-trimethoxybenzaldehyde giving the worse result (entry 6). Interestingly, the reaction using cobalt catalyst led to higher yields than by using nickel. The reaction reached good results when other aromatic aldehydes, including heteroaromatic (entry 12) or α,β -unsaturated aldehydes (entry 13), were used. The reaction with aliphatic aldehydes also gave excellent results independently of the substitution at the α -position or the presence of an isolated C-C double bond. It should be pointed out that the reaction using diethyl azodicarboxylate gave practically the same result as the diisopropyl derivative. However, when the steric hindrance of the azoderivative was increased the final yield decreased (compare entries 1, 19 and 20).

Table 3. Preparation of hydroacylation products^{a)}

Ent	R ¹	R ²	No	Yield (%) ^{b)}	3
1	<i>i</i> -Pr	Ph	3a	89 (83) ^{c)}	
2	<i>i</i> -Pr	2-MeC ₆ H ₄	3b	86 (75) ^{c)}	
3	<i>i</i> -Pr	3-MeC ₆ H ₄	3c	79 (99) ^{c)}	
4	<i>i</i> -Pr	4-MeC ₆ H ₄	3d	72 (78) ^{c)}	
5	<i>i</i> -Pr	4-MeOC ₆ H ₄	3e	67 (41) ^{c)}	
6	<i>i</i> -Pr	3,4,5-(MeO) ₃ C ₆ H ₂	3f	26 (8) ^{c)}	
7	<i>i</i> -Pr	4-FC ₆ H ₄	3g	90 (86) ^{c)}	
8	<i>i</i> -Pr	2-ClC ₆ H ₄	3h	95 (38) ^{c)}	
9	<i>i</i> -Pr	3-ClC ₆ H ₄	3i	97 (88) ^{c)}	
10	<i>i</i> -Pr	4-ClC ₆ H ₄	3j	87 (65) ^{c)}	
11	<i>i</i> -Pr	1-naphthyl	3k	87 (79) ^{c)}	
12	<i>i</i> -Pr	1-thienyl	3l	60 (60) ^{c)}	
13	<i>i</i> -Pr	C ₆ H ₅ CH=CH	3m	74 (82) ^{c)}	
14 ^{d)}	<i>i</i> -Pr	CH ₃ (CH ₂) ₂	3n	99	
15 ^{d)}	<i>i</i> -Pr	CH ₃ (CH ₂) ₇	3o	99	
16 ^{d)}	<i>i</i> -Pr	(CH ₃ CH ₂) ₂ CH	3p	99 (99) ^{c)}	
17 ^{d)}	<i>i</i> -Pr	(CH ₃) ₃ C	3q	75 (88) ^{c)}	
18	<i>i</i> -Pr	(<i>Z</i>)-EtCH=CH(CH ₂) ₅	3r	99	
19	Et	Ph	3s	99 (99) ^{c)}	
20	<i>t</i> -Bu	Ph	3t	40 (62) ^{c)}	

^{a)} Reaction carried out using compounds **1** (1mmol) and **2** (1.2 mmol) and 1mL of solvent. ^{b)} Isolated yield after column chromatography. ^{c)} Reaction carried out with NiO-Fe₃O₄ (1.03 mol%) catalyst. ^{d)} Reaction carried out during 30 min.

Conclusion

In conclusion, we have demonstrated that cobalt impregnated on magnetite is a good catalyst for the hydroacylation reaction with azodicarboxylates independently of the nature of aldehyde and using nearly stoichiometric amounts of both reagents, with the nickel catalyst having similar activity. Furthermore, this reaction could be conducted with the smallest amount of catalyst, requiring the shortest reaction time, compared to previous results in the literature. The catalyst was stable enough to be removed by a magnetic decantation and recycled ten-fold with any detrimental effect on the results.

Experimental Section

General Information. Melting points were obtained with a Reichert Thermovar apparatus. NMR spectra were recorded on a Bruker AC-300 (300 MHz for ¹H and 75 MHz for ¹³C) using CDCl₃ as a solvent and TMS as internal standard for ¹H and ¹³C; chemical shifts are given

in δ (parts per million) and coupling constants (J) in Hertz. FT-IR spectra were obtained on Jasco 4100 LE (Pike Miracle ATR) spectrophotometer. Mass spectra (EI) were obtained at 70 eV on a Himadzu QP-5000 spectrometer, giving fragment ions in m/z with relative intensities (%) in parentheses. Thin layer chromatography (TLC) was carried out on Schleicher & Schuell F1400/LS 254 plates coated with a 0.2 mm layer of silica gel; detection by UV₂₅₄ light, staining with phosphomolybdic acid [25 g phosphomolybdic acid, 10 g Ce(SO₄)₂ · 4 H₂O, 60 mL of concentrated H₂SO₄ and 940 mL H₂O]. Column chromatography was performed using silica gel 60 of 40-63 mesh. All reagents were commercially available (Acros, Aldrich, Fluorochem) and were used as received. The X-ray Fluorescence analyses were carried out on a PHILIPS MAGIX PRO (PW2400) X-ray spectrometer equipped with a rhodium X-ray tube and a beryllium window. **The incorporation of cobalt was determined by X-ray fluorescence.** The BET analyses were carried out on a automatic volumetric AUTOSORB-6 Quantachrome and its degasser unit. N₂ at 77K was used as gas. X-ray photoelectron spectroscopy analyses were carried out on a VG-Microptech Multilab 3000 equipped with a hemispheric electron analyzer with 9 channeltrons (pass energy between 2 and 200 eV) and a X-ray tube with Mg and Al anodes. TEM analyses were carried out on a JEOL JEM-2010 microscope, equipped with a X-ray detector Oxford Inca Energy TEM 100 for microanalysis (EDS). The program Fiji-win32 was used to measure the particle size distribution on TEM images. XRD analyses were obtained on a Bruker D-8 advance diffractometer cith Göebel mirror with high temperature chamber and X-ray generator Kristalloflex K 760-80F(3KW, 20-60KV and 5-80mA).

General Procedure for the Preparation of Cobalt Catalyst. To a stirred solution of the metal salt CoCl₂ · 6H₂O (1 mmol, 238 mg) or NiCl₂ · H₂O (1 mmol, 130 mg) in deionized water (120 mL) was added commercial available Fe₃O₄ (4 g, 17 mmol, powder < 5 μ m, BET area: 9.86 m²/g). After 10 minutes at room temperature, the mixture was slowly basified with NaOH (1M) until pH around 13. The mixture was stirred during one day at room temperature in air. After that, the catalyst was filtered and washed several times with deionized water (3 \times 10 mL). The solid was dried at 100 °C during 24 h in a standard glassware oven, obtaining the expected catalyst.

General Procedure for the Hydroacylation of Azodicarboxylate Compounds. To a stirred solution of the corresponding aldehyde (**2**, 1.2 mmol) in trichloroethylene (1 mL) were added the catalyst (50 mg) and the corresponding substituted azodicarboxylate (**1**, 1 mmol). The resulting mixture was stirred at 60 °C until the end of the reaction. The catalyst was removed by a magnet and the resulting mixture was quenched with water and extracted with AcOEt (3 \times 5 mL). The organic phases were dried over MgSO₄, followed by evaporation under reduced pressure to remove the solvent. The product was usually purified by chromatography on silica gel (hexane/ethyl acetate) to give the corresponding products **3**. Physical and spectroscopic data, as well as literature for known compounds, follow.

Diisopropyl 1-benzoylhydrazine-1,2-dicarboxylate (3a):^[12] White solid; mp = 120-121 °C (hexane); t_r = 15.8; R_f = 0.1 (hexane/ethyl acetate: 4/1); ¹H NMR (300 MHz, CDCl₃): δ 7.69 (m, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.4-7.45 (m, 2H), 6.87 (s, br, 1H), 4.85-5.1 (2m, 1 and 1H, respectively), 1.30 (d, J = 6.0 Hz, 6H), 1.07 (d, J = 5.4 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 171.1, 155.2, 152.8, 135.1, 131.8, 128.0 (4C), 72.3, 70.5, 21.8 (2C), 21.2 (2C); IR (ATR): ν 3275, 1756, 1740, 1684, 1251, 1047 cm⁻¹; MS (EI) m/z (%): 222 (8), 105 (100), 77 (17).

Diisopropyl 1-(2-methylbenzoyl)hydrazine-1,2-dicarboxylate (3b): Pale yellow solid; mp = 64-66 °C (hexane); t_r = 15.9; R_f = 0.53 (hexane/ethyl acetate: 3/2); ¹H NMR (300 MHz, CDCl₃): δ 7.3-7.4 (m, 2H), 7.15-7.3

(m, 2H), 6.97 (s, br, 1H), 5.03 (heptet, J = 6.2 Hz, 1H), 4.84 (heptet, J = 6.2 Hz, 1H), 2.39 (s, 3H), 1.3 (d, J = 6.2 Hz, 6H), 1.0 (d, J = 6.2 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 170.4, 155.1, 152.2, 136.1, 135.2, 130.2, 129.9, 126.2, 125.3, 72.3, 70.6, 21.9 (2C), 21.1 (2C), 9.1; IR (ATR): ν 3294, 2984, 1754, 1734, 1687, 1252, 1505 cm⁻¹; MS (EI) m/z (%): 322 (M⁺, 0.1), 120 (9), 119 (100), 91 (17); Elemental analysis calcd. for C₁₆H₂₂N₂O₅: C = 59.61, H = 6.88, N = 8.69; found: C = 59.65, H = 6.93, N = 8.59.

Diisopropyl 1-(3-methylbenzoyl)hydrazine-1,2-dicarboxylate (3c): White solid; mp = 96-98 °C (hexane); t_r = 16.3; R_f = 0.7 (hexane/ethyl acetate: 3/2); ¹H NMR (300 MHz, CDCl₃): δ 7.5 (m, 2H), 7.25-7.35 (m, 2H), 6.96 (s, br, 1H), 5.01 (heptet, J = 6.2 Hz, 1H), 4.89 (heptet, J = 6.2 Hz, 1H), 2.38 (s, 3H), 1.29 (d, J = 6.2 Hz, 6H), 1.07 (d, J = 6.2 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 171.3, 155.2, 152.9, 137.9, 135.1, 132.6, 128.9, 128.0, 125.2, 72.3, 70.6, 21.9 (2C), 21.3 (2C), 21.2; IR (ATR): ν 3273, 2985, 1741, 1689, 1519, 1252; MS (EI) m/z (%): 236 (8), 120 (9), 119 (100), 91 (18) cm⁻¹; Elemental analysis calcd. for C₁₆H₂₂N₂O₅: C = 59.61, H = 6.88, N = 8.69; found: C = 59.68, H = 7.01, N = 8.75.

Diisopropyl 1-(*p*-tolyl)hydrazine-1,2-dicarboxylate (3d):^[12] White solid; mp = 100-102 °C (hexane); t_r = 16.4; R_f = 0.7 (hexane/ethyl acetate: 3/2); ¹H NMR (300 MHz, CDCl₃): δ 7.61 (m, 2H), 7.22 (d, J = 7.9 Hz, 2H), 6.86 (s, br, 1H), 4.9-5.1 (2m, 1 and 1H, respectively), 2.40 (s, 3H), 1.29 (d, J = 5.6 Hz, 6H), 1.11 (d, J = 5.6 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 171.1, 155.2, 153.0, 142.7, 132.1, 128.7 (2C), 128.4 (2C), 72.3, 70.6, 21.9 (2C), 21.6, 21.3 (2C); IR (ATR): ν 3281, 1753, 1736, 1685, 1250, 1044 cm⁻¹; MS (EI) m/z (%): 236 (9), 120 (14), 119 (100), 91 (22).

Diisopropyl 1-(4-methoxyphenyl)hydrazine-1,2-dicarboxylate (3e):^[9a] White solid; mp = 85-87 °C (hexane); t_r = 17.4; R_f = 0.57 (hexane/ethyl acetate: 3/2); ¹H NMR (300 MHz, CDCl₃): δ 7.73 (m, 2H), 7.05 (s, br, 1H), 6.91 (d, J = 8.8 Hz, 2H), 4.85-5.05 (m, 2H), 3.85 (s, 3H), 1.28 (d, J = 6.0 Hz, 6H), 1.13 (d, J = 6.0 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 170.6, 163.9, 163.0, 153.4, 153.2, 132.3, 131.0, 113.4 (2C), 72.2, 70.5, 55.4, 21.9 (2C), 21.4 (2C); IR (ATR): ν 3258, 1748, 1719, 1698, 1251, 1024 cm⁻¹; MS (EI) m/z (%): 136 (10), 135 (100).

Diisopropyl 1-(3,4,5-trimethoxybenzoyl)hydrazine-1,2-dicarboxylate (3f):^[12] White solid; mp = 92-94 °C (hexane); t_r = 18.9; R_f = 0.3 (hexane/ethyl acetate: 3/2); ¹H NMR (300 MHz, CDCl₃): δ 7.01 (s, 2H), 6.93 (s, br, 1H), 4.85-5.05 (m, 2H), 3.89 (s, 3H), 3.88 (s, 6H), 1.3 (d, J = 6.3 Hz, 6H), 1.14 (d, J = 6.3 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 170.8, 155.3, 153.0, 152.9 (2C), 141.7, 129.9, 106.0 (2C), 72.4, 70.6, 60.9, 56.2 (2C), 21.9 (2C), 21.4 (2C); IR (ATR): ν 3283, 2979, 1746, 1719, 1699, 1587, 1248 cm⁻¹; MS (EI) m/z (%): 398 (M⁺, 5%), 196 (11), 195 (100).

Diisopropyl 1-(4-fluorobenzoyl)hydrazine-1,2-dicarboxylate (3g):^[8b] White solid; mp = 98-99 °C (hexane); t_r = 15.5; R_f = 0.8 (hexane/ethyl acetate: 1/1); ¹H NMR (300 MHz, CDCl₃): δ 1.14 (d, J = 5.9 Hz, 6H), 1.31 (d, J = 5.9 Hz, 6H), 4.9-5.05 (m, 2H), 6.95-7.0 (m, 1H), 7.12 (t, J = 7.1 Hz, 2H), 7.7-7.75 (m, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 170.2, 164.9 (d, J_{C-F} = 253.3 Hz, C), 152.8, 152.2, 131.1, 130.8 (d, J_{C-F} = 6.8 Hz, 2C), 115.3 (d, J_{C-F} = 22 Hz, 2C), 72.6, 70.7, 21.9 (2C), 21.4 (2C); IR (ATR): ν 3282, 1745, 1723, 1698, 1283 cm⁻¹; MS (EI) m/z (%): 240 (10), 154 (10), 124 (12), 123 (100), 95 (20).

Diisopropyl 1-(2-chlorobenzoyl)hydrazine-1,2-dicarboxylate (3h): Yellow oil; t_r = 16.4; R_f = 0.63 (hexane/ethyl acetate: 3/2); ¹H NMR (300 MHz, CDCl₃): δ 7.3-7.5 (m, 4H), 6.99 (s, 1H), 4.85-5.05 (2m, 1 and 1H, respectively), 1.05-1.35 (2m, 6 and 6H, respectively); ¹³C NMR (75 MHz, CDCl₃): δ 167.5, 154.9, 151.6, 136.1, 130.8, 130.2, 129.3, 127.9, 126.6, 72.6, 70.6, 21.8 (2C),

21.2 (2C); IR (ATR) ν 3312, 2983, 2937, 1739, 1257 cm^{-1} ; MS (EI) m/z (%): 256 (10), 141 (34), 139 (100), 111 (12); Elemental analysis calcd. for $\text{C}_{15}\text{H}_{19}\text{ClN}_2\text{O}_5$: C = 52.56, H = 5.59, N = 8.17; found: C = 52.42, H = 5.49, N = 8.23.

Diisopropyl 1-(3-chlorobenzoyl)hydrazine-1,2-dicarboxylate (3i): White solid; mp = 108–110 °C (hexane); t_r = 16.5; R_f = 0.7 (hexane/ethyl acetate: 3/2); ^1H NMR (300 MHz, CDCl_3): δ 7.45–7.65 (m, 3H), 7.3–7.4 (m, 1H), 7.04 (s, br, 1H), 4.9–5.1 (m, 2H), 1.3 (d, J = 6.2 Hz, 6H), 1.11 (d, J = 5.9 Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 169.8, 155.1, 152.5, 136.8, 134.2, 131.7, 129.5, 128.0, 126.1, 72.8, 70.8, 21.9 (2C), 21.3 (2C); IR (ATR): ν 3286, 2985, 2940, 1744, 1757, 1527, 1518, 1254 cm^{-1} ; MS (EI) m/z (%): 256 (12), 214 (11), 170 (17), 141 (39), 139 (100), 111 (20); Elemental analysis calcd. for $\text{C}_{16}\text{H}_{22}\text{ClN}_2\text{O}_5$: C = 52.56, H = 5.59, N = 8.17; found: C = 52.59, H = 5.48, N = 8.08.

Diisopropyl 1-(4-chlorobenzoyl)hydrazine-1,2-dicarboxylate (3j):^[9a] White solid; mp = 82–84 °C (hexane); t_r = 16.6; R_f = 0.7 (hexane/ethyl acetate: 3/2); ^1H NMR (300 MHz, CDCl_3): δ 7.65–7.7 (m, 2H), 7.3–7.4 (m, 2H), 6.95 (s, br, 1H), 4.9–5.05 (m, 2H), 1.3 (d, J = 5.2 Hz, 6H), 1.13 (d, J = 5.2 Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.2, 155.1, 152.7, 138.2, 133.4, 129.6 (2C), 128.4 (2C), 72.7, 70.8, 21.9 (2C), 21.4 (2C); IR (ATR): ν 3310, 2989, 1735, 1712, 1596, 1486, 1264 cm^{-1} ; MS (EI) m/z (%): 256 (8), 141 (33), 139 (100), 111 (14).

Diisopropyl 1-(1-naphthoyl)hydrazine-1,2-dicarboxylate (3k): White solid; mp = 102–104 °C (hexane); t_r = 19.0; R_f = 0.4 (hexane/ethyl acetate: 3/2); ^1H NMR (300 MHz, CDCl_3): δ 8.15–8.2 (m, 1H), 7.93 (d, J = 7.9 Hz, 1H), 7.86 (d, J = 7.9 Hz, 1H), 7.6–7.65 (m, 1H), 7.45–7.55 (m, 3H), 7.1 (s, 1H), 5.05–5.1 (m, 1H), 4.65–4.7 (m, 1H), 1.34 (d, J = 6.2 Hz, 6H), 0.65–0.75 (m, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 170.4, 155.3, 152.0, 134.1, 133.1, 130.5, 129.9, 128.2, 127.3, 126.4, 124.7, 124.6 (2C), 72.3, 70.7, 21.9 (2C), 20.8 (2C); IR (ATR): ν 3278, 1760, 1743, 1514, 1251 cm^{-1} ; MS (EI) m/z (%): 358 (M^+ , 6), 156 (26), 155 (100), 127 (61); Elemental analysis calcd. for $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_5$: C = 63.67, H = 6.19, N = 7.82; found: C = 63.8, H = 6.25, N = 7.9.

Diisopropyl 1-(thiophene-2-carbonyl)hydrazine-1,2-dicarboxylate (3l):^[17] Colorless oil; t_r = 16.0; R_f = 0.47 (hexane/ethyl acetate: 3/2); ^1H NMR (300 MHz, CDCl_3): δ 7.89 (dd, J = 3.9 Hz, J = 1.3 Hz, 1H), 7.6 (dd, J = 5.0 Hz, J = 1.3 Hz, 1H), 7.22 (s, br, 1H), 7.09 (dd, J = 5.0 Hz, J = 3.9 Hz, 1H), 4.95–5.1 (m, 2H), 1.25–1.35 (m, 12H); ^{13}C NMR (75 MHz, CDCl_3): δ 162.6, 155.3, 154.8, 152.6, 135.5, 133.5, 127.1, 72.6, 70.8, 21.8 (2C), 21.5 (2C); IR (ATR): ν 3299, 1736, 1234 cm^{-1} ; MS (EI) m/z (%): 228 (12), 186 (8), 142 (10), 111 (100).

Diisopropyl 1-cinnamoylhydrazine-1,2-dicarboxylate (3m):^[17] Colorless oil; t_r = 17.9; R_f = 0.53 (hexane/ethyl acetate: 3/2); ^1H NMR (300 MHz, CDCl_3): δ 7.72 (d, J = 15.7 Hz, 1H), 7.45–7.5 (m, 3H), 7.25–7.3 (m, 3H), 6.81 (s, br, 1H), 5.01 (heptet, J = 6.3 Hz, 1H), 4.93 (heptet, J = 6.3 Hz, 1H), 1.27 (d, J = 6.3 Hz, 6H), 1.15–1.25 (m, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 166.5, 155.1, 152.8, 145.8, 134.6, 130.4, 128.4 (2C), 118.8, 72.3, 70.4, 21.8 (2C), 21.7 (2C); IR (ATR): ν 3311, 1732, 1236 cm^{-1} ; MS (EI) m/z (%): 132 (10), 131 (100), 103 (16).

Diisopropyl 1-butyrylhydrazine-1,2-dicarboxylate (3n):^[8b] Colorless oil; t_r = 13.01; R_f = 0.6 (hexane/ethyl acetate: 3/2); ^1H NMR (300 MHz, CDCl_3): δ 6.84 (s, br, 1H), 4.85–5.0 (m, 2H), 2.80–2.85 (m, 2H), 1.62 (m, 2H), 1.2–1.25 (m, 12H), 0.9 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 173.7, 155.1, 152.6, 71.9, 70.2, 38.7, 21.8 (2C), 21.6 (2C), 18.0, 13.5; IR (ATR): ν 3311, 1719, 1235 cm^{-1} ; MS (EI) m/z (%): 204 (48), 173 (10), 162 (28), 146 (13), 120 (33), 118 (46), 103 (13), 102 (20), 76 (51), 71 (100), 59 (11).

Diisopropyl 1-nonanoylhydrazine-1,2-dicarboxylate (3o):^[8a] Colorless oil; t_r = 16.2; R_f = 0.7 (hexane/ethyl acetate: 3/2); ^1H NMR (300 MHz, CDCl_3): δ 6.66 (s, br, 1H), 4.9–5.1 (m, 2H), 2.85–2.9 (m, 2H), 2.85–2.9 (m, 2H), 1.6–1.7 (m, 2H), 1.2–1.35 (m, 22H), 0.87 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 173.9, 155.1, 152.6, 71.9, 70.2, 36.9, 31.7, 29.2, 29.0 (2C), 24.6, 22.5, 21.8 (2C), 21.6 (2C), 14.0; IR (ATR): ν 3314, 2981, 2925, 1720, 1244 cm^{-1} ; MS (EI) m/z (%): 205 (12), 204 (100), 162 (44), 160 (12), 141 (52), 120 (24), 118 (70), 76 (32), 71 (26), 57 (28), 55 (13).

Diisopropyl 1-(2-ethylbutanoyl)hydrazine-1,2-dicarboxylate (3p): Colorless oil; t_r = 13.6; R_f = 0.73 (hexane/ethyl acetate: 3/2); ^1H NMR (300 MHz, CDCl_3): δ 7.01 (s, br, 1H), 4.95–5.1 (2m, 1 and 1H, respectively), 3.45–3.5 (m, 1H), 1.65–1.8 (m, 2H), 1.5–1.6 (m, 2H), 1.32 (d, J = 6.3 Hz, 6H), 1.25–1.3 (m, 6H), 0.91 (t, J = 7.4 Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 177.0, 155.1, 152.6, 71.8, 70.0, 47.3, 24.7 (2C), 21.7 (2C), 21.5 (2C), 11.4 (2C); IR (ATR): ν 3311, 2970, 2937, 2878, 1719, 1230 cm^{-1} ; MS (EI) m/z (%): 302 (M^+ , <0.1%), 204 (16), 162 (9), 120 (15), 99 (46), 98 (22), 76 (11), 71 (100); Elemental analysis calcd. for $\text{C}_{14}\text{H}_{26}\text{N}_2\text{O}_5$: C = 55.61, H = 8.67, N = 9.26; found: C = 55.57, H = 8.60, N = 9.19.

Diisopropyl 1-pivaloylhydrazine-1,2-dicarboxylate (3q):^[8b] Colorless oil; t_r = 12.7; R_f = 0.73 (hexane/ethyl acetate: 3/2); ^1H NMR (300 MHz, CDCl_3): δ 6.81 (s, br, 1H), 4.95–5.1 (m, 2H), 1.2–1.35 (m, 21H); ^{13}C NMR (75 MHz, CDCl_3): δ 179.6, 155.7, 153.2, 72.1, 70.5, 42.0, 27.4 (2C), 21.8 (2C), 21.6 (2C); IR (ATR): ν 3295, 2981, 1720, 1227 cm^{-1} ; MS (EI) m/z (%): 204 (37), 162 (30), 120 (43), 118 (15), 103 (11), 85 (817), 76 (31), 57 (100).

(Z)-Diisopropyl 1-(dec-7-enoyl)hydrazine-1,2-dicarboxylate (3r): Colorless oil; t_r = 16.7; R_f = 0.47 (hexane/ethyl acetate: 4/1); ^1H NMR (300 MHz, CDCl_3): δ 6.72 (s, br, 1H), 4.90–5.1 (m, 2H), 2.90 (t, J = 6.8 Hz, 2H), 1.95–2.05 (m, 4H), 1.6–1.7 (m, 2H), 1.2–1.4 (m, 16H), 0.95 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 173.0, 155.1, 152.6, 131.7, 128.9, 72.0, 70.3, 36.9, 29.4, 28.7, 26.9, 24.5, 21.8 (2C), 21.6 (2C), 20.4, 14.3; IR (ATR): ν 3313, 1736, 1502, 1237 cm^{-1} ; MS (EI) m/z (%): 356 (M^+ , 0.08), 205 (14), 204 (100), 163 (11), 162 (49), 153 (54), 152 (32), 135 (13), 123 (816), 121 (13), 120 (27), 118 (74), 109 (11), 83 (15), 76 (43), 71 (10), 69 (37), 67 (16), 55 (31); Elemental analysis calcd. for $\text{C}_{18}\text{H}_{32}\text{N}_2\text{O}_5$: C = 60.65, H = 9.05, N = 7.86; found: C = 60.67, H = 9.03, N = 7.87.

Diethyl 1-benzoylhydrazine-1,2-dicarboxylate (3s):^[18] Colorless oil; t_r = 15.5; R_f = 0.5 (hexane/ethyl acetate: 3/2); ^1H NMR (300 MHz, CDCl_3): δ 7.68 (d, J = 7.1 Hz, 2H), 7.35–7.55 (m, 3H), 7.24 (s, br, 1H), 4.25 (q, J = 7.1 Hz, 2H), 4.15 (q, J = 7.1 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H), 1.07 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 172.1, 155.7, 153.4, 133.7, 132.0, 130.1, 128.4, 128.1, 64.0 (2C), 14.3 (2C); IR (ATR): ν 3312, 2921, 1705, 1222 cm^{-1} ; MS (EI) m/z (%): 106 (8), 105 (100), 77 (21).

Di-tert-butyl 1-benzoylhydrazine-1,2-dicarboxylate (3t): White solid; mp = 118–120 °C (hexane); t_r = 14.9; R_f = 0.67 (hexane/ethyl acetate: 3/2); ^1H NMR (300 MHz, CDCl_3): δ 8.15–8.2 (m, 1H), 7.93 (d, J = 7.9 Hz, 1H), 7.71 (d, J = 7.7 Hz, 2H), 7.51 (t, J = 7.4 Hz, 2H), 7.42 (t, J = 7.4 Hz, 2H), 6.84 (s, br, 1H), 1.50 (s, 9H), 1.23 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3): δ 171.6, 154.5, 151.7, 135.8, 131.7, 128.1 (4C), 84.4, 82.2, 28.1 (3C), 27.4 (3C); IR (ATR): ν 3336, 1760, 1721, 1703, 1280, 1063 cm^{-1} ; MS (EI) m/z (%): 180 (13), 163 (22), 136 (37), 105 (100), 77 (47), 59 (810), 57 (894), 51 (15); Elemental analysis calcd. for $\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}_5$: C = 60.7, H = 7.19, N = 8.33; found: C = 60.65, H = 7.23, N = 8.32.

Acknowledgements

This work was supported by the Spanish Ministerio de Economía y Competitividad (MICINN; CTO2011-24151) and University of Alicante. J.M.P. thanks the MICINN (FPI program) for her fellowship. We gratefully acknowledge the polishing of our English by Mrs. Oriana C. Townley.

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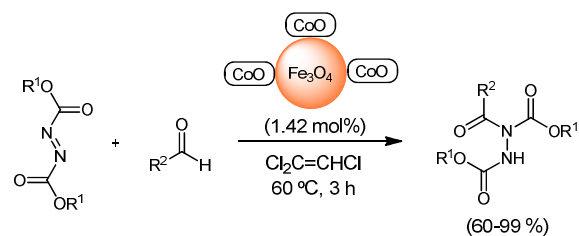
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Cobalt-Impregnated Magnetite as General
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Adv. Synth. Catal. **Year**, *Volume*, Page – Page

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