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Isotopomeric diols by "one-pot" Ru-catalyzed homogeneous hydrogenation of dicarboxylic acids

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ABSTRACT

The "one-pot" homogeneous hydrogenation of γ-butyrolactone and succinic or fumaric acid to 1,4-butandiol, have been successfully realized in the presence of the catalytic system [$Ru(acac)_3$]/triphos] [triphos:$MeC(CH_2PPh_2)_3$]. The influence of some reaction parameters on the regioselectivity and the rate of the reaction were investigated. The study was then extended to the "one-pot" synthesis of isotopomeric 1,4-butandiols by deuteration of the appropriate substrates in a deuterated solvent. 1,4-butandiol-d_8, which was fully characterized, was obtained with 96% yield and 100% isotopomeric selectivity. A mechanism was proposed to rationalize the role of catalyst, solvent and deuterium distribution.

1. Introduction

Hydrogenation of fatty acids and their methyl esters to produce alcohols has relevant industrial applications since it is one of the routes generally used for the manufacture of high alcohols. In contrast with the hydrogenation of ketones or aldehydes, the hydrogenation of esters is troublesome. Industrial plants for the hydrogenation of commercial fatty acids or esters employ heterogeneous catalysts, usually copper chromium based systems, at relatively high temperatures (200–300 °C) and hydrogen pressures (200–300 bar) [1].

Despite of a plethora of papers and patents regarding heterogeneous catalysts for the reduction of esters and acids to alcohols, a minor effort has been devoted to the application of the homogeneous hydrogenation which has involved mostly soluble ruthenium complexes.

In the past, some of us reported the hydrogenation of activated esters, i.e. dimethyl oxalate, using soluble ruthenium cluster compounds such as $Ru_4H_4(CO)_8(PBu_3)_4$ or $Ru_2(CO)_4(CH_3COO)_2(PR_3)_2$ [2]. Ethylene glycol was selectively synthesized from dimethyl oxalate by homogeneous hydrogenation in the presence of $Ru_2(CO)_4(CH_3COO)_2(PR_3)_2$. In order to avoid the decomposition of substrate the hydrogenation were carried out at 120 °C to completely convert dimethyl oxalate to methyl glycolate and then at 180 °C to hydrogenate the intermediate to diols. Also Grey and co-workers [3] reported the hydrogenation of esters which were activated by adjacent electron withdrawing groups, such as dimethyl oxalate, using the anionic ruthenium complex $K_2[(PPh_3)_3(PPh_2)Ru_2H_4]\cdot(C_6H_{14}O_3)_2$ as catalyst. Among dicarboxylic acids, up to now, the hydrogenation of dimethyl oxalate is the most widely studied and reported in the literature, and so far the reaction can be provide a benchmark reaction in this type of catalysis.

Elsevier and co-workers [4] have extensively studied the catalytic activity of the system based on [$Ru(acac)_3$] (acac = acetylacetonate) for the hydrogenation of dimethyl oxalate to ethylene glycol in the presence of a selection of mono-, di- and tridentate ligands based on N- and P-donor and Zn as promoter. They achieved the conclusion that [$Ru(acac)_3$]/triphos] system [triphos:$MeC(CH_2PPh_2)_3$] is the most efficient in relatively mild conditions (120 °C, 85 bar H_2). The authors extended the study to the hydrogenation of benzyl benzoate to benzyl alcohol in the same conditions employing the same catalytic system but fluorinated solvent and an excess of triethylamine were required [5].

Nomura et al. [6] accounted for the use of [$Ru(acac)_3$] with an excess of $P(n\text{-}C_8H_{17})_3$ in the presence of Zn for the partial conversion of methyl phenylacetate to 2-phenyl ethanol, the reaction was carried out at 200 °C and 10 bar of hydrogen pressure.

Recently the tripodal sulfur ligand $TriSulf^{Bu}$ has been used by Boardman et al. [7] for the selective homogeneous ruthenium-catalyzed hydrogenation of dimethyl oxalate to methyl glycolate.

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In the same year Milstein and co-workers [8] described an innovative catalyst for the homogeneous hydrogenation of esters, consisting in a PNN (2-(di-*tert*-butylphosphinomethyl)-6-(diethylaminomethyl)pyridine)ruthenium hydride complex, providing the hydrogenation of non-activated aromatic and aliphatic esters to the corresponding alcohols under relatively mild conditions (115–140 °C and 5.3 bar of H_2).

In 2007 we have settled a convenient procedure for the reduction of 1,4-dicarboxylic acids to isotopomeric γ-butyrolactones containing 2, 4 or 6 deuterium atoms using $Ru_4H_4(CO)_8(PBu_3)_4$ as homogeneous catalyst [9]. This catalyst shows a complete selectivity for the reduction of dicarboxylic acids to esters but, obviously it is not able to reduce esters to the corresponding alcohols.

Now we are interested to the synthesis of the corresponding isotopomeric 1,4-butandiols through deuteration of lactones or directly through the "one-pot" hydrogenation of the corresponding 1,4-dicarboxylic acids, that may even be more appealing. The use of succinic acid from renewable resources as a C_4 building block has been very recently reviewed [10]. Aware of the ability of the [$Ru(acac)_3$]/triphos] system to catalyzed the homogeneous hydrogenation of dimethyl oxalate to methyl glycolate, we have explored the activity of such system in the hydrogenation of γ-butyrolactone (GBL), succinic, fumaric or acetylenedicarboxylic acid (Scheme 1), in view of a possible one pot synthesis of deuterated isotopomeric 1,4-butandiols containing 4, 6, 8 or 10 deuterium atoms.

2. Results and discussion

2.1. Catalytic activity of $Ru(acac)_3$/triphos

All experiments were performed with the following molar ratios in order to compare the results with those reported in literature: 100/1.19 for substrate/$Ru(acac)_3$, 1.37/1 for triphos/$Ru(acac)_3$ and 0.26/1 for Zn/substrate.

Hydrogenation of fumaric acid to the corresponding 1,4-butandiol (1,4-BD) occurs through a multistep reaction. The synthesis carried out in methanol using the catalytic system $Ru(acac)_3$/triphos, leads to a mixture of products containing butandiol and the intermediate products reported in Scheme 2. A series of experiments were performed to maximize the conversion of fumaric acid (FA) to 1,4-BD: the influence of reaction variables such as temperature, solvent and reaction time were investigated. Furthermore, in order to evaluate the steps involved in the formation of 1,4-butandiol, the intermediate products succinic acid and γ-butyrolactone (GBL) were tested as starting materials in some experiments.

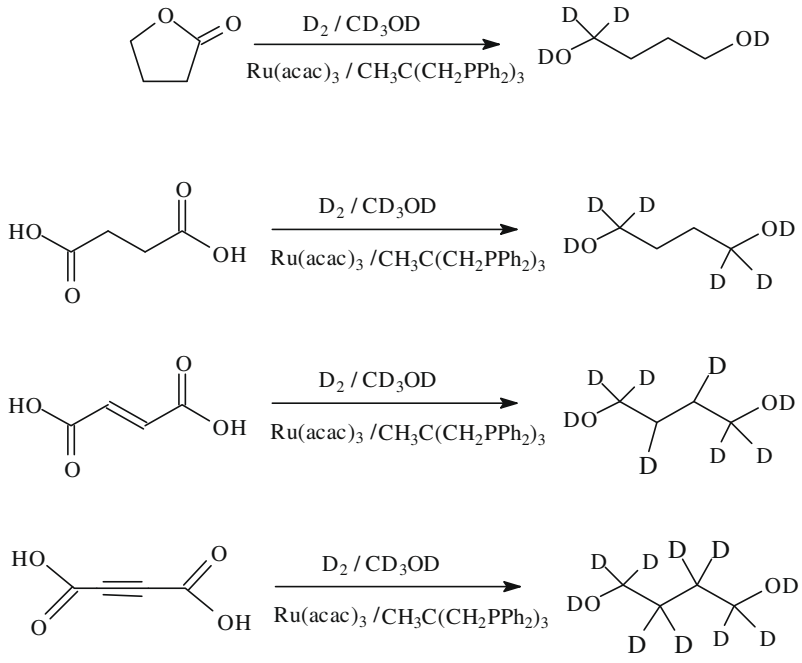
Hydrogenation of carbon–carbon double bond of fumaric acid leads to succinic acid followed by esterification of the carboxylic groups with methanol (when used as solvent) affording the corresponding methyl ester (dimethyl succinate, DS). Hydrogenation of DS to 1,4-BD proceeds through two steps. In the first step DS is converted to methyl 4-hydroxybutyrate (HB) that can be converted to 1,4-BD through the hydrogenation of the residual methyl ester group.

The intermediate HB may undergo a *trans*-esterification reaction leading to the formation of the cyclic ester γ-butyrolactone (GBL), that in the reaction mixture is in equilibrium with HB as experimentally verified even at room temperature (as a consequence of this, the GBL concentration reported, is referred to the total amount of HB and GBL). GBL may be also converted to 1,4-BD.

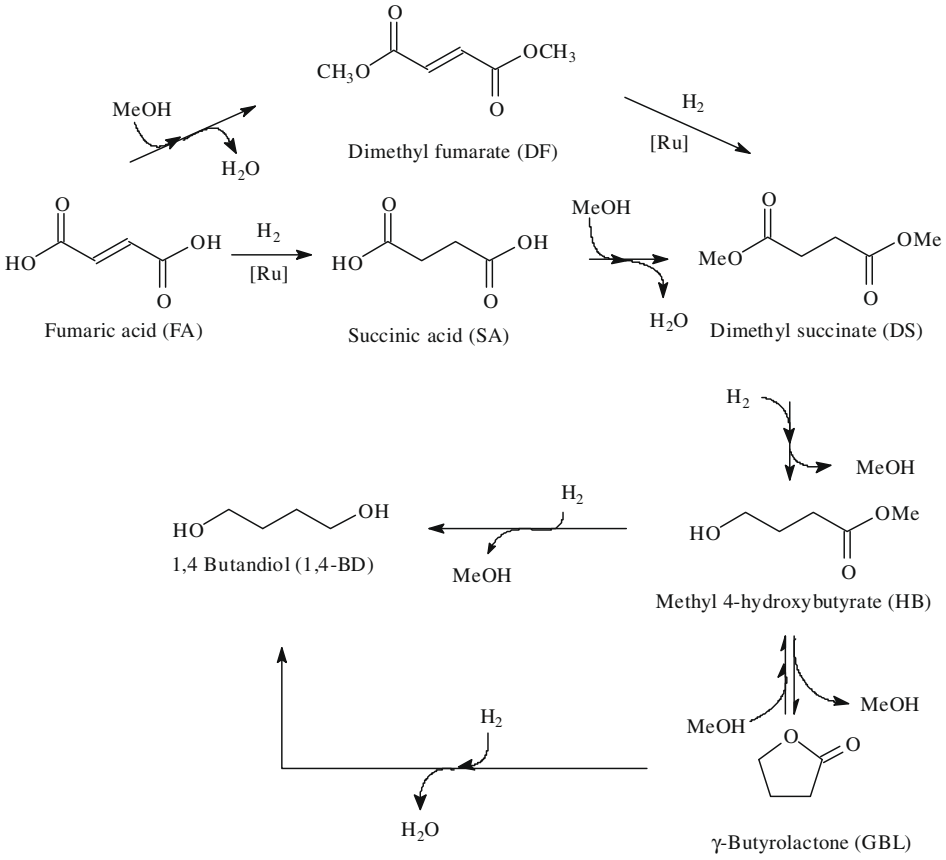
As an alternative path fumaric acid (FA) may be esterified to dimethyl fumarate (DF) in a first step and subsequently hydrogenated to dimethyl succinate (DS). The subsequent steps remain unchanged.

2.2. Reaction products composition obtained using different starting materials

Hydrogenation of fumaric acid, succinic acid or GBL in the same reaction conditions (T 120 °C, P_{H2} 80 bar) afforded a mixture of products. The relative amounts, as shown by the GC analyses reported in Table 1, are affected by the substrate tested. Residual fumaric acid was not detected, hence its conversion was 100% while the yield of the desired diol was only 23% (entry 1, Table 1). Intermediate products DS and GBL were the major products of the mixture with their relative amount of 38% and 36% together with the



Scheme 1. Synthesis of isotopomeric 1,4-butandiols from γ-butyrolactone or carboxylic acids.



Scheme 2. Hydrogenation of fumaric acid.

presence of small amount of succinic acid (3%). When the reaction was carried out starting from succinic acid the reaction products composition was very different (entry 2, Table 1). The yield of 1,4-butandiol and that one of the intermediate product (GBL) was improved presumably due to the skipping of the first hydrogenation step (reduction of fumaric acid to succinic acid). Coherently the hydrogenation of GBL shifts the reaction towards the final products (entry 3, Table 1): steps affording succinic acid and dimethyl succinate DS are avoided, hence the composition of 1,4-BD (36%) and GBL (64%) in the reaction mixture was improved.

2.3. Influence of reaction time

2.3.1. Hydrogenation of fumaric acid

Fumaric acid was reduced with the catalytic system above reported, using methanol as solvent, with a hydrogen pressure of 80 bar at 120 °C. Results of the reaction obtained by GC analysis, are reported in Table 2. Reaction carried out for 16 h (entry 4, Table 2) gave a total conversion but only traces of 1,4-BD (<1%) while the yields of intermediate products were: 38% for succinic acid, 14% for GBL and 48% for dimethyl succinate (DS).

Let the reaction going out for 48 h (entry 1, Table 2), a significant increase of the 1,4-BD yield from traces (entry 4, Table 2) to 23% (entry 1, Table 2) was observed. In the same time the GBL yield raised to 36% while DS went down to 38% (entry 1, Table 2) and the succinic acid yield decreased from 38% (entry 4, Table 2) to 3% (entry 1, Table 2).

As the reaction time was further increased the yield to 1,4-BD appreciably improved: it raised from 30% after 72 h (entry 5, Table 2) to 56% after 96 h (entry 6, Table 2). At the same time the amount of succinic acid remained almost unchanged (entries 6 and 7, Table 2) while the yield of GBL and DS decreased.

Table 1
Hydrogenation of fumaric acid, succinic acid and GBL.[a]

Entry	Substrate	Reaction products composition (%)			
		SA	DS	GBL	1,4-BD
1	Fumaric acid	3	38	36	23
2	Succinic acid	3	12	56	29
3	GBL	–	–	64	36

SA: succinic acid; 1,4-BD: 1,4-butandiol; GBL: γ-butyrolactone; DS: dimethyl succinate.

[a] Conditions: methanol (12 ml), substrate (1.770 mmol), hydrogen (80 bar), $Ru(acac)_3$ (0.021 mmol), $MeC(CH_2PPh_2)_3$ (0.029 mmol), Zn (4.6×10^{-3} mmol), temperature 120 °C, time 48 h.

Table 2
Hydrogenation of fumaric or succinic acid.[a] Influence of reaction time.

Entry	Acid	Time (h)	Reaction products composition (%)			
			SA	DS	GBL	1,4-BD
4	Fumaric	16	38	48	14	Traces
1	Fumaric	48	3	38	36	23
5	Fumaric	72	2	37	31	30
6	Fumaric	96	2	28	14	56
7	Succinic	24	4	14	76	6
2	Succinic	48	3	12	56	29
8	Succinic	72	3	10	54	33

SA: succinic acid; 1,4-BD: 1,4-butandiol; GBL: γ-butyrolactone; DS: dimethyl succinate.

[a] Conditions: solvent (12 ml), fumaric acid (1.770 mmol), hydrogen (80 bar), $Ru(acac)_3$ (0.021 mmol), $MeC(CH_2PPh_2)_3$ (0.029 mmol), Zn (4.6×10^{-3} mmol, temperature 120 °C.

Table 3
Hydrogenation of fumaric acid or GBL.[a] Influence of solvent.

Entry	Substrate	Solvent	Reaction products composition (%)			
			SA	DS	GBL	1,4-BD
1	Fumaric acid	CH_3OH	3	38	36	23
9	Fumaric acid	THF	52	–	48	–
3	GBL	CH_3OH	–	–	64	36
10	GBL	THF	–	–	98	2

SA: succinic acid; 1,4-BD: 1,4-butandiol; GBL: γ-butyrolactone; DS: dimethyl succinate.
[a] Conditions: solvent (12 ml), substrate (1.770 mmol), hydrogen (80 bar), Ru(acac)$_3$ (0.021 mmol), MeC(CH$_2$PPh$_2$)$_3$ (0.029 mmol), Zn (4.6×10^{-3} mmol), temperature 120 °C, time 48 h.

2.3.2. Hydrogenation of succinic acid

The influence of reaction time was also tested starting from succinic instead of fumaric acid while the other parameters were unchanged: three experiments lasting for 24, 48 and 72 h were performed and the results reported in Table 3. The yield of 1,4-BD were respectively 6%, 29% and 33% (entries 7, 2 and 8, respectively Table 2) that meant a slight improvement with respect to those obtained with fumaric acid. Also in these cases the yield of 1,4-BD was raised, as the reaction time increased, and obviously to a detriment of the GBL yield, that went down from 76% after 24 h of reaction (entry 7) to 54% after 72 h (entry 8). The concentration of GBL and DS showed the same trends registered in the reduction of fumaric acid when the reaction time increases, although the yield to GBL was considerably greater and, consequently, the DS yield was considerably lower.

2.4. Influence of solvent

In order to avoid the formation of the intermediate esters dimethyl fumarate (DF) and dimethyl succinate (DS) the reaction was carried out using THF instead of methanol as solvent.

2.4.1. Hydrogenation of fumaric acid

Reaction carried out in the experimental conditions reported in entry 1, Table 2 did not showed 1,4-BD (entry 9, Table 3), while the formation of GBL was considerably increased, going up to 48%.

2.4.2. Hydrogenation of GBL

The hydrogenation of GBL was also carried out in the same reaction conditions used for the hydrogenation of fumaric acid and the results are reported in Table 3. As well as for the hydrogenation of fumaric acid, using THF as solvent, starting from GBL the yield to diol was negligible (2%) (entry 10, Table 3). These results confirmed that methanol is the preferred solvent for this hydrogenation according with the results reported by Teunissen et al., suggesting its involvement in the catalytic cycle [4].

2.5. Influence of reaction temperature

The hydrogenation of fumaric acid was performed using temperature and time as referring parameters while solvent, catalyst amount and hydrogen pressure were kept always constant (Table 4). The general trend showed an increment in the formation of 1,4-BD with the temperature and, as a consequence, a decrease of the concentration for all other intermediates. In fact after 48 h for reactions run at 120, 150 and 180 °C (Table 4, entry 1, 11 and 14) the concentration of 1,4-BD raised from 23% to 81% while a reverse trend was registered for the yield of DS and GBL.

Table 4
Hydrogenation of fumaric acid.[a] Influence of reaction temperature.

Entry	Temperature (°C)	Time (h)	Reaction products composition (%)			
			SA	DS	GBL	1,4-BD
1	120	48	3	38	36	23
5	120	72	2	37	31	30
6	120	96	2	28	14	56
11	150	48	4	11	33	52
12	150	72	3	5	11	81
13	180	24	1	10	29	60
14	180	48	1	9	9	81

SA: succinic acid; 1,4-BD: 1,4-butandiol; GBL: γ-butyrolactone; DS: dimethyl succinate.
[a] Conditions: solvent (12 ml), fumaric acid (1.770 mmol), hydrogen (80 bar), Ru(acac)$_3$ (0.021 mmol), MeC(CH$_2$PPh$_2$)$_3$ (0.029 mmol), Zn (4.6×10^{-3} mmol).

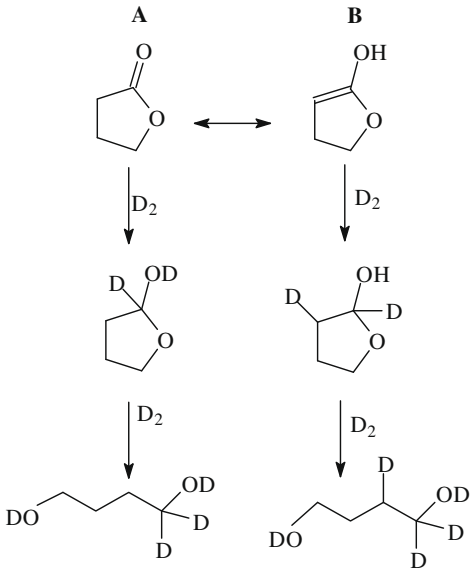
2.6. Deuteration of fumaric acid

Some preliminary tests were performed with the aim to elucidate the mechanism of the carboxylic acid or GBL hydrogenation and in the same time to evaluate the effectiveness of this method for the synthesis of isotopomeric diols through the deuteration of fumaric acid, succinic acid or GBL.

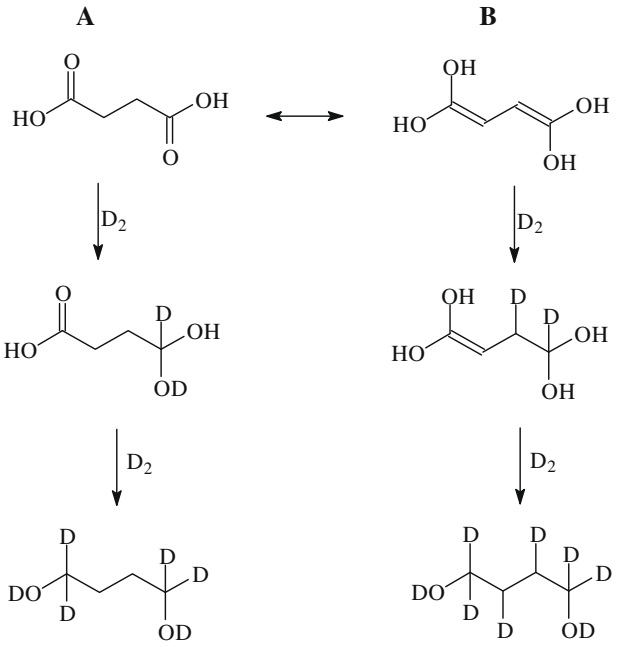
The carboxylic group of the acid or that one of GBL may be directly hydrogenated to alcohol (step A, Schemes 3 and 4) or may initially isomerize to an enolic form and subsequently the enol may be hydrogenated (step B, Schemes 3 and 4), that is in the first case a C=O hydrogenation takes place while in the second case a C=C hydrogenation has been realized.

The nearly complete conversion of fumaric acid to 1,4-BD-d$_8$ (yield 96% isotopomeric selectivity 100%) having the following distribution of deuterium: DO–CD$_2$–CHD–CHD–CD$_2$–OD is supported by GC–MS and NMR analysis. The H atoms were present in the initial positions. These results confirm the direct deuteration of the C=O bond of the carboxylic acid, that is only step A of Schemes 3 and 4 is effective.

The reaction crude showed a 1,4-BD conversion (96%) higher than the 81% obtained in the hydrogenation of fumaric acid (entry 12, Table 4), even if the same experimental conditions were adopted (with the obvious exception that hydrogen instead of



Scheme 3. Alternative steps in the GBL deuteration.



Scheme 4. Alternative steps in the succinic acid deuteration.

deuterium and dry distilled methanol instead of methanol-d_4 were employed).

In consideration of the complete conversion of fumaric acid to 1,4-BD-d_8 (DO–CD_2–CHD–CHD–CD_2–OD) this method is adequate for the synthesis of isotopomeric butandiol containing eight deuterium atoms in high yield. In the same way it will be possible to obtain a 1,4-BD-d_4 from GBL or 1,4-BD-d_6 from succinic acid or DS and the perdeuterated 1,4-BD-d_{10} from acetylenedicarboxylic acid.

The high conversion to 1,4-BD reached in the deuteration of fumaric acid is remarkable. The more suiting hypothesis regarding the increment in 1,4-BD yield may be attributed to the lower purity grade of CD_3OD for what concern the content of water; nevertheless a different behaviour of D_2 with respect to H_2 or CD_3OD with respect to CH_3OH cannot be ruled out.

Traces of water present in methanol-d_4 may have a beneficial influence on the rate of the catalytic deuteration. Van Engelen et al. [4] have reported an inhibiting effect of water on the conversion when using commercial methanol instead of the dry solvent, but a positive influence on the rate of the reaction, by trace of water in the solvent has been shown in other cases [11]. In our case, the small amount of water present in methanol-d_4 could have been able to promote the hydrogenation of fumaric acid to 1,4-butandiol, even if increasing the amount of water to 1% a negative influence was shown (yield 75%).

2.7. Characterization of DO–CD_2–CHD–CHD–CD_2–OD

The mass spectrum of deuterated 1,4-butandiol-d_8 is shown in Fig. 1, its interpretation is reported in Schemes 5–7 according to the fragmentation mechanism proposed by Horváth and Kuszmann [12]. They were the first to study the mass fragmentation of 1,4-BD and different isotopomeric 1,4-diols (DO–$(CH_2)_4$–OD and HO–CD_2–$(CH_2)_2$–CD_2–OH).

The molecular ion (*m*/*z* 98) is not observed in the spectrum as usually happen for alcohols. Hydrogen (deuterium) rearrangement of molecular ion occurs through two routes (Scheme 5). Both mechanisms (1 and 2) assume the formation of rearranged molecular ions at *m*/*z* 98 in which the cation and radical sites are separated. Molecular ions **1a**, **2a** and **3a**, were not observed, because they rapidly decompose through different fragmentation patterns.

Fragmentation of radical cation **1a** occurring at radical site is reported in Scheme 6.

The mass spectrum shows a base peak at *m*/*z* 46 (**1c**) due to an α-cleavage of **1a** loosing formaldehyde and forming **1b**, followed by the loss of water. Fragments at *m*/*z* 44 and 45 are formed through the loss of deuterium or hydrogen, respectively, from the propane radical cation **1c**.

Alternatively the fragmentation of **1a** occurs at cation site with initial loss of D_2O (*m*/*z* 20) forming **1f** followed by deuterium (**1g**) or hydrogen (**1i**) elimination. The following loss of CO from the aldehydic species **1g** leads to fragment at *m*/*z* 48 (**1h**).

Molecular ion **2a**, obtained from 1,4 deuterium rearrangement, can lose water according with the process reported in Scheme 7. The fragment obtained (**2b**) has *m*/*z* 78 and weak intensity.

An alternative route that involves the loss of water and justify the presence of the second most intense peak in the spectrum (*m*/*z* 47) is reported in Scheme 7. Molecular ion **3a**, derived from the rearrangement of ion **2a** gives the elimination of water forming **3b** followed by the α-cleavage loosing ethylene and forming the ion **3c** $[DO–CD{=}CHD]^{+\cdot}$ (*m*/*z* 47). [13] Alternatively, the loss of

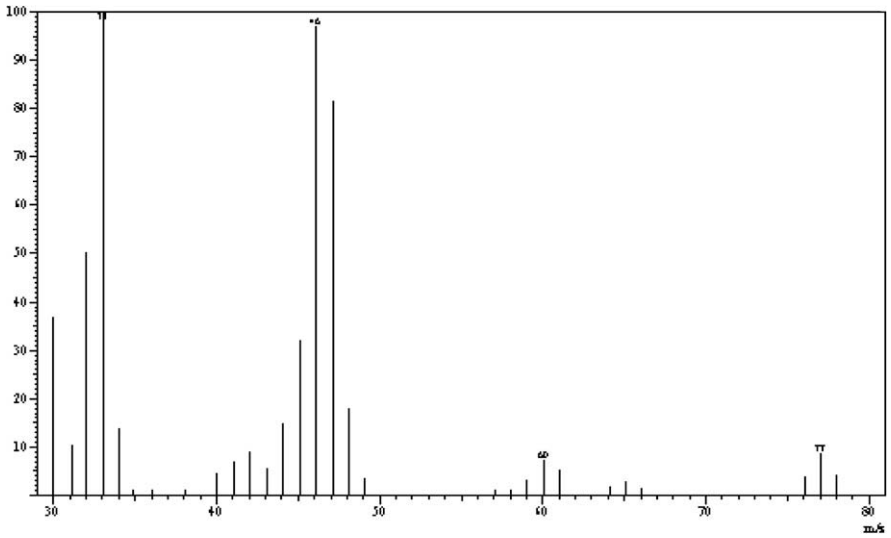
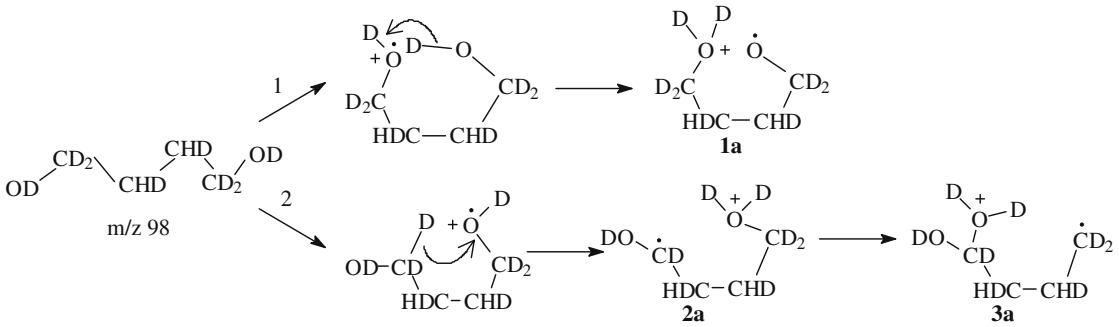
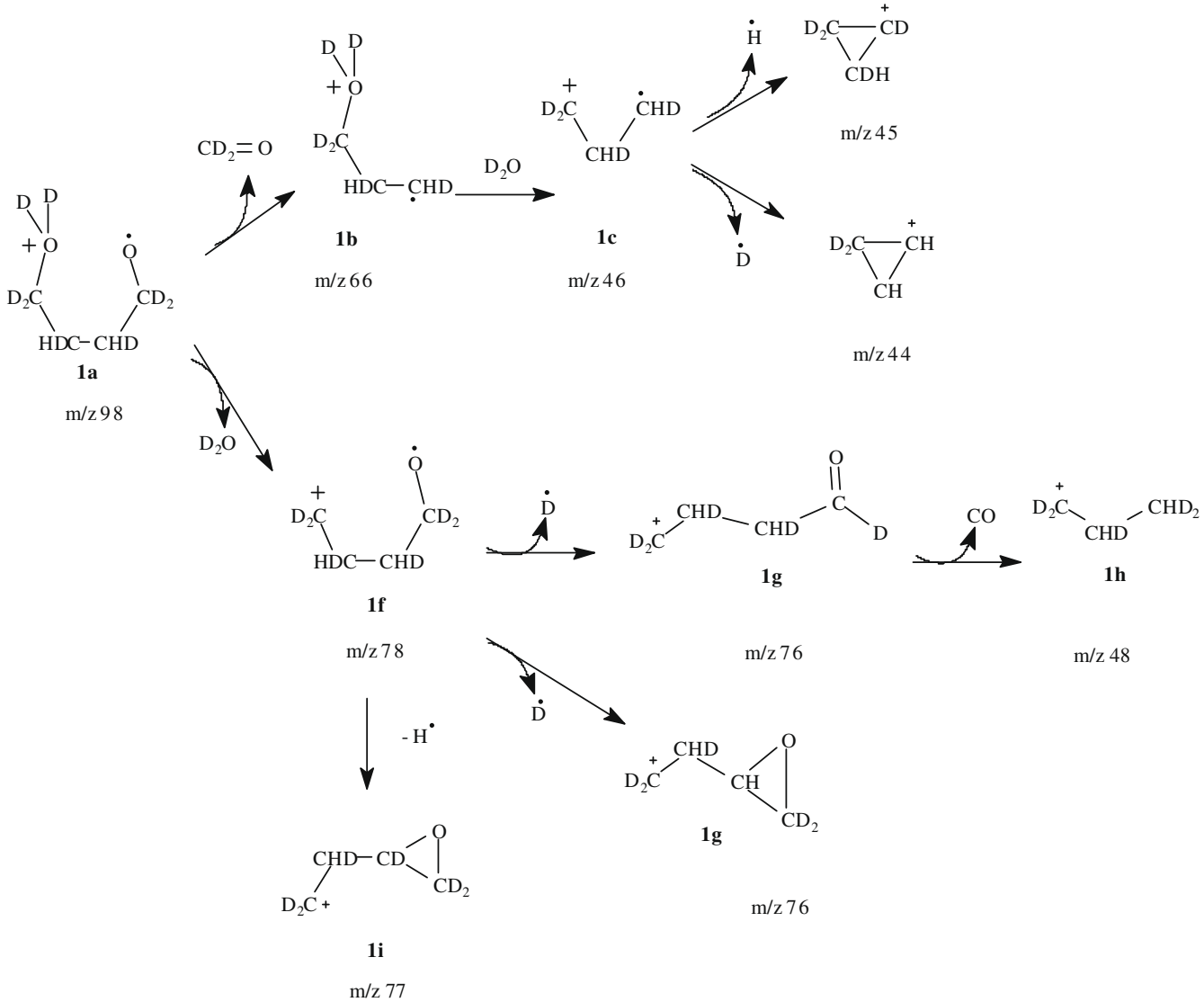


Fig. 1. Mass spectrum of 1,4-butandiol-d_8.



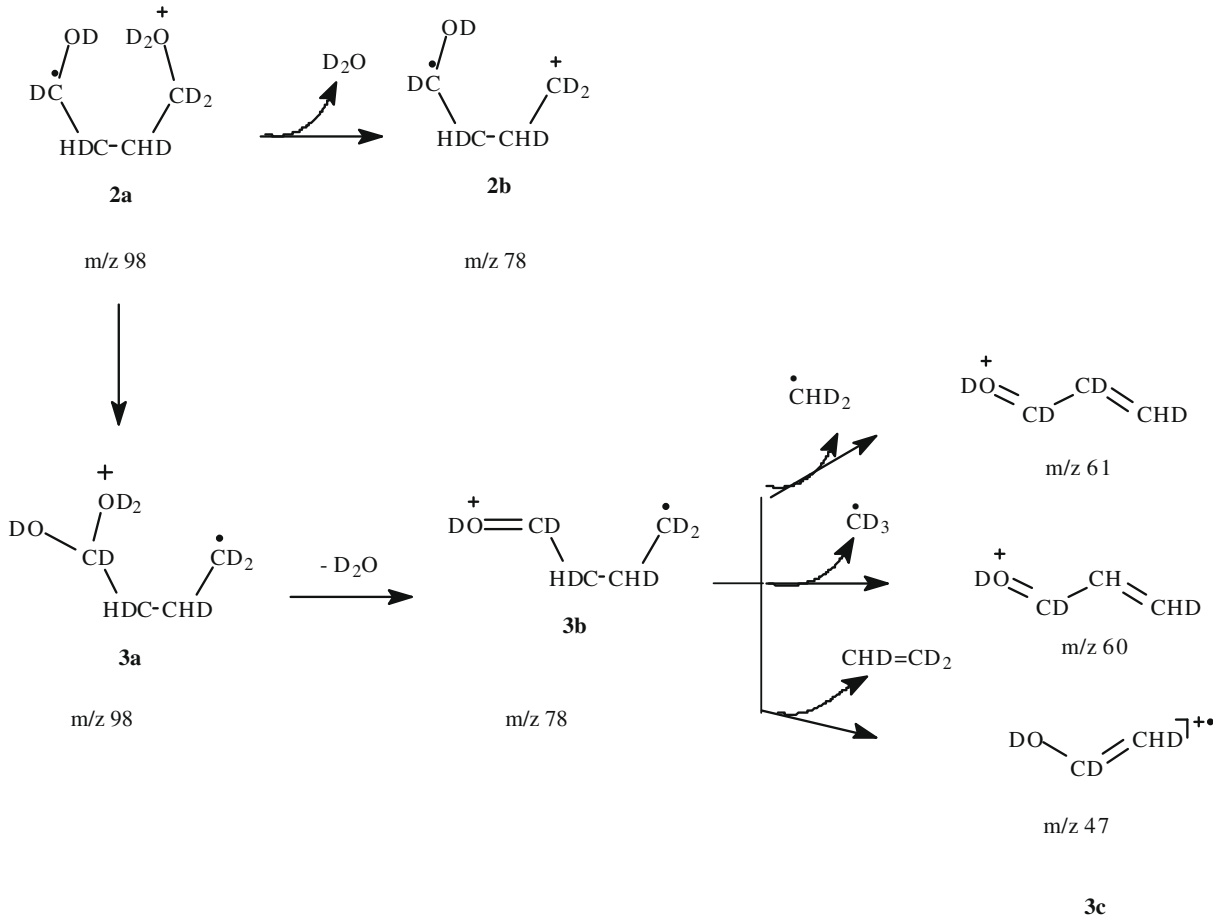
Scheme 5. Rearrangements of molecular ion.



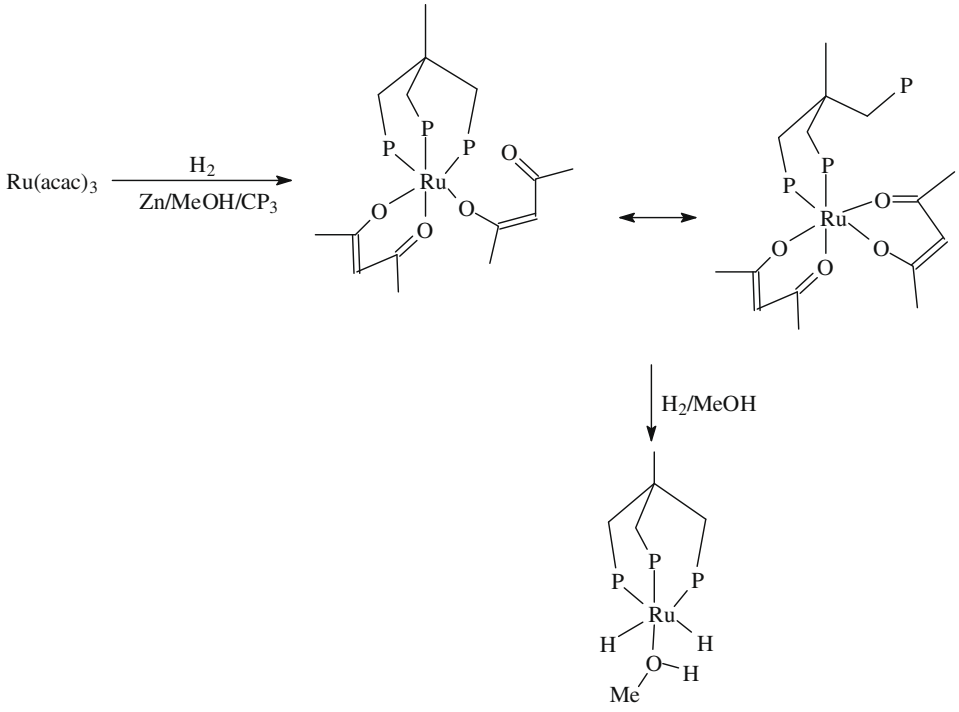
Scheme 6. Fragmentation of radical cation **1a**.

water from **3a** can be followed by the elimination of a CHD_2 radical (or CD_3 radical) through a H-rearrangement giving the weak peaks, respectively, at *m*/*z* 61 and 60.

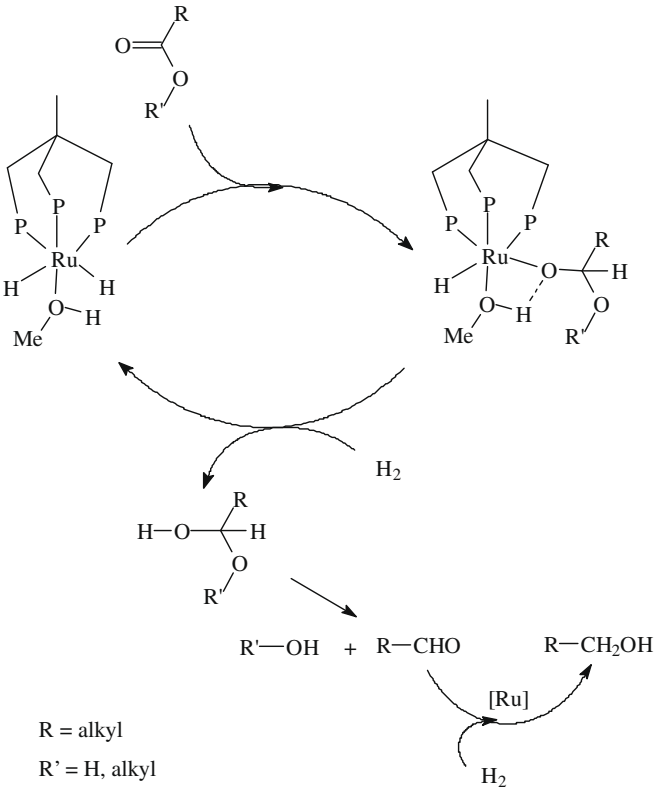
The insertion of deuterium atoms in position 2 and 3 of the fumaric acid, is confirmed also by ^1H and ^{13}C NMR spectra of the resulting diol: only one singlet is present in the ^1H NMR spectrum at 1.541 ppm (s, 2H, –C*H*D) referred to the hydrogen atoms in position 2 and 3. According to this interpretation only two signals are present in the ^{13}C NMR spectrum: a triplet centered at 28.670 ppm referred to the –CHD–group, and a quintet centered at 60.416 ppm referred to -CD_2–group Schemes 8 and 9.



Scheme 7. Fragmentation of radical cation **2a** and **3a**.



Scheme 8. Suggested synthesis of catalytic specie (CP_3:$MeC(CH_2PPh_2)_3$;P:PPh_2).



Scheme 9. Suggested catalytic cycle for carboxylic acid (R′ = H) or ester (R′ = alkyl) reduction.

2.8. Role of the catalyst

As expected the catalyst is formed in the reaction conditions from the reaction of $Ru(acac)_3$ with triphos ligand. The complex $Ru(triphos)(acac)_2$ is initially formed that reacts with hydrogen, giving an hydride, as suggested by Tenuissen et al. [14] The hydride reacts with the alcohol as solvent giving a solvento species as reported by Bakhmutov and co-workers [15] for fluorinated alcohols. This solvento species may interacts and subsequently reacts with the acid substrate giving the addition of the Ru–H moiety to the CO group. The absence of an alcohol as solvent renders more hard the formation of this complex and hence the catalyst shows a lower activity.

This specie reacting with hydrogen gives a hydrated form of the aldehyde (R′=H) or an emiacetal ($R'=CH_3$). According with those reported by Tenuissen the hydride reacts with an acid or an ester through the carbonyl group of the RCOOR′ (R′: H, CH_3) moiety giving an emiacetal that is decomposed to the aldehydic group (RCHO) and water or an alcohol (R′ = H, CH_3).

This hypothesis is supported by the reduction of the acid in an alcoholic solvent. Using THF in fact the formation of alcohol is almost suppressed.

The data reported on the deuteration of dicarboxylic acid and GBL confirm, furthermore that the reaction takes place through direct insertion of deuterium on the C=O double bond and exclude the deuteration of the enolic form of the carboxylic acids or lactone.

3. Conclusions

The hydrogenation of fumaric acid, succinic acid or GBL to the corresponding 1,4-diols with a homogeneous catalyst in relatively mild conditions was carried out with high yield and selectivity. The catalytic system $[Ru(acac)_3]$/triphos, used in this work, had never been tested before in the hydrogenation of non-activated dicarboxylic acids such as those containing more than two carbon atoms among the carboxylic groups, that generally are hardly reduced. Furthermore the use of a friendly solvent instead of more sophisticated fluorinated solvents is achieved.

As an extension of this reaction the "one-pot" deuteration of fumaric acid in deuterated solvent was realized affording a convenient route to isotopomeric 1,4-BD-d_8.

A mechanism is reported to support the data obtained such as the position of deuterium in the isotopomeric alcohols and the role of methanol as solvent.

4. Experimental section

4.1. General remarks

All manipulations were carried out according to standard Schlenk techniques in a dried nitrogen atmosphere.

4.2. Materials

The methanol (Carlo Erba) was dried according to standard procedures [16] and stored under nitrogen. The THF (Aldrich) was dried by refluxing over $LiAlH_4$ under nitrogen atmosphere, distilled (b.p. 65 °C) and stored under nitrogen. The GBL (Merck) was distilled (b.p. 205 °C) and stored under nitrogen. Commercial fumaric and succinic acid (Carlo Erba) were used as supplied. $Ru(acac)_3$ was prepared according to Braca et al. [17]. Triphos $[MeC(CH_2PPh_2)_3]$ (Aldrich) was used as supplied. CD_3OD, (tetradeuteromethanol from Aldrich, isotopic purity 99.8% D, content of water 0.0025%) was used as supplied. Deuterium was supplied by Rivoira (99.8% purity).

4.3. Instruments

Gas chromatographic analyses were carried out using a Shimadzu GC-2010 instrument equipped with a SPB™-5 capillary column (length 60 m, internal diameter 0.25 mm, film thickness 0.25 μm) and a FID detector. Injector and detector temperature were set at 280 °C. After injection, the temperature of the GC was raised from 60 to 125 °C at 15 °C/min, then from 125 to 130 °C at 2.5 °C/min. The temperature was kept at 130 °C for 3 min, then the column was heated at a rate of 15 °C/min to the final temperature of 250 °C at which was kept for 3 min.

Mass spectrometric analyses, were used to verify the identity and the isotopomeric purity of the products. They were performed on a GC–MS Shimadzu QP 5050 using a Supelco Equity-5 column, having 0.25 mm internal diameter, length 30 m and 0.25 μm film thickness. The injector temperature was 200 °C and detector temperature was 280 °C. The oven temperature was initially held at 40 °C for 5 min, then raised at 15 °C/min up to 280 °C, and finally kept at this temperature for 15 min.

Multinuclear NMR spectra were registered using a Varian Mercury 400 spectrometer operating at 399.919 MHz for ^1H and 100.570 MHz for ^{13}C. Residual hydrogen of the solvent or the ^{13}C signal of the solvent was employed as reference.

4.3.1. Catalytic reactions: general procedure

Homogeneous catalytic hydrogenations of fumaric acid, succinic acid and GBL were carried out in a 150 ml stainless steel Parr autoclave electrically thermostated (±1 °C). Zinc powder was introduced directly into the autoclave. The vessel was closed and the air evacuated. A solution of $Ru(acac)_3$, triphos, substrate and solvent

were prepared in a Schlenk tube under nitrogen atmosphere, and transferred into the autoclave by suction. The autoclave was pressurized at room temperature with hydrogen, then stirred and heated at the prefixed temperature for the established time. At the end of the reaction the autoclave was rapidly cooled to room temperature, the gas vented and the solution collected and transferred into a 50 ml Schlenk tube. A sample of the solution was taken for the MS and GC analyses. Each test was repeated three times, the mean value was reported.

4.3.2. Preparation of 1,4-BD from fumaric or succinic acid

About 0.303 mg of Zn (4.6×10^{-3} mmol) was placed in the autoclave, then the vessel was closed, and air was evacuated. 206.0 mg (1.77 mmol) of fumaric acid or 209.0 mg (1.77 mmol) of succinic acid, 8.338 mg (2.09×10^{-2} mmol) of $Ru(acac)_3$, 17.95 mg (0.029 mmol) of triphos were dissolved at room temperature in 12 ml of solvent (CH_3OH or THF) in a Schlenk tube. The mixture was introduced in the autoclave by suction, then the vessel was pressurized with hydrogen at 80 bar. The mixture was stirred at the settled temperature for the prefixed time. At the end of the reaction the autoclave was rapidly cooled, the gas vented out and the crude analyzed by GC and GC–MS techniques.

4.3.3. Preparation of 1,4-BD from GBL

About 0.303 mg of Zn (4.6×10^{-3} mmol) was placed in the autoclave, then the autoclave was closed, and air was evacuated from the vessel. And 140 μl (1.77 mmol) of GBL, 8.575 mg (2.15×10^{-2} mmol) of $Ru(acac)_3$, 18.16 mg (0.029 mmol) of triphos were dissolved at room temperature in 12 ml of solvent (CH_3OH or THF). The mixture was introduced in the autoclave by suction, then the vessel was pressurized with hydrogen at 80 bar. The mixture was stirred at the settled temperature for the prefixed time. Afterwards the autoclave was rapidly cooled, the gas vented out and the crude analyzed by GC and GC–MS techniques.

4.3.4. Preparation of 1,4-BD-d_8

The amount of reactants and the operating procedure were the same for the hydrogenation of fumaric acid: 206.0 mg (1.77 mmol) of fumaric acid, 8.338 mg (2.09×10^{-2} mmol) of $Ru(acac)_3$, 17.95 mg (0.029 mmol) of $MeC(CH_2PPh_2)_3$, 0.303 mg (4.6×10^{-3} mmol) of Zn and 12 ml of CD_3OD. The reaction was carried out for 72 h under a D_2 pressure of 80 bar, and the resulting solution was analyzed by GC, GC–MS, ^1H and ^{13}C NMR techniques.

^1H NMR (400 MHz, (CD_3OD)), δ: 1.541 ppm (singlet, 2H, –C*H*D–).

^{13}C NMR (400 MHz, (CD_3OD)), δ: 60.416 ppm (quintet, –*C*D_2–, ^1J: 21.43 Hz), 28.670 ppm (triplet, –*C*HD–, ^1J: 19.11 Hz).

MS: The MS spectrum of 1,4-BD-d_8 is reported in Fig. 1, showing: $[CD_2CDCHD]^{+\cdot}$ as base peak at 46 *m*/*z*. Interpretation of the other peaks present is reported in the text.

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