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A SELECTIVE REDUCTION OF α,β-UNSATURATED KETONES

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ABSTRACT: A selective hydrogenation of carbon-carbon double bond of α,β–unsaturated ketones are obtained when a mixture of limonene, α,β-unsaturated ketone and 10% Pd/C is refluxed with vigorous stirring for 15-45 min. The best results are obtained when a molar ratio limonene:α,β-unsaturated ketone of 3:1 and 4 molar % palladium/ketone are used. The stereoselectivity is similar to the results obtained when H_2 and Pd/C have been used in neutral solvent.
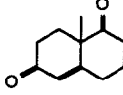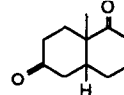
Selective hydrogenation of carbon-carbon double bond of α,β-unsaturated ketones has been for a long time a challenging problem[1-5]. Although several methods are available[6], they require special apparatus and hydrogen (potentially explosive), the synthesis and handling of hydride complexes[3], long reaction time[6-8] or give low yields[6,9]. However it has been reported that the carbon-carbon double bond of enones with extended conjugation (Ph-C=C-C=O) can be selectively hydrogenated with Pd/C using limonene as the hydrogen source[10], whose efficiency in the Catalytic Transfer Hydrogenation (CTH) is known[10-18]. We have modified and extended this method for a series of α,β-unsaturated ketones without extended conjugation, which may have different adsorption on the catalyst.

In a typical experiment limonene, 10% Pd/C and the α,β-unsaturated ketone are heated at reflux temperature. The best results are obtained when a molar ratio limonene:α,β-unsaturated ketone of 3:1 and 4 molar % palladium/ketone are used. These reaction conditions and the reaction time differ significantly from those reported by Kindler and Lührs[10]. They have used molar ratio limonene:α,β-unsaturated ketone of 15:1 and 7,5 molar % palladium/ketone employing xylol as a solvent for 1-2h. Typical results are present in the table 1.

The results observed with the ketones **5** and **7** presumably were a consequence, respectively, of a strong interaction between the ketone **5** and the catalyst resulting in the blocking of its active sites not permitting hydrogen transfer from limonene to enone and, in contrast,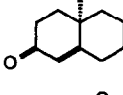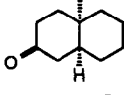 the difficult of interaction between the ketone **7** and catalyst that favors the disproportionation of the terpene[19].

In the reduction of isophorone (**9**) we obtained 80% of conversion with 100% of selectivity in saturated ketone when we used 10% Pd/C as catalyst. In this case the disproportionation of limonene was complete in 20

Table 1: Selective Reduction of α,β-Unsaturated Ketones[a]

no.	Ketone[22]	Reflux (min)	Yield (%)	Product	Selectivity (%)
1	$(CH_3)_2C=CHCOCH_3$	45	100	$(CH_3)_2CHCH_2COCH_3$	100
2	$CH_3CH=CHCOCH_3$	15	100	$CH_3CH_2CH_2COCH_3$	100
3	$C_4H_9CH=CHCOCH_3$	15	100	$C_4H_9CH_2CH_2COCH_3$	100
4	$CH_3CH=CHCOC_2H_5$	15	100	$CH_3CH_2CH_2COC_2H_5$	100
5	$CH_2=CHCOCH_3$	15	-	-	_19
6		30	100		100
7		30	-	-	_19
8		30	100		100
9		30	100		80(100)
10		30	100		100[23]
11		30	100		60[24]
12		30	100		70[24]
13		30	100		83[20]
14		30	100		96[20]

[a] Results of CTH obtained in analysis by CG/MS System
(some isolated products were characterized by nmr).

min of reflux. Extending the reaction time was inefficient as the p-menthanes and p-cymene that formed[16] were not good hydrogen donors. Using 10% Pd/BaSO$_4$ this conversion was 100% with the same selectivity. The presence of p-menthenes and some limonene was still observed in this reaction mixture after 20 min at reflux while the reduction of enone was 70%.

These results show the competition between the disproportionation of limonene and the transfer of hydrogen to acceptor, which is dependent on its adsorption on the catalyst.

The excellent stereoselectivity in favor of the *cis* isomer in the reduction of (S)-(-)-verbenone (10), (R)-(-)-10-methyl-1(9)-octal-2-one (13) and 9-methyl-5(10)-octalin-1,6-dione (14)[20] is similar to the results obtained when H$_2$ and Pd/C have been used in neutral solvent. However, mechanistic models to explain the results from the classical catalytic hydrogenation[21] cannot be indiscriminately applied to the hydrogenation which occurs by hydrogen transfer from an hydroaromatic molecule. This can be explained by the fact that this process is not a simple alternative source for hydrogen generation which in the presence of a catalyst would operate as in the classical hydrogenation. This statement is based on the observation that is necessary the simultaneous adsorption of both the acceptor (α,β-unsaturated ketone) and the donor (terpene) on the catalyst and that a competition occurs between the disproportionation of donor and the hydrogen transfer to the acceptor.

On the other hand, application of the mechanistic model formulated by Carrà to explain the cyclohexene disproportionation[25] seems to be more appropriate. In this case, hydrogen would be transferred from the donor to the enone (both adsorbed on the catalyst) on the opposite side in relation to the catalyst.

It is important to note that no allylic and/or saturated alcohols have been detected even when the reaction time was 24h. Moreover was not observed polymerization reaction. The catalyst can be recovered and re-used several times without any significant decrease in the selectivity and conversion of the enones.

Besides efficiency, simplicity, short reaction time, the use of a commercially available catalyst and no requirement of an acid or basic medium, this method presents safe and easy handling in selective reduction of carbon-carbon double bond of α,β-unsaturated acyclic and cyclic (ring with five or six members) ketones, broadening the perspectives cited by Kindler *et al* for the selective reduction of enones with extended conjugation[10] . Therefore this is a simple and useful alternative to selective reduction of carbon-carbon double bond of α,β-unsaturated ketones.

EXPERIMENTAL SECTION

All chemicals were purchased from commercial sources used without further purification, except for 3-penten-2-one (1), mesityl oxide (5) and isophorone (9), which were distilled prior the use. Mass spectra were obtained using GC/MS with electron impact ionization of 70eV and Carbowax 20M capillary column (50 x 0.25 x 0.3μm). ^{1}H NMR data were recorded at 200 MHz in $CDCl_3$ solvent with Me_4Si as internal standard. IR spectra were obtained from neat films between salt plates or from KBr pellets. Preparative thin-layers chromatography (PTLC) was performed on 20 x 20cm glass plates coated with a 1-2mm of Merck silica gel 60 F_{254}, using diethyl ether/hexane (1:1) as eluent.

General Procedure for the Catalytic Hydrogenation Transfer. In a three necked round-bottom flask equipped with a rubber septum, a reflux condenser and a thermometer, were introduced 3 mmol of α,β-unsaturated ketone, 9 mmol of limonene and 0.139 g of 10% Pd/C (0.12 mmol of Pd). The mixture was refluxed in an oil bath with vigorous magnetic stirring for 15-45 min. The reaction was monitored by gas chromatography (GLC) on GC-MS system for identification of products by comparison between their fragmentations and those of standard samples.

Reduction of mesityl oxide (5). 9.8g (100 mmol); 40.8g (300 mmol); 4.63g; 45min. After filtration to remove the catalyst, the product was isolated by fractional distillation 8.3 g (85%). The IR and ^{1}H NMR spectra of the product were identical to that of an authentic sample of methyl isobutyl ketone and with data reported in the literature[7].

Reduction of isophorone (9). The product was isolated by PTLC and confirmed by IR (film) 1710cm^{-1} ; ^{1}H NMR δ 0.80 (s, 3H); 1.00 (s,3H); 1.10-1.30 (m, 2H); 1.40-1.60 (m, 1H); 1.76-2.22 (m, 4H); MS m/z (relative intensity) 41 (31); 42 (11); 43 (6); 52 (11); 53 (60); 54 (18); 55 (34); 56 (29); 69 (46); 83 (M$^+$ 100); 125 (10); 140 (18).

Reduction of (S)-(-)-verbenone (10). After filtration to remove the catalyst, the product was isolated in 84% yield by silica gel chromatography using hexane/ethyl acetate (9:1) as eluent, and confirmed by IR (film) 1705 cm^{-1}, ^{1}H NMR δ 0.95 (s, 3H); 1.11 (d, J=7.5 Hz, 3H); 1.28 (s, 3H); 1.35 (d, J=10.4 Hz, 1H); 2.05-2.15 (m, 2H); 2.20-2.49 (m, 1H); 2.49-2.60 (m, 2H); 2.81 (dd, J=19.8 Hz, J=10.8 Hz, 1H); ^{13}C NMR δ 57.9 (C_1); 214.3 (C_2); 41.3 (C_3); 31.0 (C_4); 47.3 (C_5); 40.1 (C_6); 28.3 (C_7); 26.9 (C_8); 24.5 (C_9); 20.9 (C_{10}); MS m/z (relative intensity) 41 (18); 42 (3); 53 (7); 55 (38); 67 (22); 68 (8); 69 (15); 81 (16); 82 (17); 83 (M$^+$ 100); 95 (51); 109 (29); 119 (15); 137 (10); 152 (10).

Reduction of (R)-(-)-10-methyl-1(9)-octal-2-one (13). 0.30 g (1.83 mmol); 0.74g (5.45 mmol); 0.08 g. The product (0.24 g; 80% yield) was isolated in a manner similar to that outlined above for **10**. The ^{13}C NMR spectra of the major product (83%) was identical to that data reported in the literature[26] to the cis-10-methyl-decalone: δ 44.1 (C_1); 212.5 (C_2); 37.7 (C_3); 33.1 (C_4); 37.0 (C_5); 21.5 (C_6); 24.9 (C_7); 28.8 (C_8); 43.9 (C_9); 32.5 (C_{10}); 27.2 (C_{11}). ^{1}H NMR: δ 1.21 (s, 3H).

Reduction of 9-methyl-5(10)-octalin-1,6-dione (14). 0.30 g (1.68 mmol); 0.69 g (5.46 mmol); 0.07 g. The product (0.26 g; 85% yield) was isolated using a similar procedure to that described for **10**. The ^{13}C NMR spectra of the product was identical to that data reported in the literature[26] to the cis 9-methyl-decalin-1,6-dione: δ 211.0 (C_1); 38.3 (C_2); 23.8 (C_3); 26.5 (C_4); 43.6 (C_5); 214.0 (C_6); 37.4 (C_7); 33.6 (C_8); 48.4 (C_9); 45.9 (C_{10}); 22.8 (C_{11}). ^{1}H NMR: δ 1.32 (s, 3H).

General Procedure for the Catalytic Hydrogenation with H$_2$. A mixture of 3.00 mmol of unsaturated ketone, 9.00 mmol of p-cymene as solvent and 0.12 mmol of Pd (10% Pd/C), was hydrogenated at 200°C under 1 atmosphere of hydrogen. After 50 min, the catalyst was filtered and the product isolated and characterized by ^{1}H and ^{13}C NMR spectra.

Reduction of (S)-(-)-verbenone (10). 0.50 g (3.33 mmol); 1.35 g (9.99 mmol; 0.14 g. The product was isolated in a manner similar to that used for **10** in Catalytic Hydrogenation Transfer. The ^{1}H and ^{13}C NMR spectra of the product was identical to that obtained in the Catalytic Hydrogenation Transfer of **10**.

Reduction of 9-methyl-5(10)-octalin-1,6-dione (14). 0.50 g (2.80 mmol), 1.44 g (8.42 mmol), 0.12 g. The product was isolated in the manner described for the Catalytic Hydrogenation Transfer of **10**. The ^{1}H and ^{13}C NMR spectra of the product was identical to that obtained in the Catalytic Hydrogenation Transfer of **14**.

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19. We observed the formation of Δ^1-p-menthene and Δ^3-p-menthene during the disproportionation of limonene.The final products are p-menthanes and p-cymene like observed by Brieger[16]. No disproportionation of limonene was observed with the ketone 5. On the other hand, this process was complete with the ketone 7.

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23. We did not detect opening of four membered ring.

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