

Homogeneous hydrogenations of α , β -unsaturated compounds using pentacyanocobaltate (II) anion as catalyst system

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Abstract. Hydrogenation of some α , β -unsaturated carbonyl compounds using potassium pentacyanocobaltate (II), $K_3Co(CN)_5$, as a homogeneous catalyst has been investigated. Thus, hydrogenation of 1-carvone (I), mesityl oxide (4), 2-cyclohexenone (8) and benzalacetone (6) afforded the corresponding dihydrocompounds. Hydrogenation of β -ionone (10) afforded a mixture of the α , β -dihydrocompounds (14) and (15). In all these cases, it was observed that the reaction proceeded to completion only in the presence of added base. Hydrogenation of 5 α -androst-1-en-17 β -ol-3-one acetate (19) afforded the saturated compound, 5 α -androst-17 β -ol-3-one (20) in 60% yield. It was found that other steroid enones and dienones were not reduced by this catalyst system.

Keywords. Homogeneous hydrogenation; pentacyanocobaltate (II); α , β -unsaturated ketones.

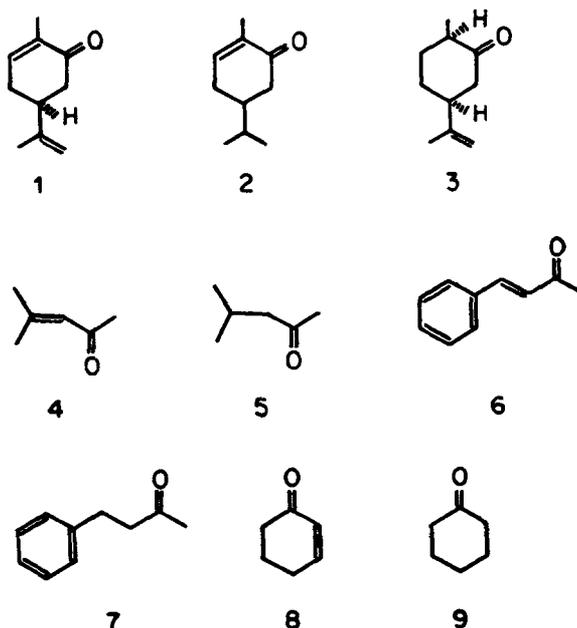
1. Introduction

Various homogeneous catalytic systems have been employed to hydrogenate α , β -unsaturated carbonyl compounds (Birch and Williamson 1976). In some of these cases, the carbonyl group along with the double bond is also reduced whereas in others high pressures are required for hydrogenation. Among the catalysts that have been successfully used in hydrogenating only the olefin part of the substrates are the hydroformylation catalyst dicobaltoctacarbonyl, $Co_2(CO)_8$; the Wilkinson's catalyst, $(Ph_3P)_3 RhCl$; and the pentacyanocobaltate (II), $K_3Co(CN)_5$ systems. In a more limited sense, the systems $(Ph_3P)_2PtCl_2/SnCl_2$ and $RuCl_2(Ph_3P)_3$ have also been used.

Owing to the facility with which the pentacyanocobaltate (II), $K_3Co(CN)_5$, species reacts with hydrogen to form a hydrido complex, this system has been used in the catalytic homogeneous hydrogenation of various organic substrates (Kwiatek *et al* 1963; Kwiatek 1967; Kwiatek 1968; Jackmann 1968). This catalyst hydrogenates a wide range of organic compounds with a fair amount of selectivity. Although the hydrogenations using this catalyst of double bonds activated by conjugation to olefins, aromatic systems, and carboxylic acids are known, detailed studies on the hydrogenation of α , β -unsaturated ketones and its suitability in organic synthesis are lacking. We describe briefly the results obtained on the hydrogenation of some unsaturated ketones using the pentacyanocobaltate (II) catalyst.

2. Results and discussion

Reduction of 1-carvone (1) using this catalyst in the absence of base (see experimental) gave only 50% of the dihydracarvone (3). However, over the same period of time, the reduction proceeded much more efficiently in the presence of base, and gave dihydrocarvone (3) in more than 90% yield. The identity of the compound was established from its spectral data, optical rotation and the melting point of the semi-carbazone derivate. It is interesting to note that the reduction of 1-carvone (1) using tris(triphenylphosphine)chlororhodium as the homogeneous catalyst system leads exclusively to carvotenacetone (2) in which the isolated double bond is selectively reduced (Birch 1966).



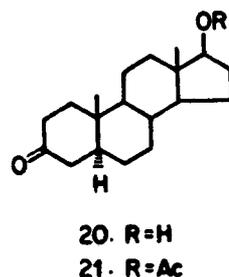
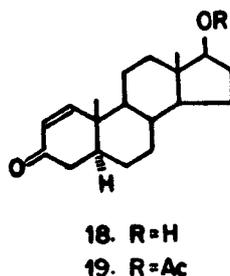
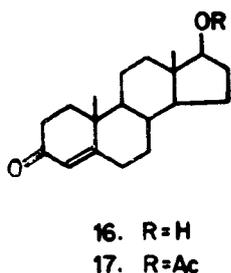
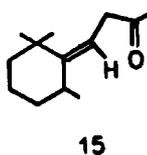
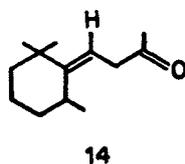
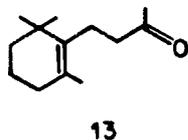
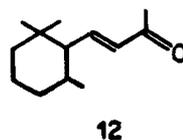
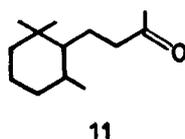
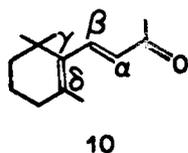
The hydrogenation of mesityl oxide (4) in the presence of base proceeded to near completion and afforded 4-methyl pentan-2-one (5) in good yield. As observed in the case of 1-carvone (1) and mesityl oxide (4), the reduction of benzalacetone (6) and 2-cyclohexenone (8) was found to go to completion only in the presence of added base, to give 4-phenylbutan-2-one (7) and cyclohexanone (9) respectively in excellent yield.

Surprisingly, it was observed that the reduction of 3, 5-dimethyl cyclohex-2-enone, both in the presence and absence of base, did not take place and the starting compound was recovered unchanged.

Hydrogenation of β -ionone (10) was expected to give the tetrahydroderivative (11) or the dihydrocompounds (12) or (13). Hydrogenation of β -ionone in the absence of base was incomplete and the spectral data of the product obtained showed the presence of starting material. However, when the hydrogenation was carried out in the presence of added base with CN/CO ratio of 5, the reaction proceeded to completion. The IR spectrum of the product showed a strong absorption at 1705 cm^{-1} due to the saturated C=O group and a weak absorption at 1670 cm^{-1} attrib-

able to a double bond. The p.m.r. spectrum showed a one proton intense triplet at δ 5.52 ($J=8$ Hz) indicating the presence of an olefinic proton coupled to the adjacent methylene protons.

In the high field region a quartet at δ 3.1 ($J=8$ Hz, $J=2$ Hz) corresponding to two protons was present. This can be assigned to the two methylene protons flanked by the keto group and the double bond having a hydrogen. Besides these, a sharp singlet at δ , 2.15 due to the ketomethyl group, a six proton intense singlet at 1.2 assignable to a gem-dimethyl group and a doublet (3H, $J=6$ Hz) centered at 1.22 showing the presence of a methyl group coupled to a tertiary proton were also present. All these spectral characteristics are in agreement with the dihydro- β -ionone structure (14). The small coupling ($J=2$ Hz) observed for the ketomethylene group can arise from the homoallylic coupling of this proton with the tertiary proton δ to the C=O group. The p.m.r. spectrum of the product also showed a singlet at δ 1.1 and a broad doublet at δ 3.45, the relative intensities of these two peaks being in the ratio of 1 : 3. As these peaks did not disappear even after purification of the product by preparative thin layer chromatography, they have been assumed to be due to the ketomethylene and gem dimethyl group of a possible geometrical isomer (15) of the dihydro- β -ionone (14) discussed earlier. The relative intensities of these signals were in the ratio of 1 : 6 indicating that the two compounds (14) and (15) were present in that ratio in the product.



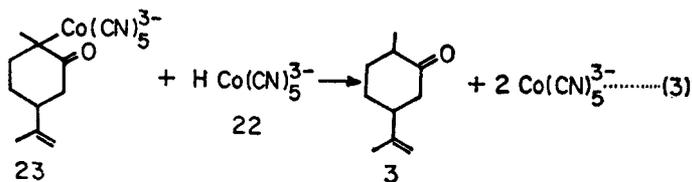
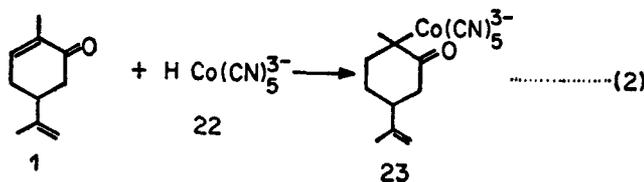
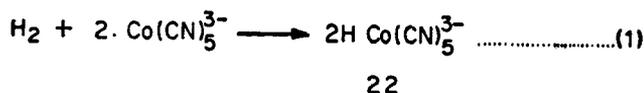
In order to gauge the utility of pentacyanocobaltate (II) in the catalytic hydrogenation of some steroid systems, the reduction of some steroidal enones and the dienones was investigated. Reduction of testosterone and its acetate (16) and (17) was

attempted. No hydrogenation was observed in either case. It was suspected that these compounds failed to get hydrogenated due to their insolubility and hence the reaction was carried out in aqueous ethanol and other solvent systems. However, both the compounds were recovered unchanged even under these conditions.

The hydrogenation of a less sterically hindered system viz., 5 α -androst-1-en-17 β -ol-3-one (19) was attempted. Although this failed in water-benzene system, hydrogenation proceeded smoothly in aqueous ethanol medium to give a mixture of 5 α -androst-17 β -ol-3-one (20) and 5 α -androst-1-en-17 β -ol-3-one (18). The two compounds were separated and characterised as their acetates. The identity of the compounds was established from their spectral data and comparison with authentic sample.

The hydrogenation of androst-1,4-diene-3,17-dione and androst-1,4-diene-17 α -methyl-17 β -ol-3-one were attempted using both benzene and ethanol as cosolvents. It was anticipated that the Δ^1 double bond would undergo reduction while the more sterically hindered Δ^4 -bond would remain unaffected. However, the starting dienones were recovered unchanged.

It is clear from the above that the cyclic α , β unsaturated ketones with or without an α -substituent are smoothly hydrogenated with this reagent whereas the β -substituted compounds are not affected. Further the presence of base facilitates the reduction. These results can be explained based on the mechanism described for 1-carvone (1) as depicted in chart 1.



Several mechanisms were advanced for the hydrogenation of conjugated dienes and carbonyl compounds with pentacyano cobaltate (II) (Kwiatek 1967). But the apparent inhibition of the β -substituted compounds, other than mesityl oxide, towards hydrogenation with this reagent gains support to the mechanism depicted in chart 1. This inhibition of the β -substituted compounds towards hydrogenation may be due to the steric factor which prevents the approach of the bulky hydrido pentacyano-

cobalt species (22) towards the substrate. Mesityl oxide, being an acyclic unsaturated ketone is not rigid and hence hydrogenation can take place.

The hydrogenation of β -ionone (10) deserves comment. Although it is a cyclic α , β , γ , δ -unsaturated ketone having a δ -substituent, it affords a mixture of the two isomers (14) and (15) on hydrogenation. The formation of these compounds may be envisaged as the initial hydrogenation of the α , β -double bond of β -ionone and subsequent isomerisation of the resulting compound (12) to the final product under the reaction conditions. Thus, equilibration of the double bond of the dihydro- β -ionone (12) results in the formation of a mixture of the (E) and (Z) isomers, (14) and (15) respectively, as observed.

Cross conjugated dienones could not be hydrogenated with this reagent. This may probably be due to the formation of a stable π -complex between the reagent and the substrate (six electron system) which prevents hydrogen transfer. However, a complex of this type could not be isolated.

3. Conclusions

Cyclic α , β -unsaturated ketones with or without an α -substituent are readily hydrogenated to the corresponding dihydrocompounds in the presence of pentacyanocobaltate (II) under homogeneous conditions. Substitution at the β -position in the cyclic compounds hinders hydrogenation. Mesityl oxide and β -ionone are also hydrogenated.

3.1. Experimental

All melting points and boiling points reported are uncorrected. The IR spectra were recorded on a Perkin-Elmer Model 700 spectrometer and the p.m.r. spectra on a Varian HA-100D or T-60 spectrometer. Chemical shifts are quoted relative to tetramethylsilane (TMS) as internal standard.

4.1. General procedure for hydrogenation of unsaturated compounds using potassium pentacyanocobaltate (II)

The procedure followed for hydrogenation of substrates using potassium pentacyanocobaltate (II) was essentially that described by Kwiatek 1967.

The reaction vessel consists of a three-necked flask (500 ml) equipped with a pressure equalizing funnel (100 ml). It was connected to the hydrogenator through its middle neck. The third neck was tightly closed using a septum cap. The hydrogenation was carried out at room temperature (25° to 30°C) under a slight positive hydrogen pressure. Three different procedures were followed to carry out the hydrogenation.

4.2. Method A

To a solution of cobaltous chloride (7.1 g) in water (100 ml) taken in the three-necked flask, a solution of potassium cyanide (10.1 g) in water (100 ml) was added under an

atmosphere of hydrogen with stirring using a magnetic stirrer. A pale pink precipitate of cobalt cyanide first appears which dissolves in excess of the cyanide to give an olive green solution of pentacyanocobaltate (II). The solution was stirred until hydrogen absorption stopped. The colour of the solution changed from olive green to pale yellow. The organic substrate (ca. 1 g) (either as the pure compound in the case of a liquid or as a solution in the case of a solid) was then introduced into the reaction flask through the septum cap with a syringe and the mixture stirred for 12 to 18 h. At the end of this period, the reaction mixture was extracted with a suitable organic solvent (ether, benzene or methylene chloride), the combined organic extract was washed with water and dried over anhydrous sodium sulphate. Removal of the solvent afforded the product.

4.3. Method B

A solution of cobaltous chloride (7.1 g) and water (60 ml) was taken in the three-necked flask and treated with a solution of potassium hydroxide (5 g) in water (40 ml). A solution of potassium cyanide (10.1 g) in water (100 ml) was then added in an atmosphere of hydrogen through the dropping funnel with vigorous stirring. The solution was saturated with hydrogen. The organic substrates (1g) was introduced into the reaction vessel through the septum cap using a syringe and the mixture stirred for 12 to 20 h. The resulting mixture was extracted with a suitable solvent. The combined organic extract was washed with water and dried over anhydrous sodium sulfate. Removal of the solvent afforded the product.*

4.4. Method C

To a solution of cobaltous chloride (3.6 g) in water (10 ml) a solution of the substrate (0.5 g) in ethanol (40 ml) was added followed by a solution of potassium hydroxide (2.5 g) in water (5 ml). A solution of potassium cyanide (5.1 g) in water (40 ml) was added to this through the dropping funnel under an atmosphere of hydrogen with vigorous stirring. About 100 ml of hydrogen was absorbed rapidly and the colour of the solution turned to pale yellow. The stirring was continued for 24 h, most of the ethanol was distilled off in vacuum and the residue was extracted with methylene chloride. The combined organic extract was washed with water, dried and the solvent was distilled off to afford the reaction product.

4.5. Hydrogenation of 1-carvone

(i) Hydrogenation of 1-carvone (1) (5.0 g) (Method A) followed by careful fractional distillation of the product afforded dihydrocarvone (3) (2.4 g, 48%), b.p. 212-214°/685 mm (lit. b.p. 220-22°/760 mm); IR (neat): ν_{\max} 1720 (saturated C=O) and 1640 cm^{-1} (C=C); PMR δ (CCl_4): 0.96 (d, $J=6$ Hz, 3H, $\text{CH}-\text{CH}_3$), 1.75 (s, 3H, $=\text{C}.\text{CH}_3$), 2.0-2.5 (m, 8H) and 4.72 (s, 2H, $=\text{CH}_2$); (Found: C, 78.7; H, 10.8 Calculated for $\text{C}_{10}\text{H}_{16}\text{O}$: C, 78.98 and H, 10.53%) Semicarbazone m.p. 188-189° (m.p. 189-190°) (Marshall *et al* 1967).

(ii) Hydrogenation of 1-carvone (I) (5.0 g) (Method B) afforded dihydrocarvone (3) (4.45 g) b.p. 212-214°/685 mm.

*The products obtained from a number of experiments were combined for further purification.

4.6. Hydrogenation of mesityl oxide

(i) Hydrogenation of mesityl oxide (4) (1 g) (Method A) afforded a mixture (0.9 g; 90%) of the starting ketone (4) and 4-methyl pentan-2-one (5). IR (neat): ν_{\max} 1710 and 1670 cm^{-1} .

(ii) Mesityl oxide (5 g) was hydrogenated (Method B) and the resulting product on distillation yielded 4-methyl pentan-2-one (5) (4.5 g, 90%), b.p. 113-115°/680 mm IR (neat): ν_{\max} 1710 cm^{-1} ; PMR: δ (CCl_4): 1.16 [d, $J=6$ Hz, 6H, $\text{HC}(\text{CH}_3)_2$], 1.45=2.0 (m, 3H) and 2.1 (s, 3H, COCH_3) (Found: C, 65.05; H, 10.51, calculated for $\text{C}_6\text{H}_{12}\text{O}$; C, 65.45; H, 10.95%). Semicarbazone m.p. 132° (m.p. 130°, Salkind and Bebukishwili 1909).

4.7. Hydrogenation of benzalacetone (6)

(i) Hydrogenation of benzalacetone (6) (5 g) (Method A) afforded an oil which on distillation gave 4-phenylpentan-2-one (7) (2.9 g, 58%) as a colourless oil, b.p. 225/680 mm. (b.p. 235°/760 mm, Karrer *et al* 1930); IR (neat): ν_{\max} 1700 (sat. $\text{C}=\text{O}$) and 1600 cm^{-1} (aromatic $\text{C}=\text{C}$); PMR δ (CCl_4): 2.14 (s, 3H, $\text{CO}-\text{CH}_3$), 2.82 (2t, 4H, $-\text{CH}_2-\text{CH}_2-$) and 7.2 (s, 5H, aromatic) (Found: C, 65.6; H, 11.00. Calculated for $\text{C}_{10}\text{H}_{12}\text{O}$: C, 65.45 and H, 10.91%). Semicarbazone m.p. 142° (m.p. 142-144°) (Karrer *et al* 1930).

(ii) Hydrogenation of benzalacetone (6) (5 g) (Method B) followed by distillation of the product gave the pentanone (7) (9.2 g, 92%).

4.8. Hydrogenation of 2-cyclohexenone (8)

(i) Hydrogenation of 2-Cyclohexenone (8) (1 g) (Method A) gave a mixture of the unsaturated ketone (8) and cyclohexanone (9) (0.9 g); IR (neat): ν_{\max} 1710 and 1680 cm^{-1} .

(ii) Hydrogenation of 2-cyclohexenone (8) (5 g) (Method B) yielded cyclohexanone (4.4 g, 88%). Semicarbazone prepared in the usual way had a m.p. 165° and was identified with an authentic sample.

4.9. Hydrogenation of β -ionone (10)

Hydrogenation of β -ionone (10) (1g) (Method B) followed by short path distillation of this product afforded 4-(2', 6', 6'-trimethylcyclohexylenyl) butan-2-one (14) (0.91 g) as a mobile colourless liquid b.p. 75-80°/2mm (lit. b.p. 136°/18mm) IR (neat); ν_{\max} 1700 (saturated $\text{C}=\text{O}$) and 1670 cm^{-1} ($\text{C}=\text{C}$): PMR δ (CCl_4): 1.1 (d, $J=6$ Hz, 3H, $\text{CH}-\text{CH}_3$) 1.2 [s, 6H, $\text{C}(\text{CH}_3)_2$] 1.2-1.64 (m, 6H) 2.15 (s, 3H, COCH_3); 3.1 (dd, $J=8$ Hz, 2H, 2H, $=\text{CH}-\text{CH}_2\text{CO}$) and 5.52 (t, $J=8$ Hz, 1H, $=\text{CH}-\text{CH}_2$): 0.92 (s, 1H, $\text{C}(\text{CH}_3)_2$ of 15 and 3.4 [br.d, $J=7$ Hz, 0.4H, $=\text{CH}-\text{CH}_2-\text{C}$ of 15]; (Found: C, 80.09; H, H, 11.23. Calculated for $\text{C}_{13}\text{H}_{22}\text{O}$: C, 80.41 and H, 11.34%).

The 2, 4-dinitrophenylhydrazone prepared in the usual way had m.p. 96° (m.p. 102°) (Miki and Hara, 1956).

4.10. Hydrogenation of 5 α -Androst-1-en-17 β -ol-3-one acetate

(i) Hydrogenation of the acetate (19) (Method A and B) using benzene as the solvent afforded a solid which was found to be identical with the starting material (m.p. and m.m.p., IR spectra).

(ii) The acetate (19) (500 mg) was hydrogenated following the method C. The product (0.46 g) was treated with acetic anhydride (3 ml) and pyridine (0.5 ml) and left overnight. The reaction mixture was poured into ice-water mixture and warmed over a water bath for 1 h. It was then allowed to cool and the solid separated was filtered, washed with water and dried. Preparative layer chromatography of the solid (EtOAc: Hexane, 1 : 4) afforded dihydrotestosterone acetate (21) (290 mg) ($R_f=0.6$) identical with an authentic sample (m.p. and m.m.p. 158-159°); (m.p. 158°) (Ruzicka and Goldberg 1936), IR(nujol): ν_{\max} 1730 (OCOCH₃) and 1705 cm⁻¹ (saturated C=O); PMR δ (CDCl₃): 0.80 (s, 3H, C-18-CH₃), 1.03 (s, 3H, C-19-CH₃), 1.03-2.5 (m, methylene and methine protons), and 2.05 (s, CH, OCOCH₃) and 4.62 (t, J=7 Hz, CHOCOCH₃); and the starting material (19) ($R_f=0.5$) identical with the authentic sample in all respects. (m.p. and m.m.p. 126°), (m.p. 122°, Butenandt and Dannenberg, 1940); IR (nujol): ν_{\max} 1740 (OCOCH₃) and 1680 cm⁻¹ (conjugated C=O).

Acknowledgements

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