CATALYTIC HYDROGENATION OF ETHYL α-ACETYLAMINO-β-KETOBUTYRATE ON MODIFIED METAL CATALYSTS

I. P. Murina, A. A. Vedenyapin,
and E. I. Klabunovskii

UDC 542.941.7:547.466

We have recently shown that on hydrogenation of the threonine precursor ethyl α-acetylamino-β-ketobutyrate (I) on a Raney nickel catalyst modified with (RR)-(+)-tartaric acid, the ethyl ester of N-acetyl-allo-threonine (allo-II) can be obtained in 82% yield with 100% selectivity [1]. In the present work we have studied the effect of metal catalysts on the sterically directed pathway for this process.

EXPERIMENTAL

PMR spectra were recorded on a Bruker WM-256 instrument (internal standard TMS), IR spectra were recorded on a Specord UV-VIS instrument, and spectropolarimetric analysis was performed using a Spectropol-1 instrument. GLC analysis of the catalysts was carried out on a LKhM-8MD instrument with flame ionization detector [glass column of length 2.5 m, Chromatone N-AW-DMCS (0.16-0.20 mm) treated with 5% silicone SE-30], 140°C, nitrogen carrier gas (30 cm^3/min), ethyl ester of N,O-diacetyl-L-threonine used as internal standard. The initial substrate was characterized in [1].

Catalysts. Skeletal Cu—Pd (SCPC) and Pd (SPC) catalysts were prepared by leaching Pd—Cu—Al and Pd—Al alloys with a 10% aqueous solution of NaOH at 50°C as in [2]. SCPC contained 15.1 at.% Pd. For preparation of supported Ni—Pd/Al_2O_3 (NPC), Cu—Ru/SiO_2 (CRC), and Ru/SiO_2 (RC) catalysts, $PdCl_2$, $Ni(NO_3)_2 \cdot 6H_2O$, $CuCl_2 \cdot 2H_2O$, and $RuCl_3$ salts of analytically pure grade were used with γ-Al_2O_3 (Ryazan works) and A-300 Aerosil (Kalush plant) supports. The content of the metal phase in NPC and CRC was 10%. The weight ratios of the metals were: Ni:Pd = 8:2 in NPC, Cu:Ru = 8:2 in CRC-2, and Cu:Ru = 5:5 in CRC-5. The Ru/SiO_2 catalyst contained 0.5 and 5.0 wt.% Ru for RC-0.5 and RC-5 respectively. The supported catalysts were obtained according to [3] and reduced in a current of H_2:N_2 (1:10) at 360°C (NPC) and 450°C (CRC, RC). Before reduction, NPC was calcined in a current of N_2 at 450°C.

Modification of the catalysts, hydrogenation of (I), and separation of the catalysts from the catalyzate were carried out as in [1].

The composition of the products was determined using PMR and GLC. In addition to the intended products (allo-II) [retention time (t) 15.5 min] and the ethyl ester of N-acetylthreonine (threo-II) (t = 15.8 min) in the hydrogenation on CRC and RC (SiO_2 support) two by-products were formed: (III) (t = 5.5-6 min) and (IV) (t = 13 min). In order to identify them the appropriate syntheses were carried out.

threo-2,5-Dimethyl-4-carboethoxy-Δ^2-oxazoline (III) Hydrochloride. This was obtained as in [4] from (allo-II), mp 107°C (from $CHCl_3$). IR spectrum (KBr pellet, ν, cm^{-1}): 1750 C=O, w, ether), 1645 (C=N), 1585, 1530. PMR spectrum ($CDCl_3$, δ, ppm, J, Hz): 1.23 t (3H, CH_3CH_2O, J = 7.0), 1.50 d (3H, C^5—CH_3, $J_{CH_3-H^5}$ = 6.5), 2.05 s (3H, C^2—CH_3), 4.20 q (2H, $CH_3\underline{C}H_2O$, J = 7.0), 4.28 d (1H, C^4—H, $J_{H^4-H^5}$ = 2.5), 5.42 d. q (1H, C^5—H, $J_{H^5-H^4}$ = 2.5, $J_{CH_3-H^5}$ = 6.5), 8.90 br. s (1H, N·HCl). The constants of (III) obtained from standard (allo-2) coincided with those given.

Control Experiment. Compound (I) (1 g, 5 mmole) in 8 ml of EtOH was agitated in a vibrating autoclave for 10-20 h at 75°C and p_{H_2} = 0.5 MPa in the presence of 0.5 g SiO_2 previously treated with a solution of tartaric acid at pH 5.0 and 50°C for 1 h. A yellow oil was obtained, containing 80% (I) and 20% (IV) (t = 10 and 13 min respectively).

The stereoselectivity of the reaction was determined by two methods: 1) by PMR from the intensity ratio of the chemical shifts of the α-protons in (threo-II) (4.53 ppm) and (allo-II)

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow.
Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 5, pp. 999-1001, May, 1988. Original article submitted December 31, 1986.

0568-5230/88/3705-0869$12.50

TABLE 1. Hydrogenation of (I) at 75°C in Ethanol

Catalyst	[Tartaric acid], %	p, MPa	τ, h	Degree of conversion, %	Composition of catalyzate, %			
					(threo-II)	(allo-II)	(III)	(IV)
SCPC	5,0	10,0	23	85	–	85	–	–
SCPC	5,0	7,5	16	90	–	90	–	–
SPC	5,0	7,5	16	80	4	74	–	–
NPC-2	5,0	10,0	18	95	2	93	–	–
NPC-2	5,0	10,0	15	80	10	70	–	–
CRC-2	nil	0,5	9	25	1	2	12	10
CRC-2	0,5	0,5	9	88	4	8	13	63
»	0,5	10,0	9	81	3	5	25	48
»	5,0	10,0	12	65	20	10	21	14
CRC-5	nil	10,0	24	80	10	11	18	41
CRC-5	5,0	10,0	22	90	15	10	22	41
RC-0.5	nil	10,0	9	15	2	3	3	7
RC-0.5	5,0	10,0	9	18	2	4	3	9
RC-5	5,0	10,0	15	93	23	58	11	1
RC-5*	5,0	10,0	15	93	21	53	16	3

*Hydrogenation carried out in CH_3COOH.

(4.60 ppm) in $CDCl_3$, these were assigned in [1]; 2) by GLC after acylation of the catalyzate using $(CH_3CO)_2O$ [1, 5]; standard (threo-II) and (allo-II) (t = 20.0 and 22.8 min respectively) were obtained and characterized in [1].

DISCUSSION

Hydrogenation of (I) to (II) was carried out in EtOH at 75°C and a pressure of 0.5-10 MPa in the presence of the catalysts described above. The results are given in Table 1, from which it can be seen that on skeletal CPC modified with tartaric acid, (I) is hydrogenated as on a Raney nickel catalyst [1] with 100% selectivity to (allo-II) with yields amounting to 85-90%, which is somewhat higher than the case for the Ni catalyst. The increase in yield of the intended product when changing from the Raney Ni catalyst to SCPC may be due to the absence in the latter of by-product oxazoline derivatives (III). The 100% selectivity of hydrogenation on these skeletal catalysts is confirmed by the formation of pure (III) from (allo-II).

On all the other catalysts investigated a mixture of (threo-II) and (allo-II) is formed in different ratios depending on the type of catalyst (Table 1). Moreover, when (I) is hydrogenated on CRC and RC, by-products (III) and (IV) are formed. It may be concluded from the results of the control experiment that (IV) is formed from (I) on the surface of SiO_2. We have not established the structure of (IV) but as (I) has a tendency to undergo aldol-type reactions [6] it may be presumed that (IV) is a product of such a reaction and is a cyclic compound such as diketopiperazine. On the skeletal Pd catalyst and on NPC on Al_2O_3, (allo-II) is mainly formed in high yield, similar to the yields on SCPC, but the stereoselectivity of reaction in this case is somewhat lower because of the formation of (threo-II). Although the degree of conversion of (I) on CRC and RC-5 is high (93%), there is a considerable amount of (IV) in the products in the case of CRC, and the yield of the intended products (allo-II) and (threo-II) $\leq$ 30% (Table 1). In contrast to the other catalysts, on CRC modified with a 5% solution of tartaric acid more (threo-II) than (allo-II) is formed.

Comparison of the hydrogenation of (I) on unmodified and modified catalysts using CRC as a model shows that modification can affect the sterically directed pathway of this process and the yield of the intended product, which has been demonstrated previously [1] for a Ni catalyst. Despite modification of the catalysts with a chiral agent, hydrogenation of (I) does not proceed enantioselectively.

Thus, out of all the catalysts investigated under the conditions of this experiment, the most suitable for the synthesis of (allo-II) are the skeletal copper–palladium and nickel catalysts modified with a 5% solution of tartaric acid at pH 5.0 and 50°C.

CONCLUSIONS

1. We have prepared a skeletal Cu–Pd catalyst modified with tartaric acid, on which there is 100% selectivity in the hydrogenation of ethyl α-acetylamino-β-ketobutyrate with a yield of N-acetyl-allo-threonine ethyl ester of about 90%.

2. It is shown that the nature of the metal phase of the catalysts has an effect on their activity, selectivity, and diastereoselectivity in this process.

LITERATURE CITED

1. A. A. Vedenyapin, I. P. Murina, T. I. Kuznetsova, and E. I. Klabunovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 2584 (1986).
2. A. A. Vedenyapin, T. I. Kuznetsova, E. I. Klabunovskii, et al., Izv. Akad. Nauk SSSR, Ser. Khim., 2206 (1983).
3. T. I. Kuznetsova, A. A. Vedenyapin, and E. I. Klabunovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 1002 (1984).
4. K. Pfister, C. A. Robinson, A. S. Shabica, and M. Tishler, J. Am. Chem. Soc., 71, 1101 (1949).
5. S. V. Shlyapnikov, M. Ya. Karpeiskii, and E. F. Litvin, Biokhimiya, 28, 664 (1963).
6. H. Kawasaki, Nippon Kagaky Zazzi, 78, 1251 (1957); Chem. Abs., 54, 4404e (1960).

STUDY OF THE KINETICS OF THE OXIDATION OF PALLADIUM(II) BY INORGANIC FREE RADICALS IN ACIDIC AQUEOUS SOLUTIONS BY PULSE RADIOLYSIS

A. V. Gogolev, V. P. Shilov,
and A. K. Pikaev

UDC 541.15:541.127:542.943:546.982

It is well known [1] that Pd is formed in a relatively large amount besides other products in the fission of uranium. It is evident that the radiolytic reactions of ions of this metal in aqueous solutions should be taken into account in nuclear fuel reprocessing technology. To predict these reactions it is necessary to know the rate constants for the reactions of these ions with the shortlived products from the radiolysis of aqueous solutions. In this communication the results are presented of studying by pulse radiolysis the reactivity of Pd(II) ions towards the radicals $OH^{\bullet}$, $NO_3^{\bullet}$, and $SO_4^{\bullet -}$ in acidic aqueous solutions.

EXPERIMENTAL

We used a microsecond pulse radiolysis unit based on a U-12 linear accelerator using 5 MeV electron energy (pulse length 2.3 μsec). The doses per pulse, measured by the thiocyanate method [2], were (1 to 3) × 10^{17} eV/g (average radical concentration $\sim 10^{-5}$ M). The optical absorption of the radicals was recorded for the corresponding absorption bands [3]. Solutions of Pd(II) ions were prepared by dissolving a weighed sample of Pd in concentrated HNO_3, followed by double evaporation with chemically pure grade of perchloric acid to the moist salt. The residue was dissolved in 2.5 M $HClO_4$. The initial solution contained 9 mmole/liter $Pd(ClO_4)_2$ in 2.3 M $HClO_4$. The molar extinction coefficient of the $Pd(ClO_4)_2$ solution at 380-390 nm was 83 liter/(mole·cm), which agrees with the data in [4]. To prepare the nitric and sulfuric acid solutions a known amount of chemically pure grade of HNO_3 or H_2SO_4 solution was added to the $Pd(ClO_4)_2$ solution.

DISCUSSION

When an electron pulse acts on nitric acid solutions of Pd(II) optical absorption which belongs to $NO_3^{\bullet}$ and Pd(III) arises in the UV and visible parts of the spectrum. They are formed from the reactions

$$HNO_3(H^+ + NO_3^-) + OH^{\bullet} \rightarrow NO_3^{\bullet} + H_2O \qquad (1)$$

$$Pd(II) + OH^{\bullet} \xrightarrow{H^+} Pd(III) + H_2O \ . \qquad (2)$$

The $NO_3^{\bullet}$ radicals also appear as a result of the direct action of radiation on HNO_3. For wavelengths corresponding to the absorption bands of $NO_3^{\bullet}$ (630 nm) a decrease is observed in the optical absorption to a certain constant value after the end of a pulse (Fig. 1). This is caused by the reaction

---

Institute of Physical Chemistry. Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 5, pp. 1001-1004, May, 1988. Original article submitted April 28, 1987.

0568-5230/88/3705-0871$12.50