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Hydrogenation on Granular Palladium-containing Catalysts: II.* Hydrogenation of Nitroheterocyclic Compounds

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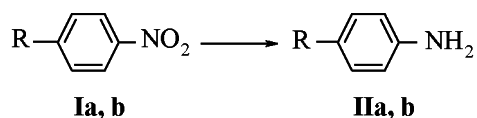
Abstract—Nitroheterocyclic compounds were reduced in a classical reactor with an agitator equipped with a cell for fixed bed of catalyst. As catalysts were applied granular palladium catalysts (0.5% of Pd on γ-Al$_2$O$_3$ and 2% of Pd on granulated carbon). Anilines and 3-amino-2(1H)-pyridones were obtained in high yield at reduction of the appropriate nitro compounds, and the activity of the catalyst samples only slightly decreased. Yet aminopyrazoles and aminoimidazoles obtained by hydrogenation on palladium were very sensitive to the presence of air even as hydrochlorides. In the course of hydrogenation of nitropyrazoles and nitroimidazoles the activity of the catalyst markedly decreased.

We have formerly described [1] a construction of reactor providing a possibility to use in a classical reactor with agitator granular palladium-containing catalysts (GPC), e.g. commercial ShPAK-0.5 (0.5% of Pd on γ-Al$_2$O$_3$), for hydrogenation of alkynes into alkenes. Although hydrogenation of nitro group is comprehensively described in the literature [2, 3], the interest is conserved to performing this process under milder conditions (at room temperature, with no strong acids or alkali). Therefore we undertook investigation of GPC application to hydrogenation of nitro compounds from aromatic and heterocyclic series.

We found that at hydrogenation of nitrobenzenes **Ia, b** in the reactor of the previously described construction [1] (with a fixed bed of GPC and a turbo-type agitator) the rate of hydrogen consumption was 1.5–3 times higher than in a classical rotating autoclave. This difference in rates is apparently due to the considerably more efficient stirring.

The rate of hydrogen consumption depends also on the presence of a solvent. For instance, on diluting the trifluoromethoxynitrobenzene (**Ia**) with methanol (1:1) resulting in decreased viscosity of the reaction medium the hydrogenation rate increased approximate-

ly twice, but further dilution did not accelerate the process.

The repeated use of the catalyst (lifetime) is of great interest. We found that decrease in the catalyst activity significantly depended on the procedure of nitrobenzene charging. When after hydrogenation run the reactor was opened in air, we observed a considerably reduced catalyst activity (procedure A). If the fresh portion of nitrobenzene was charged immediately after the hydrogenation product discharge (procedure B) the catalyst activity was only slightly reduced (Table 1).

The chemical yield changed insignificantly and in both procedures approached 97–95% (according to GLC of the reaction mixture) and after distillation it was 91–89%.

Table 1. Duration of several successive hydrogenation runs on a single portion of catalyst[a]

Run no.	Time, h	
	A	B
1	4	4
2	10	5
3	12	5
4	23	5
5	35	6

Ia, b   **IIa, b**

I, II, R = CF$_3$O (**a**), CF$_2$ClO (**b**).

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* For communication I see [1].

[a] Into the reactor was charged 50 of ShPAK-0.5 and in each run 160 g of compound **Ia**, 200 ml of methanol. The hydrogenation was performed at 44—46°C, 40—42 at.

Table 2. Yields, melting points, and elemental analyses of compounds **IIa, b, IVa–c, VIa, b, VII, IX**

| Compd. no.	Yield, %	mp, °C bp (*p*, mm Hg)	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
IIa	89	65–69 (7)[a]	47.3	3.2	7.6	$C_7H_6F_3NO$	47.46	3.39	7.91
IIb	91	93–95(7)	43.0	3.6	7.1	$C_7H_6ClF_2NO$	43.41	3.10	7.24
IVa	82	125–128 (BuOAc)	54.1	5.7	25.2	$C_5H_6N_2O$	54.54	5.45	25.45
IVb	90	208–209 (DMF)	60.3	7.7	21.1	$C_7H_{10}N_2O$	60.87	7.25	20.29
IVc	75	145–146 (benzene–hexane, 1 : 1)	57.2	6.3	13.7	$C_{10}H_{14}N_2O_3$	57.14	6.67	13.33
VIa	55	111–113 (benzene)	42.8	4.7	29.1	$C_5H_7N_3O_2$	42.55	4.96	29.79
VIb	37	145–147 (benzene)	59.7	4.8	27.0	$C_{10}H_{10}N_4O$	59.41	4.95	27.72
VII	41	232–233 (Ac$_2$O)	45.2	4.6	19.7	$C_8H_9N_3O_4$	45.49	4.26	19.91
IX	63	247–249 (MeOH)	53.3	6.1	23.4	$C_8H_{11}N_3O_2$	53.04	6.08	23.20

[a] 73–75°C (10 mm Hg) [4].

Similarly a hydrogenation was carried out with several 2-hydroxy-3-nitropyridines **IIIa–c**. The pattern of the process was like that of nitrobenzenes **Ia, b** hydrogenation: the hydrogenated products were fairly stable and were obtained in a high yield (75–90%) on evaporating methanol.
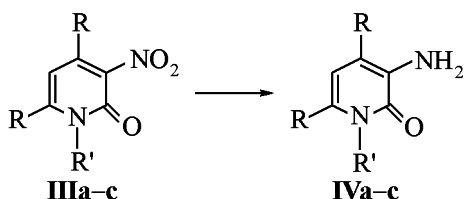
**I, II, R,R′ = H (a), Me, H (b), Me, CH$_2$COOMe (c).**

In going to hydrogenation of nitropyrazoles **Va–c** and nitroimidazole (**VIII**) the products obtained were considerably less stable than amines **IIa, b, IVa–c**. Although 4-aminopyrazoles with electron-withdrawing substituents **VIa, b** were isolated in a pure state,
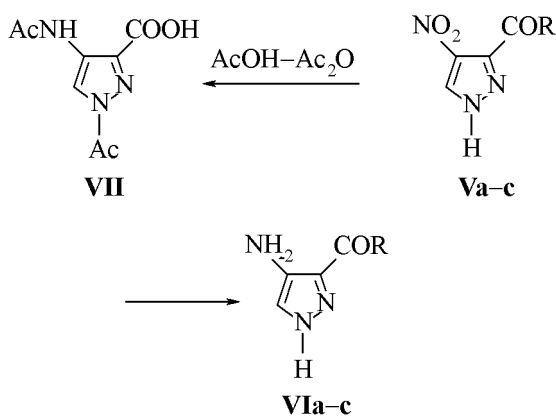
V, VI, R = OMe (**a**), NHPh (**b**), COOH (**c**).

the hydrogenation products of 4-nitropyrazole-3-carboxylic acid (**Vc**) and 4(5)-nitro-2-methylimidazole (**VIII**) we failed to obtain of sufficient purity even when the substances were separated as hydrochlorides (the peaks in the ^{1}H NMR spectra were strongly broadened due to the presence of a paramagnetic compound, presumably, of palladium complexes). At the same time the hydrogenation of pyrazole **Vb** with aluminum amalgam in methanol afforded product **VIb** that was considerably more stable than the same compound prepared by hydrogenation on a palladium catalyst (the product did not turn dark on storage for 2 months).

The hydrogenation of compounds **Vc, VIII** in acetic acid in the presence of acetic anhydride afforded the corresponding acetylated compounds **VII, IX** that turned out to be quite stable.
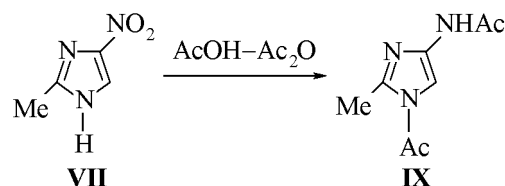
The structure of compounds synthesized was confirmed by ^{1}H NMR and mass spectra and by elemental analyses (Tables 2, 3).

It is commonly assumed that palladium on carbon support shows the maximal activity. Therefore we tested a new granular catalyst, 2% Pd on granulated carbon. This catalyst unexpectedly did nit notably accelerate the hydrogenation: at the same weight of Pd per 1 gram of the compound to be hydrogenated the hydrogenation rate increased only 1.05–1.2 times

Table 3. ^{1}H NMR and mass spectra of compounds **IIa, b, IVa–c, VIa, b, VII, IX**

Compd. no.	δ, ppm (DMSO-d_6)^a	m/z (I_{rel}, %)
IIa	5.0 br.s (2H, NH$_2$) 6.6 d (2H, Ar) 6. 9d (2H, Ar)	–
IIb	3.7 br.s (2H, NH$_2$) 6.65 d (2H, Ar) 7.0 d (2H, Ar)	193 (63) 107 (100) 92 (69) 85 (53) 80 (52)
IVa	4.95 br.s (2H, NH$_2$) 6.0 t (1H, CH^5) 6.4 d (1H, CH^4) 6.6 d (1H, CH^6) 11.2 br.s (1H, NH)	110 (100) 82 (28) 81 (22) 55 (43) 54 (45)
IVb	1.93 s (3H, CH$_3$) 2.04 s (3H, CH$_3$) 4.4 br.s (2H, NH$_2$) 5.7 s (1H, CH^5) 11.26 br.s (1H, NH)	138 (100) 109 (23) 95 (43)
IVc	2.00 s (3H, CH$_3$) 2.18 s (3H, CH$_3$) 3.7 s (3H, OCH$_3$) 4.4 br.s (2H, NH$_2$) 4.75 s (2H, CH$_2$CO) 5.85 s (1H, CH^5	210 (100) 187 (45) 179 (18) 150 (47) 121 (22)
VIa	3.8 s (3I, OCH$_3$) 4.8 br.s (2H, NH$_2$) 7.1 s (1H, CH) 12.8 br.s (1H, NH)	141 (100) 114 (14) 110 (19) 109 (32)
VIb	4.7 br.s (2H, NH$_2$) 7.0–7.8 m (6H, Ph+CH) 9.5 br.s (1H, NHCO) 12.65 br.s (1H, NH)	202 (80) 110 (95) 93 (100) 40 (43)
VII	2.17 s (3H, CH$_3$CO) 2.7 s (3H, CH$_3$CO) 8.7 s (1H, CH) 9.2 br.s (1H, NHCO)	211 (9) 169 (29) 127 (62) 109 (32)
IX	2.2 s (3H, CH$_3$) 2.55 s (3H, CH$_3$CO) 2.65 s (3H, CH$_3$CO) 7.6 s (1H, CH) 8.4 br.s (1H, NHCO)	181 (8) 139 (13) 129 (58) 97 (27) 87 (67)

^{a} ^{1}H NMR spectrum of compound **IIb** was recorded in DCl$_3$.

as compared with that on catalyst of composition 0.5% of Pd on γ-Al$_2$O$_3$.

EXPERIMENTAL

^{1}H NMR spectra were registered on spectrometer Bruker WM-250 at operating frequency 250.13 MHz in DMSO-d_6. Mass spectra were measured on Finnigan Mat instrument (electron impact, 70 eV). Nitrobenzenes Ia, b were obtained by procedure [5]. The catalyst ShPAK-0.5 was prepared as in [1].

Hydrogenation of nitro compounds on ShPAK-0.5 catalyst. General procedure for compounds **Ia, b, IIIa–c, Va, b**. Nitro compounds (0.25–0.9 mol) were dissolved in 200–300 ml of methanol (compound **IIIb** was dissolved in DMF), and the solution was charged into the reactor with 50 ml of the catalyst. The hydrogenation was performed at 30–40°C and 20–40 at till the hydrogen consumption stopped (4–8 h). Then the solution was discharged, the solvent was evaporated, and the residue was distilled (with compounds **IIa, b**) or recrystallized. The yields, melting points and solvents for recrystallization are listed in Table 2.

Hydrogenation of nitro compounds Vc, VIII in the presence of acetic anhydride. General procedure. In a mixture of 300 ml of Ac$_2$O and 150 ml of AcOH was dissolved 0.05 mol of nitro compound, and the solution was charged into the reactor with 50 ml of ShPAK-0.5 catalyst. The hydrogenation was carried out at 25–28°C, 10 at for 10–12 h. Then the solution was discharged, evaporated to the volume of ~30 ml, and cooled. The separated precipitate was filtered off and recrystallized. The yields, melting points and solvents for recrystallization are listed in Table 2.

Procedure for preparation of catalyst with composition 2% Pd on granulated carbon. In 200 ml of distilled water at heating to 70°C was dissolved 1.79 g of PdCl$_2$, the solution was acidified with hydrochloric acid to pH 2. To 50 g (56 ml) of granulated carbon in a wide beaker was added the above solution of palladium chloride, and the beaker was maintained at 70°C till water totally evaporated. Then the catalyst was placed into a muffle and heated at a rate 100 deg h^{-1} till 400°C and kept at this temperature for 2 h. The calcined catalyst was placed into a quartz reactor with electric heating, and hydrogen was passed through for 1 h at 180–200°C.

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