3. P. Baviani, F. Rose, A. Vartanian, and C. Warolin, French Patent Application No. 2473522; Ref. Zh. Khim., 160124P (1982).
4. J. L. H. Van Gelder, A. H. M. Raeymaekers, L. F. C. Roevens, and W. J. Van Laerhoven, U.S. Patent No. 3983133 (1976); Ref. Zh. Khim., 110173P (1977).
5. K. Körmendy and F. Ruff, Acta Chim. Hung., 112, No. 1, 65 (1983).
6. H.-L. Pan and T. L. Fletcher, J. Heterocycl. Chem., 9, 859 (1972).
7. W. L. Mosby, Heterocyclic Systems with Bridgehead Nitrogen Atoms, Part 1, Interscience (1961), pp. 183, 467.
8. Chau-der Li, Men Hui Lee, and A. C. Santorelli, J. Med. Chem., 22, 1030 (1979).
9. F. Claudi, P. Franchetti, M. Grifantini, and S. Martelli, J. Org. Chem., 39, 3508 (1974).
10. H. W. Heine and A. C. Brooker, J. Org. Chem., 27, 2943 (1962).
11. V. A. Anisimova, M. V. Levchenko, Yu.V. Koshchienko, and A. F. Pozharskii, USSR Inventor's Certificate No. 952847; Byull. Izobret., No. 31, 126 (1982).
12. A. V. El'tsov, K. M. Krivozheiko, and M. B. Kolesova, Zh. Org. Khim., 3, 1518 (1967).

MECHANISM OF THE CATALYTIC OXIDATION OF NITROGEN-CONTAINING METHYL-SUBSTITUTED HETEROCYCLES TO HETARYL ALDEHYDES

L. Ya. Leitis, R. A. Skolmeistere,
and M. V. Shimanskaya

UDC 542.943.7:547.821.2

An interrelationship between the electronic structures of methyl derivatives of nitrogen-containing heterocyclic compounds and the character of the interaction with the catalyst, the mechanism of heterogeneous-catalytic oxidation, and the selectivity of the process was established.

The heterogeneous-catalytic oxidation of methyl-substituted heterocycles by air oxygen is one of the most promising methods for the preparation of oxygen-containing derivatives such as aldehydes.

The high reactivities of heterocyclic compounds necessitate the purposeful selection of catalysts that ensure the selective oxidation of the methyl group without destroying the ring. In this paper we present several principles of the reaction mechanism that may serve as a basis for the creation of optimal catalytic systems. As model catalysts we used vanadium-containing systems of the oxide and phosphate type, which have shown their worth in the partial oxidation of nitrogen-containing methyl-substituted heterocycles [1].

A comparison of the rates of partial oxidation of methyl derivatives of pyridine, quinoline, and pyrazine in the presence of vanadyl phosphate with their electronic structures showed that an important factor for the oxidation of these compounds to hetaryl aldehydes is the magnitude of the positive charge on the ring carbon atom bonded to the methyl group to be oxidized [$q_{C(CH_3)}$] [2]. The investigated methyl-substituted heterocycles can be arbitrarily divided into two groups that differ with respect to the character of the interaction with the catalyst and the mechanism of oxidation. One group is made up of compounds with higher $q_{C(CH_3)}$ values (0.05-0.2 according to the MO LCAO CNDO/2 method) that contain oxidizable methyl groups in the 2 and 4 positions of the ring. 3-Methyl derivatives with positive charges $q_{C(CH_3)} < 0.05$ are included in the other group. Under comparable conditions, substantial differences in the selectivity with respect to hetaryl aldehydes are observed for compounds of both groups. In the first case the selectivity is no lower than 40% (44-100%), and in the second case the selectivity is no less than 3-10%.

Institute of Organic Synthesis, Academy of Sciences of the Latvian SSR, Riga 226006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 64-67, January, 1987. Original article submitted June 16, 1986.

0009-3122/87/2301-0052$12.50

TABLE 1. Valence State of Vanadium in a Vanadium–Molybdenum Oxide Catalyst (V–Mo, 1:9)

Oxidizable compound	Ratio to the overall vanadium content, %							
	before work		in the steady state			after reduction of the catalysts		
	V^{5+}	V^{4+}	V^{5+}	V^{4+}	V^{3+}	V^{5+}	V^{4+}	V^{3+}
2-Methylpyridine	70,4	29,6	50,6	35,3	14,1	40,0	33,3	26,7
3-Methylpyridine	70,4	29,6	70,1	29,9	—	70,0	30,0	—
4-Methylpyridine	70,4	29,6	39,4	60,6	—	—	89,3	10,7

According to IR spectroscopic investigations, the primary interaction of nitrogen heterocycles with the surfaces of vanadium-containing catalysts consists in complexing of the nitrogen atom with the Lewis acid centers — vanadium ions [1].

The experimental data make it possible to represent the subsequent transformations of the organic molecule in the following way: The methyl group of the adsorbed heterocyclic compound interacts with the basic center of the catalyst surface (the doubly bonded oxygen atom of the vanadyl ion [3]), which leads to dissociation of the C–H bond and to the formation of an RCH_2^+ carbonium ion and a surface hydroxy group. The conclusion regarding the character of the intermediate particle was drawn on the basis of the positive value of the ρ constant in the equation that describes the interrelationship between the rate of accumulation of pyridinecarbaldehydes and the inductive constants [2]. The formation of hydroxy groups in the interaction of methylpyridines with vanadium oxide was established by IR spectroscopy [1]. The liberated electrons are transmitted to the catalyst, as a result of which the vanadium ions are reduced to a significant extent in the case of the 2- and 4-methyl derivatives. The effect of the structure of the methyl-substituted heterocycle on the reducing capacity was studied with respect to isomeric methylpyridine models. Under comparable conditions, the strongest reducing agent from the point of view of the overall degree of reduction is 4-methylpyridine, in the presence of which the percentage of V^{4+} ions in a catalyst functioning under steady-state conditions is 60.6% (Table 1), but 2-methylpyridine reduces to a greater extent — 14.1% of the ions; V^{5+} is reduced to the trivalent state. In the presence of 3-methylpyridine the composition of the vanadium ions does not change during oxidation under comparable conditions. According to the data in [4], the reverse reoxidation of the individual vanadium oxides proceeds quite readily (the energy of activation for the reaction $V^{3+} \rightarrow V^{4+}$ is 6.3 kJ/mole, as compared with 21 kJ/mole for the reaction $V^{4+} \rightarrow V^{5+}$). Stabilization of vanadium in the lower oxidation states in the vanadium–molybdenum catalysts is evidently achieved through molybdenum trioxide. Reduction of vanadium in vanadium-containing catalysts was observed in the oxidation of other organic compounds also, viz., toluene, benzene, and furfural [5-7]. Since 3-methylpyridine displays weak reductive properties relative to vanadium–molybdenum catalysts at higher temperatures (above 430°C), it might be concluded that the reducing capacities of methylpyridines correspond qualitatively to their reactivities in vapor-phase oxidation and decrease in the order 4- > 2- > 3-methylpyridine.

In an inert medium the ability of methylpyridines to reduce vanadium changes in the same order (Table 1). In the case of 2-methylpyridine ~ 50% of the V^{4+} ions are reduced to V^{3+}. The formation of a small amount of trivalent vanadium was also established in the reduction of 4-methylpyridine; the V^{5+} ions are reduced completely. 3-Methylpyridine is inactive under the investigated reduction conditions.

The principal reaction products detected in the interaction of methylpyridines with vanadium–molybdenum and vanadium–phosphate catalysts in the presence of oxygen and in an inert gas are similar and consist of pyridinecarbaldehydes and carbon dioxide.

The data set forth above constitute evidence that oxygen not only from the surface of the catalyst but also from the volume participates in both processes — oxidation and reduction — in the formation of products of complete and partial oxidation. A comparison of the rates of the overall conversion of the methylpyridines and the accumulation of pyridinecarbaldehydes under conditions of catalytic oxidation and reduction of the catalyst [8] shows that in the oxidation of 2- and 4-methylpyridines the pyridinecarbaldehydes are formed chiefly through oxygen of the catalyst lattice (the rates in oxidation and reduction are comparable). In the complete oxidation of these compounds (this pertains to 2-methylpyridine to a greater degree), in addition to lattice oxygen, oxygen of the gas phase also participates in the process (the rate of formation of CO_2 in catalytic oxidation is greater than in the reduction of the catalyst). Air oxygen primarily participates in the oxidation of 3-methylpyridine, both in the complete and partial oxidation.

It follows from the information stated above that 2- and 4-methyl derivatives of heterocycles are oxidized via a stepwise mechanism, whereas the 3-substituted derivatives are oxidized via an associative mechanism. The kinetic data are also in agreement with this conslusion. For example, whereas the rate of overall oxidation of 2-methylpyridine and the formation of pyridine-2-carbaldehyde is described by an equation of the Mars—van Krevelen type [9], this mathematical model is not applicable for the description of the rates of oxidation of 3-methylpyridine. The rates of the overall conversion of 3-methylpyridine and the accumulation of pyridine-3-carbaldehyde vary as a function of the concentrations of the reagents in accordance with the equations

$$W_{tot} = k_{tot}\, c_{MP}\, c_{O_2}^{0.9} \text{ and } W_{PA} = k_{PA}\, c_{MP}^{0.7}\, c_{O_2}^{0.9},$$

where k_{tot} and k_{PA} are constants, and c_{MP} and c_{O_2} are the concentrations of 3-methylpyridine and oxygen in the reaction mixture.

Thus nitrogen-containing heterocyclic compounds that have a relatively large positive charge $q_{C(CH_3)}$ participate in acidic-basic and redox interaction with the catalyst and are oxidized via a stepwise mechanism with high selectivity. For compounds with a lower charge on the corresponding ring carbon atom, in which the oxidizable methyl group participates to a lesser extent in conjugation with the nitrogen heteroatom, the prevailing process is an acidic-basic type of interaction with the catalytic system [8], and oxidation proceeds via an associative mechanism with low selectivity with respect to the product of partial oxidation.

EXPERIMENTAL

The vanadium—molybdenum oxide catalyst was prepared by evaporation of a solution of ammonium vanadate and molybdate and calcination of the resulting precipitate in a stream of air at 350-420°C for 10 h. After pressing of the powder, the pellets were separated with selection of the 0.25-0.5 mm fraction. The oxidation and reduction reactions were carried out in the microreactor described in [2]. Helium was used to create an inert medium. The steady state of the catalyst was acheived by carrying out the reaction at 420°C and an oxygen—oxidizable compound molar ratio of 6. The pulse magnitude was 0.4 μl, and the air and helium flow rates were 40 ml/min. Reduction of the catalyst was carried out at 400-420°C. The kinetics of the oxidation of 3-methylpyridine were studied in the gradient-free flow reactor described in [9] at 370-430°C; the space velocities were 6000-24,000 h^{-1}, and the 3-methylpyridine and oxygen molar concentrations were 0.2-0.8 and 2-10 mmole/liter, respectively.

The reaction products were analyzed chromatographically [2]. The valence of vanadium was determined by titration with a 0.01 N solution of potassium permanganate and Mohr's salt in the presence of phenylanthranilic acid [10].

LITERATURE CITED

1. L. Ya. Leitis, in: Advances in Heterogeneous Catalysis in the Chemistry of Heterocyclic Compounds [in Russian], Zinatne, Riga (1984), p. 64.
2. L. Ya. Leitis, R. A. Skolmeistere, L. O. Golender, D. P. Yansone, P. A. Meksh, and M. V. Shimanskaya, Khim. Geterotsikl. Soedin., No. 2, 75 (1986).
3. H. Miyata, G. Nakagawa, T. Ono, and Y. Kubokawa, J. Chem. Soc., Faraday Trans. 1, 79, 2343 (1983).
4. A. Bielanski, K. Dyrek, and E. Servicka, J. Catal., 66, 316 (1980).
5. G. Gut and R. Brauchbar, Chimia, No. 18, 212 (1964).
6. B. Grzybowska-Swierkosz and J. Haber (eds.), Vanadium Catalysts for Processes of Oxidation of Aromatic Hydrocarbons, Polish Scientific Publishers, Warsaw—Kraków (1984).
7. A. K. Strautina, É. E. Paulan, and M. V. Shimanskaya, Izv. Akad. Nauk Latv. SSR, Ser. Khim., No. 5, 530 (1969).

8. L. Ya. Leitis, R. A. Skolmeistere, and M. V. Shimanskaya, in: Summaries of Papers Presented at the Fourth All-Union Conference on the Mechanisms of Catalytic Reactions [in Russian], Vol. 2, Moscow (1986), p. 57.
9. R. A. Skolmeistere and L. Ya. Leitis, Kinet. Katal., 23, 1499 (1981).
10. V. N. Muzgin, L. B. Khamzina, V. A. Zolotovkin, and I. Ya. Bezrukov, The Analytical Chemistry of Vanadium [in Russian], Nauka, Moscow (1981), p. 159.

NITRATION OF 3,5-DICARBONYL DERIVATIVES OF 4-PHENYL-1,4-DIHYDROPYRIDINE

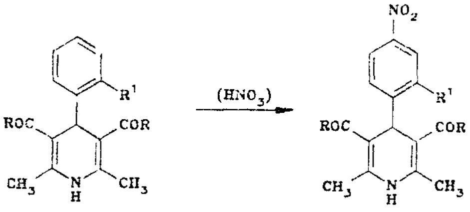
G. D. Tirzit, I. P. Skrastin'sh,
and G. Ya. Dubur

UDC 547.827:542.951

The nitration of the phenyl ring of 4-phenyl-1,4-dihydropyridines with retention of the 1,4-dihydropyridine structure was accomplished.

In connection with the ever increasing interest in 1,4-dihydropyridine (1,4-DHP) derivatives as physiologically active compounds, it has become necessary to study their reactivities. Up until now, the most characteristic reaction of 1,4-DHP was assumed to be oxidation; it has now been shown that these compounds also undergo other reactions, but little study has been devoted to their nitration — treatment with nitric acid usually leads to oxidation of pyridine [1]. Only 4,4-dialkyl-3,5-dicyano-1,4-DHP derivatives, which are extremely resistant to oxidation, are nitrated at the 2- and 6-methyl groups [2, 3].

In the present research we have shown that 3,5-dicarbonyl derivatives of 4-phenyl-1,4-DHP are nitrated relatively easily in a solution of sulfuric acid at low temperatures by nitric acid *in status nascendi* with the formation of the corresponding 4-(p-nitrophenyl)-1,4-DHP.



I II

I, II a R=CH_3, b, d R=OCH_3, c R=OC_2H_5; a—c R'=H, d R'=$OCHF_2$

With respect to their melting points (Table 1) and UV spectra (Table 2), the IIa-c obtained by this method correspond to the previously described compounds obtained by the Hantzsch method. The structures of IIa-c were also confirmed by the PMR, IR, and mass spectra (Table 2). Compound IId was synthesized for the first time. It is interesting to note that only the p-nitro compounds are obtained in all cases, i.e., the dihydropyridine ring acts as a p-orienting substituent. An attempt to nitrate the pivalyl derivative of I [R = $C(CH_3)_3$] was unsuccessful, since splitting out of tert-butyl alcohol and destruction of the molecule occur under the conditions used.

EXPERIMENTAL

The UV spectra were obtained with a Hitachi UV-vis 557 spectrophotometer. The IR spectra of mineral oil suspensions of the compounds were recorded with a Perkin-Elmer IR-580B

Institute of Organic Synthesis, Academy of Sciences of the Latvian SSR, Riga 226006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 68-69, January, 1987. Original article submitted December 20, 1985.

0009-3122/87/2301-0055$12.50