STUDY OF OPTICALLY ACTIVE HETEROLIGAND CHELATE COMPLEXES. VII. HETEROLIGAND COMPLEXES AS MODELS OF INTERMEDIATE COMPLEXES IN ENANTIOSELECTIVE HYDROGENATION CATALYSIS

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The current concepts on the mechanism of the asymmetric hydrogenation of dicarbonyl compounds on modified catlaysts do not explain all the available experimental data. In particular, the Groenewegen and Sachtler hypothesis [1] is inapplicable in the case of the hydrogenation of the symmetric β-diketone, acetylacetone (acac). To explain the mechanism of asymmetric hydrogenation, a hypothesis has already been previously advanced [2, 3] on the intermediate formation of ternary catalyst—modifier—substrate complexes. The recently found correlation between the optical yield of the hydrogenation of dicarbonyl compounds on copper, nickel, and cobalt skeleton catalysts modified by amino acids (AA), and the stability of the corresponding heteroligand chelates [4] makes it possible to assume that the ternary complexes are structurally similar to heteroligand chelates.

We used the chiroptic methods to study the structure of heteroligand chelates of Cu, Ni, and Co(II) with acac and chiral aromatic AA in solution, and we found that the acac ligand in these chelates has a folded structure [5-9]. Indications [10, 11] on the absence of aromaticity of the chelate ring of acac confirm this conclusion. The conformations of acac and configurations of AA for Ni chelates (λ-acac and S-AA or δ-acac and R-AA) and those for Co chelates (δ-acac and S-AA or λ-acac and R-AA) [8, 9] are oppositely related. The Cu chelates apparently have a relationship similar to Ni chelates. We attempted to explain the available literature and our experimental data on the asymmetric hydrogenation of acac, ethyl acetoacetate (EAA), and methyl acetoacetate (MAA), by considering the intermediate complex as a heteroligand chelate bound to the catalyst surface by the apical bond of the metal ion at which the distribution of the chelate on the metal surface is the most favorable for binding the phenyl of the aromatic AA to the metal (the phenyl effect [12]). The relationships between the configuration of the chiral (AA) and the conformation of the prochiral (acac, EAA, MAA) ligands used were the same as in the case of chelates in solution [8, 9].

Figure 1A gives a schematic illustration of the acac ligand of planar Cu and Ni chelates (view from the side further away from metal) in a λ conformation; Fig. 1B — possible distribution of the intermediate complex on the catalysts plane during hydrogenation of acac over the S-Phe modified Cu or Ni catalysts. To exclude the diastereoselective effect [3] during the examination of the hydrogenation scheme of acac, which results from both the enantioselective action of the catalyst, and the asymmetric induction in the substrate, we shall limit our discussion to the stage of the hydrogenation of acac to a ketol (pentan-2-ol-4-one). The hydrogenation proceeds preferably with simultaneous addition of hydrogen atoms from the side of the catalyst surface. Then in the situation of Fig. 1B (λ-acac, S-Phe), the addition of hydrogen proceeds better by path a then b (path a is sterically more favorable, since it is shorter than b), which leads to S-pentan-2-ol-4-one (the alternative path b leads to the R-ketol).

In the case of EAA, only the carbonyl group is hydrogenated. The two variants of its distribution in the transition complex are illustrated in Figs. 1C and D (EAA in the λ conformation and S-Phe). The complex in Fig. 1C leads to R-, and in Fig. 1D to S-ethyl β-hydroxybutyrate. The molecular models show that when the bond length at the metal ion—catalyst surface is commensurable with the coordination bonds of this metal, the EAA orientation illustrated in Fig. 1C (path c of hydrogen) is more favorable. An opposite orientation of EAA is possible at a more elongated metal ion—catalyst surface bond, and at a longer hydrogen path d (Fig. 1D). In this case, also the first EAA orientation (Fig. 1E) is sterically possible,

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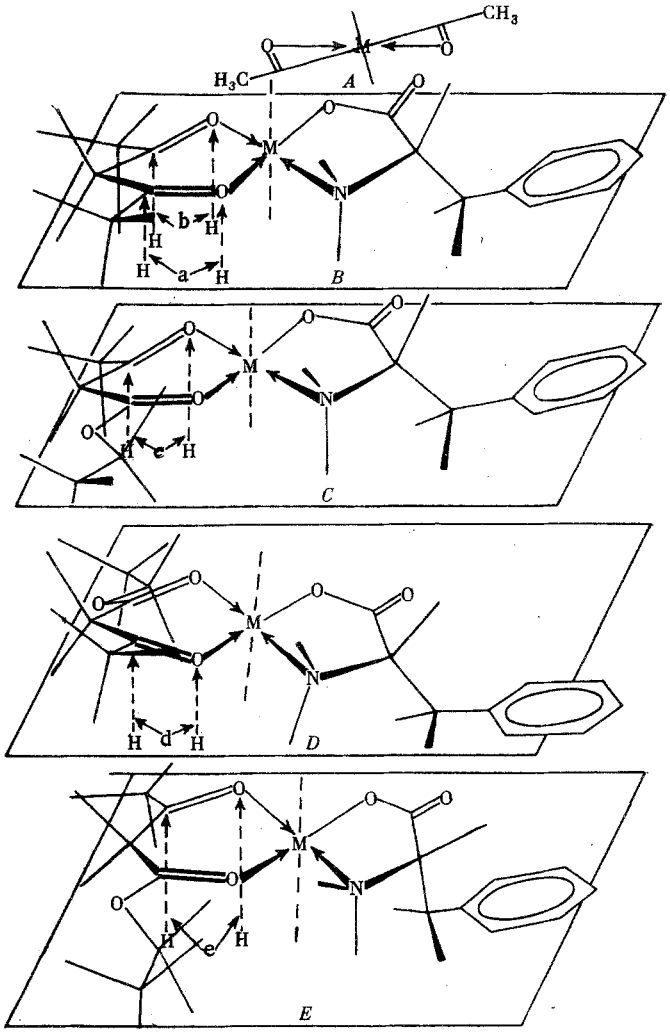

Fig. 1. Models of intermediate complexes in hydrogenation of acac and EAA over S-Phe modified Cu and Ni catalysts.

but variant D is more favorable (in the case of complex D, the addition of hydrogen to the carbonyl to be hydrogenated is sterically more favorable, since path d is shorter than e). Thus, during the hydrogenation of EAA it is theoretically possible to assume that it is possible to obtain different configurations of the products, depending on the conditions which change the length and strength of the metal ion–catalyst surface bond (for example, the method of preparation of the catalyst, the conditions of modification, etc.). In the series of Co, Ni, and Cu catalysts, a transition from a C type complex to a D type complex becomes more probable when there is an appropriate change in the configuration of the product from R to S, since in this series the length of the apical bonds of the metal chelates increases (in particular, that of copper).

The Co(II) complexes have a symmetry different from that of Cu and Ni complexes, and an inverse relationship between the AA configuration and the acac ligand conformation [8, 9], but it can be assumed that the formtion of an excess of an optical isomer during the hydrogenation of acac can, in this case, take place by the same mechanism as for Cu and Ni (taking into account the inverse configuration — conformation relationship). The configurations of the hydrogenation product proposed by examining the transition complexes in Fig. 1 change into the antipodal configurations with change in the configuration of the modifier.

Our experimental data and those of other authors [14-16] (Table 1) on hydrogenation confirm the proposed mechanism of the enantioselective hydrogenation. In fact, the predicted configuration of the product agrees with that experimentally obtained during the hydrogenation of acac over Cu, Ni, and Co catalysts, and also during the hydrogenation of EAA over Cu and Co catalysts modified by Phe, Trp, and Tyr, and during the hydrogenation of MAA over a Phe-modified

TABLE 1. Parameters of Enantioselective Hydrogenation of β-Dicarbonyl Compounds over Skeleton Cu, Ni, and Co Catalysts, Modified by Amino Acids (pressure 90-100 atm, time of hydrogenation 5-12 h)

Modifier	Catalyst	Substrate (solvent)	Conditions of modification in H_2O		Conditions of hydrogenation		Degree of conversion, %*	Optical yield, %	Configuration of product	Explainable configuration	Ref.
			C_{mod}, %	T., °C	Amount of catalyst (substrate), g	T., °C					
S-Phe	Cu	acac (EtOH)	1	20	0,5(5,8)	130	20	1,2	*S*(+)	*S*	[14]
S-Trp	Cu	acac (EtOH)	1	20	0,5(5,8)	130	74	1,4	*S*(+)	*S*	[14]
R-Tyr	Cu	acac (EtOH)	0,1	20	0,5(5,8)	130	29	0,2	*R*(−)	*R*	[14]
S-Phe	Cu	acac	1	20	0,5(5,8)	130	63	1,4	*S*(+)	*S*	[14]
S-Trp	Cu	acac	1	20	0,5(5,8)	130	57	1,8	*S*(+)	*S*	[14]
R-Tyr	Cu	acac	0,1	20	0,5(5,8)	130	54	0,5	*R*(−)	*R*	[14]
R-Phe	Ni	acac	1	100	1(19,44)	80	25,3	2,1	*R*(−)	*R*	
S-Phe	Ni	acac	1	100	1(19,44)	80	28,2	2,1	*S*(+)	*S*	
R-Trp	Ni	acac	1	100	1(19,44)	80	4,8	3,2	*R*(−)	*R*	
R-Tyr	Ni	acac	1	100	1(19,44)	80	32,5	2,3	*R*(−)	*R*	
R-Phe	Co	acac	1	100	1(19,44)	80	14,1	1,0	*S*(+)	*S*	
S-Phe	Co	acac	1	100	1(19,44)	80	19,1	1,0	*R*(−)	*R*	
R-Trp	Co	acac	1	100	1(19,44)	80	20,00	0,7	*S*(+)	*S*	
R-Tyr	Co	acac	1	100	1(19,44)	80	26,3	0,4	*S*(+)	*S*	
S-Phe	Cu	EAA (EtOH)	1	20	0,5(5)	130	6,0	9,3	*S*(+)	*S*	[15]
S-Trp	Cu	EAA (EtOH)	1	20	0,5(5)	130	11,5	7,1	*S*(+)	*S*	[15]
R-Tyr	Cu	EAA (EtOH)	0,1	20	0,5(5)	130	47,0	3,4	*R*(−)	*R*	[15]
S-Phe	Ni	MAA pH 7	2	0	<1,5(17)	60		~7,6	*R*(−)	*S*	[16]
S-Phe	Ni	MAA pH 7	2	40	<1,5(17)	60		~1,9	*R*(−)	*S*	[16]
S-Phe	Ni	MAA pH 7	2	70	<1,5(17)	60		0			[16]
S-Phe	Ni	MAA pH 7	2	100	<1,5(17)	60		~3,3	*S*(+)	*S*	[16]
S-Trp	Ni	MAA pH 7	2	0	<1,5(17)	60		~9,1	*R*(−)	*S*	[16]
S-Trp	Ni	MAA pH 7	2	100	<1,5(17)	60		~5,2	*R*(−)	*S*	[16]
S-Tyr	Ni	MAA pH 7	0,44	100	<1,5(17)	60		2,4	*R*(−)	*S*	[16]
S-Phe	Co	EAA	1	100	1(20,5)	80	7	1,3	*S*(+)	*S*	
R-Trp	Co	EAA	1	100	1(20,5)	80	24,5	3,4	*R*(−)	*R*	
R-Tyr	Co	EAA	1	100	1(20,5)	80	20,5	0,5	*R*(−)	*R*	

*For acetylacetone, yield of ketol, %.

Ni catalyst, T_{mod} > 70°C, through complex D. The change in the configuration of the product with the decrease in the temperature of modification during the hydrogenation of MAA over Phe-modified Ni catalyst, and the inversion of the configuration during the hydrogenation of MAA over Trp- and Tyr-modified Ni catalysts, in contrast to Phe-modified Ni, T_{mod} 100°C, can be explained by the transition from complex D to complex C or E.

We tried to relate the change in the value of the optical yield in the series of the amino acids used with a given metal catalyst to a change in the value of the circular dichroism (CD) of the conforamtional transition in acac (EAA) ligand (as a measure of its conformational distortion) in this series of the AA used as a second ligand in the corresponding heteroligand chelate, modeling the ternary hydrogenation complex. For this purpose, in addition to the CD spectra of heteroligand Cu, Ni, and Co(II) chelates with acac and aromatic AA already studied in [6, 8, 9], we obtained the CD spectra of similar chelates with EAA instead of acac (except for the spectra of Ni chelates, unavailable because of low values of observed CD). Figure 2 shows that these chelates, formed in the solution when $M(AA)_2$ is mixed with $M(EAA)_2$, have CD spectra in the region of d–d transitions and in the long-wave part of the charge-transfer bands, responsible for the conformational distortions of the β-dicarbonyl ligand, similar to the CD spectra of the corresponding heteroligand chelates with acac [6, 9]. We can therefore assume that the heteroligand Cu and Co(II) chelates have similar conformation of the chelate rings with acac and EAA ligands, respectively, at the same configuration of the

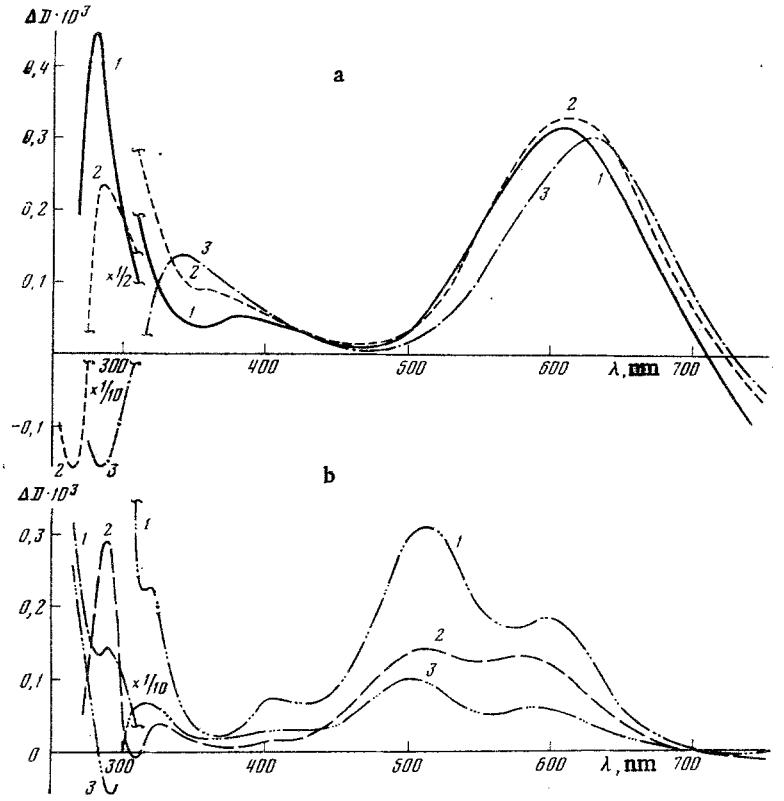

Fig. 2. Circular dichroism spectra (length of cuvette 10 mm, C, mmole/liter). a) Mixtures of $Cu(D\text{-}Phe)_2$ (C 1.3) and $Cu(EAA)_2$ (1:1) (1), $Cu(D\text{-}Tyr)_2$ (C 1) and $Cu(EAA)_2$ (1:1) (2), $Cu(D\text{-}Trp)_2$ (C 0.9) and $Cu(EAA)_2$ (1:1) (3) in DMSO. b) Mixtures of $Co(D\text{-}Phe)_2$ (C 0.74) and $Co(EAA)_2$ (1:5) (1), $Co(D\text{-}Tyr)_2$ (C 0.275) and $Co(EAA)_2$ (1:5) (2), and $Co(D\text{-}Trp)_2$ (C 0.265) and $Co(EAA)_2$ (1:5) (3) in DMFA.

AA ligand. Thus, the correspondence between the configuration of the AA ligand and the conformation of the acac ligand in the Cu(acac)(AA) and Co(acac)(AA) chelates discovered by us, can be extended to the corresponding Cu chelates with EAA ligand (see Fig. 1).

The circular dichroism of the transition in the 360-380 nm region of the Cu(EAA)(AA) chelate, and of the transition in the 315-325 nm region of the Co(EAA)(AA) chelate, as with the CD of the corresponding transitions in the Cu(acac)(AA) [6] and Co(acac)(AA) [9] chelates, is the result of the conformational effect, and is a measure of the conformational distortion of the β-dicarbonyl ligand, EAA. Figure 3 shows the correlation between the values of the CD maxima, corresponding to the conformational distortions of the acac and EAA ligands of all the heteroligand complexes studied, and the optical yield of the enantioselective hydrogenation of acac and EAA in the corresponding systems. We should note that this correlation is approximate, since the optical yield also depends on the ratio between the modified and unmodified centers of the catalyst. However, we can assume that the ratio between these centers does not substantially change during modification under the same conditions in our series of the AA-modifiers. Figure 3 shows that the increase in the conformational distortion of the acac ligand of the heteroligand chelates in the series of the given amino acids studied, used as second ligand, corresponds to an increase in the optical yield of the acac hydrogenation in the same series of AA, modifiers for all the metals studied. In the case of Cu (Fig. 3a), the deviation from the linear dependence may be a result of using a concentration of Tyr (0.1%) as a modifier, which is one order of magnitude lower than that of Phe and Trp (1%). All this confirms our proposed hypothesis on the hydrogenation of acac through an intermediate type B complex (see Fig. 1). In accordance with the proposed hydrogenation scheme, we can assume that the optical yield during the hydrogenation of EAA depends on the orientation of the EAA molecule in the intermediate complex (C or D). Therefore, the influence of the value of the conformational distortion of the EAA ligand on the optical yield is shown as a result of the influence of this distortion on the orientation of EAA. But if increase in distortion can increase the probability of a given orientation of EAA in the intermediate complex (for

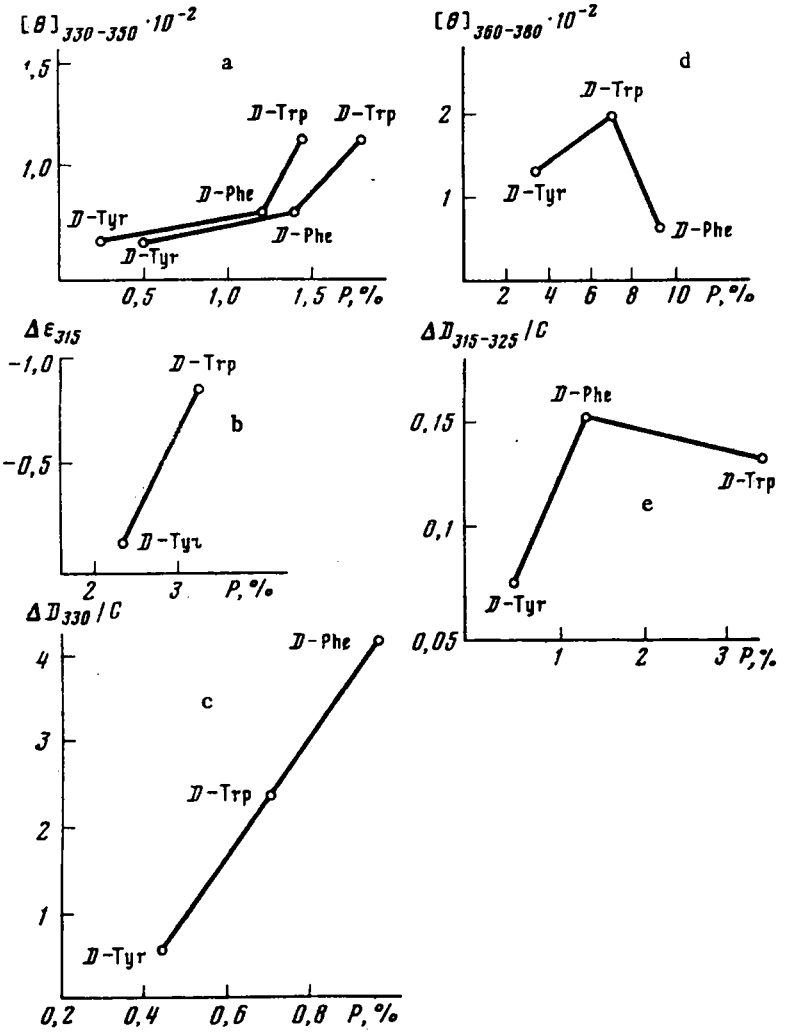

Fig. 3. Correlation between the conformational Cotton effects of heteroligand Cu, Ni, and Co(II) complexes with acac(EAA) and D(R)-amino acids (l = 10 mm) and the optical yield of the acac (or EAA) hydrogenation in the corresponding systems: a) Cu—acac—AA; b) Ni—acac—AA; c) Co—acac—AA; d) Cu—EAA—AA; e) Co—EAA—AA.

example, for Co, the probability of complex D), then this must lead to decrease in the synchronous character of the addition of the hydrogen atoms to the double bond of the carbonyl, which decreases the rate of hydrogenation through this complex. Therefore, in this case, the extent of the conformational distortion (foldability) of the EAA ligand should, in fact, have an optimal value for the maximal optical yield, as illustrated in Fig. 3d, e.

EXPERIMENTAL

The amino acid complexes of Cu and Co(II), $Cu(EAA)_2$ and $Co(EAA)_2$, were prepared by methods described in [17-20]. The CD spectra were measured on the "Jobin-Yvon-III" dichrograph in the 250-750 nm range at concentrations of the solutions of from 0.53 to 2.55 mmole/liter.

Raney Ni was obtained from the Ni/Al alloy (50:50) by leaching at 50°C for 1 h with 20% NaOH. Skeletal Co was obtained from the Co/Al alloy (30:70) by leaching at 65°C in a continuous flow with 2% NaOH. The two catalysts were washed with water to a neutral reaction.

The modification was carried out with 1% aqueous solutions of AA at a pH corresponding to the values of their isoelectric point, in a thermostated cell, at 100°C for 90 min, in an Ar current. After modification, the catalyst was washed twice with water, twice with absolute MeOH, and then with a small amount of acetylacetone [or ethyl acetoacetate (EAA)].

Acetylacetone [bp 45°C (10 mm), n_D^{17} 1.452] and EAA [bp 63°C (5 mm), n_D^{16} 1.4211] were used chromatographically pure. They were preliminarily dried over Na_2SO_4 and freshly distilled.

The hydrogenation was carried out in a glass ampul in a 0.5-liter rotating autoclave at p_{H_2} 100 atm, and 80°C. The amount of the catalyst used was 1 g, acac (or EAA) 20 ml. In the case of acac, the time of hydrogenation was calculated so that the process could be interrupted at the stage of formation of pentan-2-ol-4-one. The catalyst was then filtered off, and the catalyzate distilled in vacuo. Further treatment of the product to isolate pentan-2-ol-4-one was carried out by the method described in [13]. In the case of EAA, during the distillation of the products, the fraction boiling at 88°C (30 mm) was collected (EAA and ethyl β-hydroxybutyrate).

The hydrogenation products of acac were chromatographed on the LKhM-8MD chromatograph, flame-ionization detector; a metallic column, 600 × 0.3 cm, with 0.5% PEG 2000 + 0.5% KOH on NaCl was used, at 96°C; the flow rate of He was 60 ml/min. The hydrogenation product of EAA was analyzed on a 300 × 0.3 cm column with 15% Carbowax 20 M on a silanized Chromaton (0.4-0.6 mesh) at 100°C; flow rate of He was 60 ml/min.

The specific rotation of the hydrogenation products of acac and EAA was determined on a "Spectropol-1" spectropolarimeter at 589 and 360 nm.

CONCLUSIONS

A mechanism is proposed for the enantioselective hydrogenation of acetylacetone and ethyl acetoacetate (methyl acetoacetate) over skeletal Cu, Ni, and Co catalysts modified by aromatic amino acids, using stereochemical regularities found for heteroligand Cu, Ni, and Co(II) complexes, with acetylacetone (ethyl acetoacetate) and aromatic amino acids in solution.

LITERATURE CITED

1. J. A. Gruenewegen and W. M. H. Sachtler, J. Catal., 38, 501 (1975).
2. E. I. Klabunovskii, Stereospecific Catalysis [in Russian], Nauka (1968).
3. E. I. Klabunovskii and A. A. Vededenyapin, Zh. Fiz. Khim., 51, 3005 (1977).
4. A. A. Vedenyapin, Dissertation, Moscow (1979).
5. E. I. Klabunovskii, V. A. Pavlov, Yu. S. Airapetov, Ya. D. Fridman, V. A. Petukhov, I. P. Yakovlev, S. R. Piloyan, and L. Ya. Mikhailyuk, Izv. Akad. Nauk SSSR, Ser. Khim., 1047 (1978).
6. V. A. Pavlov, E. I. Klabunovskii, S. R. Piloyan, Yu. S. Airapetov, and E. G. Rukhadze, Izv. Akad. Nauk SSSR, Ser. Khim., 1052 (1978).
7. V. A. Pavlov, E. I. Klabunovskii, S. R. Piloyan, and Yu. S. Airapetov, Izv. Akad. Nauk SSSR, Ser. Khim., 1331 (1978).
8. V. A. Pavlov, S. R. Piloyan, E. I. Klabunovskii, V. S. Psalidas, I. P. Yakovlev, and E. G. Rukhadze, Izv. Akad. Nauk SSSR, Ser. Khim., 1711 (1979).
9. V. A. Pavlov, S. R. Piloyan, and E. I. Klabunovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 1714 (1979).
10. B. Bock, K. Flatau, H. Junge, M. Kuhr, and H. Musso, Angew. Chem. Int. Ed. Engl., 10 (4), 225 (1971).
11. M. Kuhr and H. Musso, Angew. Chem., Int. Ed. Engl., 8 (2), 147 (1969).
12. G. V. Smith and J. A. Roth, J. Catal., 4, 406 (1965).
13. T. Tanabe, Bull. Chem. Soc. Jpn., 46, 1482 (1973).
14. Yu. S. Airapetov, Dissertation, Moscow (1979).
15. A. A. Vedenyapin, Yu. S. Airapetov, E. I. Klabunovskii, Ya. D. Fridman, and L. Ya. Mikhailyuk, Izv. Akad. Nauk SSSR, Ser. Khim., 2385 (1977).
16. Y. Izumi, M. Imaida, H. Fukawa, and S. Akabori, Bull. Chem. Soc. Jpn., 36, 155 (1963).
17. G. M. Glaudi, Ann. Chim., 50, 581 (1960).
18. R. G. Charles and M. A. Pawlikowski, J. Phys. Chem., 62, 440 (1958).
19. R. W. Hay and B. P. Caughley, Austral. J. Chem., 20, 1829 (1967).
20. T. Shigematsu and M. Tabushi, Bull. Chem. Soc. Jpn., 41, 2656 (1968).