SPECTRAL STUDY OF FORMATION OF ISOMERIC MEISENHEIMER COMPLEXES FROM 1-SUBSTITUTED 3,5-DINITROBENZENES AND ACETONE

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Meisenheimer complexes of four derivatives of 3,5-dinitrobenzoic acid with acetone anion have been prepared and their NMR spectra measured; thereby their structures have been confirmed except for complexes from 3,5-dinitrobenzamide. In all the cases formation of two isomeric complexes have been observed. Symmetrical complexes are formed faster, however, they are transformed gradually into more stable unsymmetrical ones. The kinetics of formation, isomerization and reverse reactions of Meisenheimer complexes have been studied in methanol–acetone medium.

Reaction of picryl ethers with alkoxide ions produces[1] the complexes *I* and *II*, the latter being formed much faster; but being less stable[2], the complex *II* is transformed into the complex *I*. The Meisenheimer complex *II* resembles in both its stability and electronic spectrum the complex *III* formed by reaction of 1,3,5-trinitrobenzene with alkoxide ions[3]. 1-Substituted 3,5-dinitrobenzenes (*IV*) (X means an electron-withdraving substituent) react with alkoxide ions to give two products, *viz*, 4- and 2-adducts. The former ones are formed quickly, but they are less stable and are transformed into the latter ones[4]. Besides the Meisenheimer complexes from alkoxide ions, also complexes from other nucleophiles were studied inclusive of anions of C-acids especially acetone. Anions of C-acids react more slowly, but the Meisenheimer complexes formed are much more stable[5,6]. In the reactions with compounds of the type *IV*, again the symmetrical adducts *V* are formed first, and they are converted into more stable adducts[7,8] *VI*.

The aim of this work was to study the formation, isomerization and reverse reactions of these complexes and verify the structure of the newly isolated Meisenheimer complexes by NMR spectra. The complexes of the types *Va–d* and *VIa–d* were studied where X means $COOCH_3$ (*a*), $CON(CH_3)_2$ (*b*), $CON(CH_2)_5$ (*c*), and $CONH_2$ (*d*).

EXPERIMENTAL

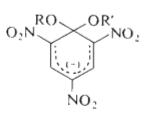
Methyl ester (*VIa*), dimethylamide (*VIb*) and amide (*VId*) of 3,5-dinitrobenzoic acid and N-(3,5-dinitrobenzoyl)piperidine (*VIc*) were prepared from 3,5-dinitrobenzoic acid or acid chloride by known methods. Their structure and purity was verified by NMR spectra. Dimethyl sulphoxide was dried with CaO, distilled and kept over molecular sieves. The other chemicals used were commercial reagents of analytical grade.

Preparation of Meisenheimer complexes from compounds IVa—d *and acetone.* 0·5 g of the respective derivative *IV* was dissolved in about 10 ml acetone, and 1 ml 0·5M sodium methoxide in methanol was added thereto. Immediately the solution turned intensively coloured due to formation of the mixture of complexes *V* and *VI*. After about one minute (or longer time in several cases) the product was precipitated by addition of 50 ml dry ether, collected by suction and washed several times with dry ether. The solid Meisenheimer complexes were carefully handled to avoid their getting wet, as they are considerably hygroscopic. The substances prepared were kept in an evacuated desiccator over P_2O_5.

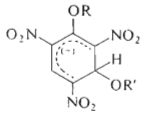
^{1}H NMR *spectra* were measured with the use of a Tesla BS 487A apparatus at 80 MHz at room temperature. 0·1M solutions of the complexes in hexadeuteriodimethyl sulphoxide were prepared for the measurements, hexamethyldisiloxane being used as internal standard (9·95τ). The values of chemical shifts were measured by a universal frequency counter with the accuracy of ± 1 Hz, and the values of coupling constants were read from calibrated graph-paper with the accuracy of $\pm 0{\cdot}2$ Hz.

Electronic spectra. For measurements of electronic spectra of the Meisenheimer complexes *VIb* and *VIc* the five days old solutions (used for NMR spectra measurements) were diluted with a mixture acetone–methanol (9 : 1 by vol.) to final concentration of about 10^{-4}M, and the spectra were measured immediately with the use of a Unicam SP 800 spectrophotometer and 1 cm cells in the wavelength range 350 to 700 nm. The solution of the compound *VIa* was prepared in a different way. The reaction mixture prepared from the compound *IVa*, acetone and 0·5M sodium methoxide in methanol was precipitated with ether first after 3 days. During this time all the primary compound *Va* was converted into *VIa*. The separated complex was purified by repeatedly dissolving in acetone and precipitating with ether. The electronic and NMR spectra were measured by the same method as in the previous cases. Electronic spectrum of the complex *Vc* was constructed from the measured extinction changes in the reverse reaction of the mixture of *Vc* and *VIc* giving the starting substrate (the isomer *Vc* reacts faster by about two orders of magnitude) and from the value of extinction coefficient in the isosbestic point of the both complexes.

Kinetic measurements. In informative kinetic experiments spectra of the reaction solution were measured at definite time intervals (Unicam SP 800 spectrophotometer, 1 cm cells, wavelength range 350 to 700 nm, temperature 20°C). The rate of formation of the complexes was followed by measuring (immediatelly and after definite time intervals) the spectra of the solutions prepared by injecting 35 µl 0·1M methanolic solution of *IVa—c* into 2·8 ml of a mixture of acetone, methanol and sodium methoxide located in the cell. The rate of isomerization reactions was followed similarly, however, only a part of methanol was put in the starting mixture before injection of the substrate, the remaining methanol being added after conversion of almost all the substrate into complexes. The rate of reverse reactions was followed practically in the same way as that of isomerization except for that 1M methanolic solution of acetic eventually chloroacetic acid was added besides methanol at the end. The rate constants of formation, isomerization and reverse reactions were determined by measurements with a Zeiss VSU-2P spectrophotometer. The reaction solutions were prepared in the same way as those for the abovementioned informative experiments measured with the Unicam spectrophotometer. The rate of formation of the both isomeric Meisenheimer complexes was measured at the wavelength corresponding to the isosbestic point of the both isomers (Table I). The rates of isomerization and reverse reactions were measured at the wavelengths 655 and 560 nm corresponding to λ_{max} of the isomers *Vc* and *VIc*, respectively. The rate of reverse decomposition of neutral forms of Meisenheimer complexes (the mixture *Vc* and *VIc* was acidified in methanol with hydrochloric acid) was measured at the wavelength 440 nm found by the way of trial; at this wavelength the absorbance of the complex formed by acidification of *Vc* is about 3× greater than that of the complex from *VIc*. As the rate of the



I



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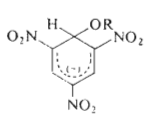

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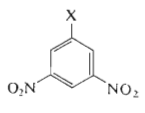

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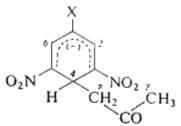
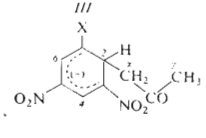


V



VI

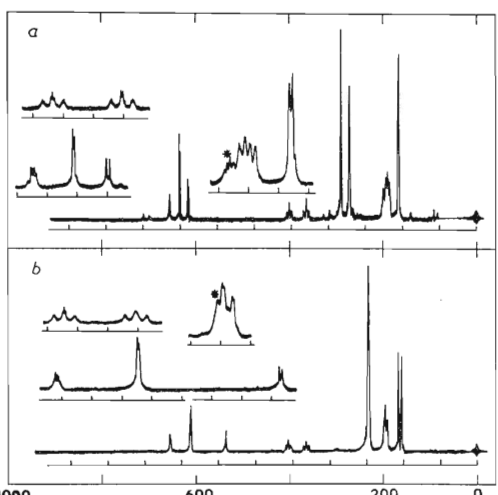


FIG. 1

^{1}H NMR Spectra of Complexes *a Va* + *VIa*, *b Vb* + *VIb* in Solutions of Hexadeuteriodimethyl Sulphoxide

The multiplet marked with asterisk belongs to the solvent.

reverse reaction of the complex formed from *VIc* is only about 6× smaller than that of the complex from *Vc*, it was only possible to determine directly the rate constant of the slower reaction from the linear part of the time dependence of the absorbance change. However, therefrom it was possible to calculate the absorbances of the protonated complex *VIc* at individual time intervals, and these values in turn could be used together with the experimentally determined absorbance values (at the same time intervals) for determination of the absorbance of the second complex and hence also determination of its decomposition rate constant.

RESULTS AND DISCUSSION

Interpretation of NMR *spectra.* Fig. 1 gives the spectra of the Meisenheimer complexes formed by reaction of *IVa* resp. *IVb* with acetone anion. From character of the spectra it is obvious that a mixture of isomeric complexes is present in the both cases. Three multiplets having chemical shifts 5·39, 1·73 and 2·20τ (curve a in Fig. 1) belong to the protons 2, 4 and 6 of the complex *VIa*, respectively. The multiplets having the chemical shifts 4·94 and 1·98τ belong to the protons 4 and 2 + 6 of the complex *Va*, respectively. The values of chemical shifts and coupling constants of the complexes *Va* and *VIa* agree with the values given by Crampton[7]. The spectrum of ring protons of complexes *Vb* and *VIb* has a similar character (curve b in Fig. 1), however, the signals of the proton 6 of the complex *VIb* and the protons 2 and 6 of the complex *Vb* are shifted towards higher fields. Another difference is encountered in chemical shifts of the γ protons. Whereas the difference in the respective chemical shifts is only 1·5 Hz in the case of complexes formed from the ester *VIa*, the difference of 6 Hz is observed in the case of complexes *Vb* and *VIb*. This fact is obviously connected with that the $N(CH_3)_2$ groups, in contrast to OCH_3 group, are non-equivalent in the two isomers. In contrast to the derivatives of N,N-dimethylbenzamide, the hindrance to rotation about C—N bond in complexes *Vb* and *VIb* is so small that no splitting of the bands occurs.

Character of spectra of the complexes *Vc* and *VIc* is analogous to that of *Vb* and *VIb*. The values of coupling constants and chemical shifts are given in Table II. (As the concentrations of the both isomeric complexes are comparable in fresh mixtures, the NMR measurements of the mixtures were repeated after several days, when the more stable isomers *VI* predominated, whereby the ascription of all absorptions in NMR spectra was enabled.)

NMR spectra of the complexes prepared from *IVd* contained only broad absorption bands which could not be interpreted. The broadening of bands was probably caused by the presence of small amount of radicals[1].

Kinetics and mechanism of reaction of 1-*substituted* 3,5-*dinitrobenzenes with acetone.* Formation of the Meisenheimer complexes by the methoxide-catalyzed reaction of 1-substituted 3,5-dinitrobenzenes with acetone in methanol–acetone media can be represented by Eqs (*A*) and (*B*).

$$CH_3COCH_3 + CH_3O^{(-)} \rightleftharpoons CH_3OH + CH_3COCH_2^{(-)} \qquad (A)$$

$$V \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} IV + CH_3COCH_2^{(-)} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} VI \qquad (B)$$

Eq. (*A*) represents a rapid antecedent equilibrium, whereas Eq. (*B*) describes the rate-limiting attack of substrate *IV* by acetone anion. In Fig. 2 the formation of the Meisenheimer complexes *Vc* and *VIc* and their isomerization are recorded. The both complexes are formed at comparable rates, but the less stable symmetrical complex *Vc* is converted into the more stable isomer *VIc* in the course of reaction. From spectra of the both isomers (Fig. 3) and from the absorbances at λ_{max} of the both complexes (Table I) measured at such reaction conditions, that the rate of formation of the both isomers is many times higher than that of isomerization, it was calculated that the rate constants ratio is 1·9 in favour of the isomer *Vc*.

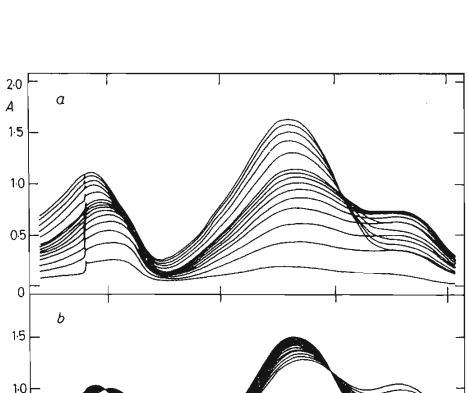


FIG. 2

Spectral Records *a* of Formation of *Vc* + *VIc* from *IVc* and Acetone Anion and their Isomerization in 29·5% by Vol. Methanol in Acetone at 20°C ($[CH_3O^-] = 7 . 10^{-3}$M; $\Delta t = 2$ and 10 minutes for the first ten and the other records, respectively) and *b* of Isomerization of *Vc* + *VIc* in 14% by Vol. Methanol in Acetone ($[CH_3O^-] = 5 . 10^{-3}$M, $\Delta t = 6$ min)

Reaction of acetone with the compound *IVb* has practically the same course as that with *IVc* under the same conditions. Methyl ester *IVa* is 30× more reactive, and the rate of formation of the complex *Va* is, roughly estimated, about 2–3 times greater than that of *VIa*. Informative kinetic experiments showed that the reaction of acetone with *IVd* has similar course to that of *IVb* and *IVc*. However, neither structure of the complexes nor their representation could be determined from NMR spectra. In electronic spectra of the reaction mixture the long-wave bands of the both complexes *Vd* and *VId* strongly overlapped each other, which considerably complicated the evaluation of kinetic experiments. Due to that the kinetics of reaction of acetone with the compound *IVd* was not further studied.

Experimental rate constants of formation of the isomeric complexes were determined by measuring the absorbance increase in the isosbestic point of the both

TABLE I

Visible Spectral Data of Complexes *V* and *VI*
Acetone–methanol medium, 10% by vol. methanol.

Complex	$\lambda_{1,max}$ nm	$\lambda_{2,max}$ nm	$\varepsilon_1 . 10^{-4}$	$\varepsilon_2 . 10^{-4}$	λ_{isosb} (complex)[a]
VIa	547	417	1·4	1·4	585 (*Va*)
VIb	553	385	1·7	1·1	600 (*Vb*)
VIc	560	385	1·3	0·8	603 (*Vc*)
Vc	655	407	1·0	0·6	603 (*VIc*)

[a] Wavelength of isosbestic point with the complex given.

TABLE II

Values of Chemical Shifts of Protons (τ) and Coupling Constants (J, Hz) in Complexes *V* and *VI* in Dimethyl Sulphoxide

Complex	H_2	H_4	H_6	$J_{2,4}$	$J_{2,6}$	$J_{4,6}$	H_α	H_γ	$J_{2,\alpha;4,\gamma}$
Va	1·98	4·94	1·98	0·8	—	0·8	7·56	7·86	5·6
VIa	5·39	1·73	2·20	1·0	~0	1·9	7·63	7·89	5·6
Vb	2·25	4·91	2·25	0·7	—	0·7	7·52	7·87	5·2
VIb	5·37	1·71	3·20	1·0	~0	1·7	7·49	7·96	5·5
Vc	2·31	4·93	2·31	1·0	—	1·0	7·52	7·87	5·5
VIc	5·44	1·75	3·27	0·8	~0	1·8	7·52	7·98	6·0

isomers (Table I), in order that the kinetic study of the complex formation be not complicated by simultaneous isomerizations. In all the cases the reactions were 1. order in the substrates used. Dependence of the experimental rate constant (k_{exp}) on methoxide ion concentration was linear in the whole range studied ($1{\cdot}8 \cdot 10^{-3}$M to $14{\cdot}1 \cdot 10^{-3}$M). The dependence extrapolated to the zero methoxide concentration crosses the origin. The facts found agree with the mechanism suggested (Eqs (*A*) and (*B*)). Decrease in methanol concentration results in an exponential increase of the experimental rate constant in the range of 50 to 19% by vol.; then its increase is even steeper (Fig. 4). The main reason for this rate constant increase is obviously the fact that basicity of the medium strongly increases (and hence also the concentration of acetone anion) with decreasing concentration of protic methanol. This basicity is expressed quantitatively by the basicity function H_- which is not known for methanol–acetone medium, however, its values for methoxide ion in dimethyl sulphoxide–methanol medium are given in[9]. The dependence of $\log k_{exp}$ on this acidity function is practically linear its slope being 0·7.

In acetone solution containing 15·5% by vol. methanol the value of $k_{exp}/[CH_3O^-]$ is 2·5 and 2·4 l mol^{-1} s^{-1} for *IVb* and *IVc*, respectively; with 26·0% by vol. methanol these values are 0·35 and 10·2 l mol^{-1} s^{-1} for *IVc* and *IVa*, respectively.

As the reaction produces simultaneously two complexes, the rate constant k_{exp} is a sum of rate constants of formation of the both complexes. Rate of formation of the symmetrical complex *V* can be described by Eq. (*1*). An analogous equation

$$v_1 = k_1[IV][CH_3COCH_2^{(-)}] = k_{exp}k_1[IV]/(k_1 + k_2) = \\ = k_{1,2}[IV][CH_3O^-] \qquad (1)$$

holds for formation of the unsymmetrical isomer *VI*. k_1 and k_2 are the rate constants

TABLE III

Dependence of Rate Constants of Formation (l mol^{-1} s^{-1}) and Reverse Reaction (s^{-1}) and Equilibrium Constants of Isomeric Complexes *Vc* and *VIc* on Concentration of Methanol in Acetone

For individual *k*'s see Eqs (*A*) and (*B*).

% CH_3OH by vol.	$k_{1,2}$	$k_{-1} \cdot 10^4$	$K_1 \cdot 10^{-2}$	$k_{2,2}$	$k_{-2} 10^6$	$K_2 \cdot 10^{-4}$
8·3	19·5	1·66	1 170	10·2	2·86	357
18·8	1·59	3·0	53	0·84	5·23	16·0
26·0	0·232	5·0	4·63	0·122	8·69	1·4

of reaction of the substrate with acetone anion (Eqs (*A*) and (*B*)), and $k_{1,2}$ is the rate constant of the formation of the symmetrical isomer *V* related to methoxide ion.

Study of the isomerization is complicated by competitive reactions which cause a decrease in concentration of the complexes. Rate of these side reactions increases with both increasing methoxide and decreasing methanol concentrations. Probably the both isomeric complexes undergo subsequent reactions with methoxide or acetone anion.

Isomerization rate constants were determined for the reaction *Vc* → *VIc*. The reaction was followed at λ_{max} of the both isomeric complexes and the ratio of the rates of isomerization and side reactions was estimated from the absorbance changes at the both wavelengths. Only those experiments were considered where the isomerization was substantially faster than the side reactions. From the results it follows that the isomerization reaction rate is independent of methoxide concentration, but it increases with increasing methanol concentration: for acetone solutions containing 29·5 and 22·5% by vol. methanol the rate constants k_{is} were found to be $2{\cdot}1 \cdot 10^{-4}$ and $1{\cdot}4 \cdot 10^{-4}$ s^{-1}, respectively. A probable mechanism of the isomerization reaction follows from Eqs (*A*) and (*B*). The complex *Vc* is decomposed into the starting substrate and acetone anion which again react to give the both complexes *Vc* and *VIc*. The reverse reaction of the complex *VIc* is inasmuch slower than that of *Vc*

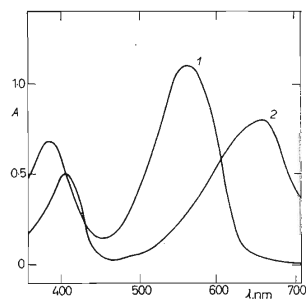


FIG. 3

Visible Spectrum of *VIc* Measured in Medium of 10% by Vol. Methanol in Acetone ($[VIc] = 8{\cdot}3 \cdot 10^{-3}$M) (*1*) and Calculated Spectrum of *Vc* for the Same Medium and Concentration (*2*)

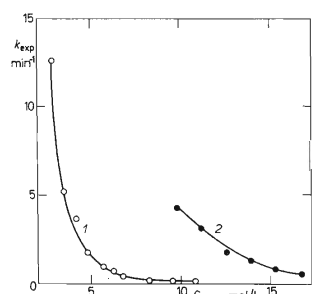


FIG. 4

Dependence of Experimental Rate Constant k_{exp} of Formation of Complexes *Vc* + *VIc* (*1*) and *Va* + *VIa* (*2*) on Methanol Concentration in Acetone at 20°C and $7 \cdot 10^{-3}$M Concentration of CH_3O^- Ions

that it can be neglected. Under the conditions used concentration of the substrate is much less than that of the complexes, and it is inversely proportional to concentration of acetone anion and hence to the methoxide concentration, too. As the rate of formation of the complexes is directly proportional to methoxide concentration, the resulting isomerization rate is independent of methoxide concentration. Concentration of the substrate is negligible as compared to that of the complexes, so that k_{is} can be defined by Eq. (2) derived from Eqs (*A*) and (*B*) on the basis of the Bodenstein steady state approximation.

$$k_{is} = k_{-1}k_2/(k_1 + k_2) \qquad (2)$$

When the reaction solution containing the both isomeric Meisenheimer complexes is neutralized with acetic acid, the reactions leading to formation of the complexes are practically stopped. The only reactions taking place under these conditions are reverse decomposition reactions of the both complexes giving the starting substrate and acetone anion which is converted very rapidly into acetone.

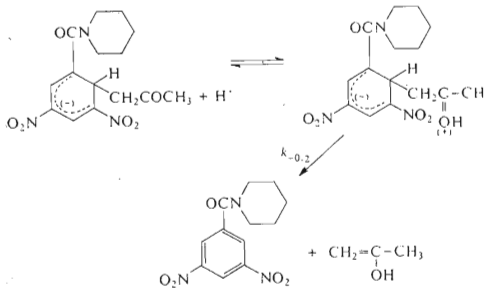
Kinetic of the reverse reaction was again followed with complexes *Vc* and *VIc*. The rate constant values increase with methanol concentration (Table III). Rate of the reverse reaction of the complex *Vc* is about 60× greater than that of *VIc*, and this ratio is practically independent of methanol concentration. Rate of the reverse reaction is defined by kinetic equation $v = k_{-1}$ [complex]. Its combination with Eq. (*1*) can define the equilibrium constant K_1 (Eq. (*3*)) of the complex *Vc* (and similarly K_2 for the complex *VIc*). The constants K_1 and K_2 differ from the

$$K_1 = [Vc]/[IVc][CH_3O^-] = k_{1,2}/k_{-1} \qquad (3)$$

equilibrium constants defined according to Eq. (*B*) for formation of the complexes by that the denominator contains methoxide concentration instead of concentration of acetone anion. The values of constants K_1 and K_2 rapidly increase with decreasing methanol concentration (Table III) which is caused, first of all, by the increase of the rate constants $k_{1,2}$ resp. $k_{2,2}$ and, to a lesser extent, by decrease of rate constants of reverse reactions.

Relation between isomerization constant k_{is} and rate constant k_{-1} is given in Eq. (*2*). Experimentally found k_{is} for 29·5% by vol. methanol concentration is $6{\cdot}1 \cdot 10^{-4}\ s^{-1}$, whereas k_{is} calculated from k_{-1} is $6{\cdot}0 \cdot 10^{-4}\ s^{-1}$.

The reverse reaction of the Meisenheimer complexes is acid-catalyzed. If the reaction mixture is acidified with methanolic hydrogen chloride, the protonation of complexes is practically complete, and the reverse reaction becomes practically independent of acidity of the medium. The rate constants $k_{-0,1}$ and $k_{-0,2}$ of the protonated complexes *Vc* and *VIc* are $5{\cdot}13 \cdot 10^{-2}$ and $8{\cdot}25 \cdot 10^{-3}\ s^{-1}$ for 29·5% by vol. methanol concentration, and $6{\cdot}08 \cdot 10^{-2}$ and $1{\cdot}44 \cdot 10^{-3}\ s^{-1}$ for 18·9% by



vol. methanol concentration, respectively. In contrast to the negatively charged Meisenheimer complexes, in this case the rate constants increase with decreasing methanol concentration. The ratio of the rate constants of the both isomers is about 10× lower than that of the negatively charged complexes, which can be due to their far greater reactivity. The only reaction products which can be considered here are the starting substrate *IVc* and enol form of acetone, so that the reaction can be described by Scheme 1. A somewhat different mechanism can also be considered where the proton is originally added to vicinal nitro or amide group, and it is transferred to oxygen atom of acetonyl group in further reaction course.

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