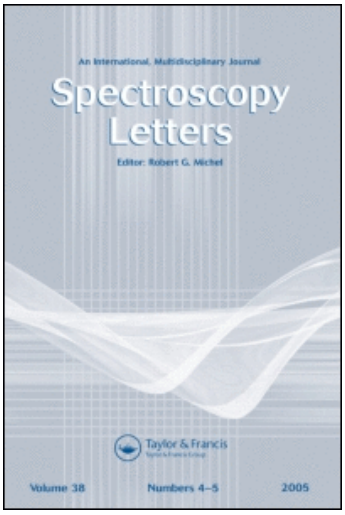

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Structural Elucidation Using ^{1}H-NMR, ^{13}C-NMR, and Mass Spectroscopic Study of 3-(Ethoxy-hydroxy-methyl)-quinolin-2(1*H*)-one and 2-Benzyloxy-3-formylquinoline

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Structural Elucidation Using ^{1}H-NMR, ^{13}C-NMR, and Mass Spectroscopic Study of 3-(Ethoxy-hydroxy-methyl)-quinolin-2(1*H*)-one and 2-Benzyloxy-3-formylquinoline

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Abstract: A convenient method has been developed for the synthesis of the 2-phenylfuro [2,3-*b*]quinoline system. It was found that 3-formylquinolin-2(1*H*)-one, when reacted with benzylchloride in dry ethanol in presence of potassium carbonate, yielded two intermediates, a hemi-acetal and an *O*-substituted product. The elucidation of these structures by means of ^{1}H-NMR, ^{13}C-NMR, and mass spectroscopic methods is reported. Some interesting mass spectral fragmentations were observed for some of the synthesized compounds.

Keywords: 2-Benzyloxy-3-formylquinolines, ^{13}C-NMR, 3-(ethoxy-hydroxy-methyl)-quinolin-2(1*H*)-one, ^{1}H-NMR, mass fragmentation, structural elucidation

INTRODUCTION

Studies on furoquinolines[1–6] are growing steadily in the field of synthetic organic chemistry, and their derivatives are much valued due to their medicinal properties. Numerous species of the plant family Rutaceae are known to produce furo[2,3-*b*]quinolines and they have been isolated in different varieties. Typical examples of the alkaloids are dictamnine, isodi-catmnine, lunacrine, and platedesmine. All these alkaloids have the basic skeleton furo[2,3-*b*]quinoline. Quinoline derivatives[7,8] are widely used as fungicides and antibacterial agents. Substituted diaminoquinolinequinones

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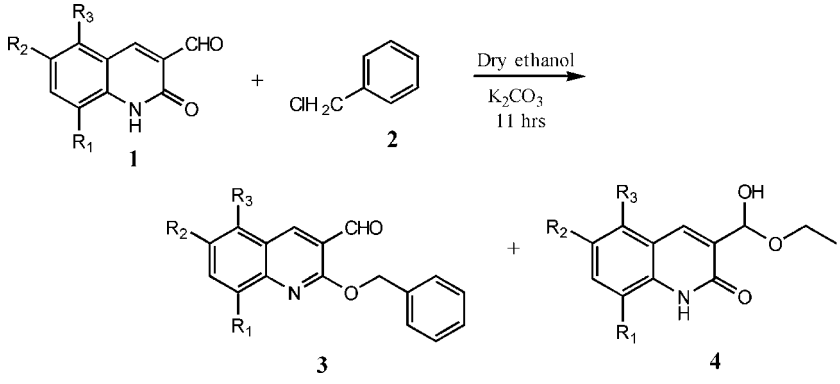
are effective in inhibiting aerobic glycolysis of tuberculoses, and 6-acetyl-amino-7-amino-5,8-quinolinequinones are highly potent against tubercle bacilli including those that developed resistance to isonicotinic hydrazides.[9] Apart from these, furo[2,3-*b*]quinolines and their derivatives are reported to exhibit various pharmacological properties,[10,11] which prompted us to synthesize the hitherto unreported furo[2,3-*b*]quinoline system.

Hence, the preparation of the furo[2,3-*b*]quinolines system and their "structural elucidation" tend to play a vital role in organic synthesis and pharmacological studies.

Herein, we report the synthesis of 2-phenylfuro[2,3-*b*]quinolines in two steps. In this connection, we employed a convenient procedure starting from 3-formylquinolin-2(1*H*)-one. In the first step, compound **1** was reacted with benzylchloride in dry ethanol in the presence of fused potassium carbonate and kept refluxed in a water bath for about 11 hr. Thin-layer chromatography (TLC) studies show the formation of two products. The expected nucleophilic attack of the O end of the starting substrate with benzyl chloride yielded one of the intermediates as a major product, and the effect of alcohol on formyl group yielded hemi-acetal as another intermediate. It is interesting to note that *hemi-acetal* or *hydroxy ether* have been obtained in the above reaction. Usually, hemi-acetals are formed by the treatment of aldehydes with alcohols in presence of acid catalyst or base catalyst. Hemi-acetals are stable toward base catalyst, but unstable toward acid catalyst because they are easily hydrolyzed by acids. We used K_2CO_3 as a base catalyst and we successfully trapped the hemi-acetal and hence allowed the formation of the product 2-benzyloxy-3-formylquinoline over hemi-acetal.

Our endeavors ended up with some active intermediates 3-(ethoxy-hydroxy-methyl)-quinolin-2(1*H*)-one and 2-benzyloxy-3-formylquinoline (Scheme 1). These active intermediates pave the path for the construction



Scheme 1.

of newer heterocycles, and their biological screening is of future interest. Hence, the structural elucidation of **3** and **4** and their derivatives warranted complete spectral investigation. This paper describes the systems and structural elucidation of **3(a–e)** and **4(a–e)** by ^{1}H-NMR, ^{13}C-NMR, and mass fragmentation studies.

EXPERIMENTAL

Reagent-grade aniline, phosphorous oxychloride, and dimethylformamide were used after the usual purification methods [for the preparation of the compounds **1(a–e)**]. Similarly, the solvents such as petroleum ether, ethyl acetate, ethanol, and methanol were purified by standard reported procedures. The reactions were performed under dry condition at 100°C for stipulated period of time. The solvents and reagents used for the synthesis were of reagent grade and were purified by standard methods. Petroleum ether (Pet-ether) used was of boiling range 60–80°C. Anhydrous sodium sulfate was used to dry the solutions of organic extracts. Purification of the crude products was carried out using chromatographic columns packed with activated silica gel (60–120 mesh). The purity of all the compounds was checked by TLC on silica gel plates, and the spots were detected by exposure to iodine vapors.

IR spectra were recorded with a Shimadzu 8201 FT spectrophotometer (USA) as KBr pellets, while the absorption frequencies were expressed in reciprocal centimeters (cm^{-1}).

The ^{1}H-NMR spectra of all the products obtained were recorded with a Brucker AMX-400 MHz spectrometer (USA) in $CDCl_3$ solution; chemical shifts are expressed in ppm (δ) relative tetra methyl silane (TMS). ^{13}C-NMR were also recorded on the same AMX-400 MHz spectrometer and are ^{1}H-decoupled. The mass spectra were recorded on a Jeol JMS-D-300 mass spectrometer (UK).

Preparation of 2-Phenylfuro[2,3-*b*]quinolines (5a–e)

We have hereby attempted to synthesize furo[2,3-*b*] quinoline starting from 3-formylquinolin-2(1*H*)-one. The aim has materialized in two steps as explained below. In the first step, reaction of benzyl chloride with 3-formylquinolin-2(1*H*)-one in dry ethanol in the presence of potassium carbonate, yielded a major intermediate 2-benzyloxy-3-formylquinoline along with hemi-acetal. *O*-arylkylated intermediate was taken for the next step, and it undergoes an intramolecular condensation by the action of methanolic sodium methoxide to give 2-phenylfuro[2,3-*b*]quinolines.

The respective 2-benzyloxy-3-formylquinolines (0.001 mol) were mixed with freshly prepared methanolic sodium methoxide (2.3 g, 0.0434 mol)

with constant stirring for about 1 hr. The reaction mixture was then refluxed for about 8 hr. After the completion of the reaction inferred through TLC, it was poured into crushed ice (200 g) and neutralized with 4 N HCl solution. The solid obtained was filtered off and purified by column chromatography over silica gel using petroleum ether-ethyl acetate (80 : 20) as eluents to give desired product (Scheme 2).

Spectral Data for the Compounds 5(a–e)

5a: IR (KBr, γ_{max}) 1598 cm^{-1}; ^{1}H-NMR ($CDCl_3$)(δ/ppm) 5.51 (s, 1H, C_3-H), 7.12–7.81 (m, 10H, Ar-H).

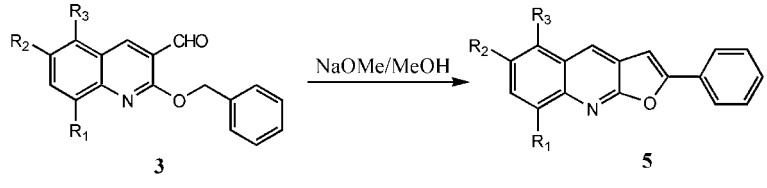
5b: IR (KBr, γ_{max}) 2862 cm^{-1}, 1590–1610 cm^{-1}; ^{1}H-NMR ($CDCl_3$)(δ/ppm) 5.53 (s, 1H, C_3-H), 7.08–7.82 (m, 9H, Ar-H), 2.31 (s, 3H, CH_3).

5c: IR (KBr, γ_{max}) 2892 & 2923 cm^{-1}, 1595 cm^{-1}; ^{1}H-NMR ($CDCl_3$)(δ/ppm) 5.56 (s, 1H, C_3-H), 7.11–7.90 (m, 9H, Ar-H), 3.92 (s, 3H, OCH_3).

5d: IR (KBr, γ_{max}) 2873 cm^{-1}, 1590–1605 cm^{-1}; ^{1}H-NMR ($CDCl_3$)(δ/ppm) 5.43 (s, 1H, C_3-H), 7.13–7.87 (m, 9H, Ar-H), 2.37 (s, 3H, CH_3).

5e: IR (KBr, γ_{max}) 2872, 2934 cm^{-1}, 1595–1610 cm^{-1}, ^{1}H-NMR ($CDCl_3$) (δ/ppm) 5.55 (s, 1H, C_3-H), 7.05–7.85 (m, 8H, Ar-H), 2.41 (s, 3H, C_8- CH_3), 2.32 (s, 3H, C_5-CH_3).

Table 1 lists the ^{1}H-NMR and ^{13}C-NMR spectral data of **3(a–e)**, and Table 2 lists the ^{1}H-NMR and ^{13}C-NMR spectral data of **4(a–e)** with the assignment of chemical shifts. The ^{13}C-NMR of **5(a–e)** was obtained as a noisy one and so not included.



3 **5**

where,

a) R_1=R_2=R_3=H
b) R_1=CH_3, R_2=R_3=H
c) R_1=O-CH_3, R_2=R_3=H
d) R_1=R_3=H, R_2=CH_3
e) R_1=R_3=CH_3, R_2=H

Scheme 2.

Table 1. ^{1}H-NMR and ^{13}C-NMR spectral data of compounds **3(a–e)**

Compound	Chemical shift, δ/ppm (J, Hz). values for quinoline aromatic protons and carbons, respectively					Carbons C_2, C_3, C_{4a}, C_{8a}, respectively	C_3-CHO	C_2-O-CH_2	Phenyl protons and carbons C_1', C_2', & C_2'', C_3' & C_3'', C_4', respectively
	C_4-H	C_5-H	C_6-H	C_7-H	C_8-H				
3a	s, 7.71; 129.37	7.65 d, $J = 7.8$ Hz; 127.99	7.30 t, $J = 7.1$ Hz; 115.77	7.76 t, $J = 7.5$ Hz; 125.63	7.93 d, $J = 7.4$ Hz; 119.96	162.46, 134.27 136.38, 142.09	s, 8.91; 190.65	s, 3.35; 46.32	m, 6.79–7.22; 132.38, 123.56, 115.77, 126.98
3b	s, 7.80; 129.45	7.58 d, $J = 7.8$ Hz; 128.02	7.26 t, $J = 7.6$ Hz; 126.32	7.68 d, $J = 8.0$ Hz; 123.42	C_8-CH_3 s, 2.60; 135.33, 24.1	163.24, 134.44 136.23, 143.01	s, 8.94; 191.23	s, 3.42; 48.24	m, 6.80–7.20; 132.38, 120.12, 114.09, 126.79
3c	s, 7.93; 129.51	7.61 d, $J = 8.0$ Hz; 128.30	7.32 t, $J = 7.8$ Hz; 126.13	7.81 d, $J = 7.9$ Hz; 123.11	C_8-OCH_3 s, 3.92; 151.43, 56.37	162.51, 134.17 135.44, 142.98	s, 8.92; 190.73	s, 3.43; 47.03	m, 6.82–7.21; 132.42, 121.34, 115.32, 126.88
3d	s, 7.90; 128.99	s, 7.60; 128.04	C_6-CH_3 s, 2.5; 135.27, 24.06	7.82 d, $J = 7.9$ Hz; 123.46	7.94 d, $J = 7.8$ Hz; 126.11	163.02, 134.36 136.19, 143.07	s, 9.01; 191.41	s, 3.40; 46.41	m, 6.80–7.21; 133.01, 119.32, 115.47, 126.78
3e	s, 7.90; 129.02	C_5- CH_3 s, 2.57; 138.13, 23.04	7.44 d, $J = 7.8$ Hz; 127.01	7.65 d, $J = 7.8$ Hz; 124.30	C_8- CH_3 s, 2.52; 136.76, 24.12	163.72, 134.87 136.22, 144.21	s, 8.89; 192.05	s, 3.45; 48.47	m, 6.78–7.20; 134.13, 120.11, 116.32, 127.45

Table 2. ^{1}H-NMR & ^{13}C-NMR spectral data of compounds **4(a–e)**

Compound	Chemical shift, δ/ppm (J, Hz) quinoline aromatic protons and carbons, respectively					Carbons C_2, C_3, C_{4a}, C_{8a}, respectively	C_3-CH	C_3-CHOH	OCH_2CH_3	CH_2CH_3	NH bs
	C_4-H	C_5-H	C_6-H	C_7-H	C_8-H						
4a	s, 8.12; 130.33	7.40 d, J = 8.1 Hz; 128.70	7.23 t, J = 7.5 Hz; 116.35	7.51 t, J = 8.1 Hz; 123.02	7.62 d, J = 7.8 Hz; 119.99	163.69, 137.83, 130.92, 138.70	s, 7.27; 97.43	s, 5.81	q, 3.80 J = 7.2 Hz; 63.09	t, 1.20 J = 6.9 Hz; 15.73	12.00
4b	s, 8.10; 130.50	7.44 d, J = 8.0 Hz; 128.10	7.31 t, J = 7.4 Hz; 115.37	7.60 d, J = 8.0 Hz; 122.70	C_8-CH_3 s, 2.58; 135.34, 22.31	163.82, 137.88 130.87, 138.53	s, 7.25; 98.33	s, 5.80	q, 3.82 J = 7.2 Hz; 64.01	t, 1.22 J = 6.9 Hz; 16.01	12.10
4c	s, 8.15; 131.07	7.40 d, J = 8.0 Hz; 127.83	7.28 t, J = 7.4 Hz; 114.99	7.66 d, J = 7.9 Hz; 124.00	C_8-OCH_3 s, 3.92; 154.09, 57.30	164.11, 138.21 131.07, 139.24	s, 7.21; 99.07	s, 5.82	q, 3.84 J = 7.2 Hz; 63.84	t, 1.20 J = 7.2 Hz; 16.12	12.12
4d	s, 8.10; 130.06	s, 7.45; 127.55	C_6-CH_3 s, 2.54; 134.44, 23.04	7.54 d, J = 8.0 Hz; 122.74	7.62 d, J = 7.8 Hz 115.37	165.03, 137.21 131.02, 138.42	s, 7.24; 98.88	s, 5.80	q, 3.90 J = 7.2 Hz; 64.27	t, 1.20 J = 6.9 Hz; 15.86	12.10
4e	s, 8.12; 130.41 21.44	C_5-CH_3 s, 2.53; 122.73	7.42 d, J = 7.8 Hz; 120.06	7.58 d, J = 7.8 Hz; 116.41	C_8-CH_3, s, 2.50 128.33 23.02	164.16, 138.73 131.22, 140.03	s, 7.32; 98.45	s, 5.81	q, 3.88 J = 7.2 Hz; 63.43	t, 1.24 J = 6.9 Hz; 15.73	12.10

RESULTS AND DISCUSSION

The exclusive products **3(a–e)** and **4(a–e)** have been characterized by analytical and spectroscopic data. The ^{1}H-NMR spectrum of compound **3a** revealed two sharp singlets at δ 8.91 and δ 3.35, which indicate the presence of an aldehyde proton and methylene protons, respectively. Quinoline aromatic protons exhibit their resonances at

δ 7.93 (d, 1H, C_8-H, $J = 7.4$ Hz)

δ 7.76 (t, 1H, C_7-H, $J = 7.5$ Hz)

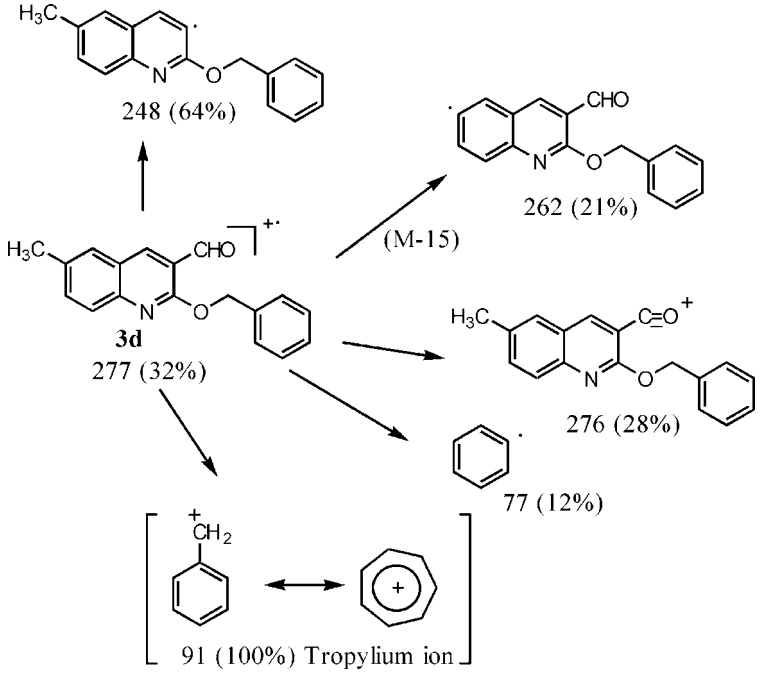
δ 7.30 (t, 1H, C_6-H, $J = 7.1$ Hz)

δ 7.65 (d, 1H, C_5-H, $J = 7.8$ Hz)

δ 7.71 (s, 1H, C_4-H)

and the substituted phenyl aromatic protons exhibit their resonances at δ 6.79–7.22 as an unresolved multiplet.

In its ^{13}C-NMR spectrum, a peak at 190.65 corresponds to aldehyde carbon and two peaks observed at 162.46 and 46.32 indicate the C_2 carbon of the quinoline ring and methylene carbon of the substituted benzyl



Scheme 3.

moiety, respectively. All the remaining peaks observed between 115.77 and 142.09 ppm are due to aromatic carbons.

The mass spectrum of the compound **3d** showed a molecular ion peak at m/z 277 (32%) (M^+). The M-28 peak observed at m/z 248 (64%) clearly shows the cleavage of formyl group of **3d**, and a base peak observed at m/z 91 (100%) accounts for tropylium ion (benzyl cation) and indicates the deduction of the benzyl moiety from the parent compound **3d** (Scheme 3).

The Mass fragmentation pattern of the compound **3d** is shown in Scheme 3.

The solvent medium, ethanol, acts as one of the substrate and attacks the compound **1** thereby yielding an intermediate **4**, but in poor yield as it is believed to be less stable than the intermediate **3**. An interesting spectral interpretation of second product **4a** is discussed as follows. In its ^{1}H-NMR spectrum **4a**, three singlets observed at δ 5.81, δ 8.12, and δ 12.00 indicate the resonances due to $-$OH, C_4-H, and N-H protons, respectively. A triplet observed at δ 1.20 and a quartet at δ 3.80 clearly indicates the presence of ethyl group. A fine singlet at δ 7.27 corresponds to methine proton at C_3-position.

Quinoline aromatic protons exhibit their resonances at

δ 7.62 (d, 1H, C_8-H, $J = 7.8$ Hz)

δ 7.51 (t, 1H, C_7-H, $J = 8.1$ Hz)

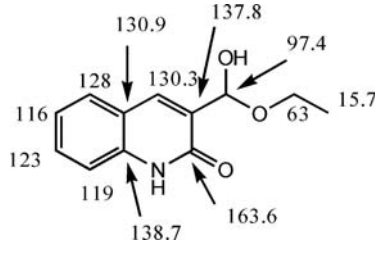
δ 7.23 (t, 1H, C_6-H, $J = 7.5$ Hz)

δ 7.40 (d, 1H, C_5-H, $J = 8.1$ Hz)

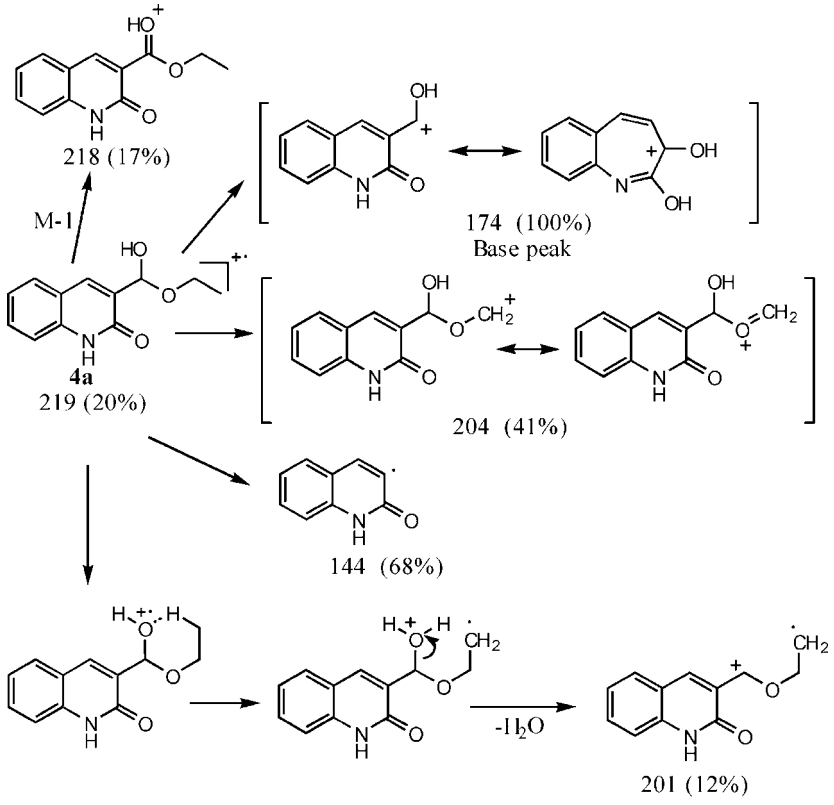
In its ^{13}C-NMR spectrum, peak at 163.69 corresponds to carbonyl carbon, and peaks at 15.73 and 63.09 indicate the presence of methyl and methylene carbons, respectively, in the structure.

A complete interpretation of the ^{13}C-NMR spectral values is given in Scheme 4.

The mass spectrum showed the molecular ion peak at 219 (20%) [M^+]. The base peak observed at m/z 174 and other fragmentations shown in



Scheme 4.



Scheme 5.

Scheme 5 confirmed our assignment. All the above spectral data correspond to the hemiacetal structure as 3-(ethoxy-hydroxy-methyl)-quinolin-2(1*H*)-one. Because the 1H-NMR and 13C-NMR obtained are very clear to predict the exact structure of the products, we need not go for 2D experiments like heteronuclear multiple bond correlation (HMBC) and heteronuclear single quantum correlation (HSQC). The methods adopted are effective enough to derive the structure of the newer derivatives. Along with the above spectral methods, the interesting mass fragmentation study has also helped to confirm the structure of the compounds **3** and **4**.

The mass-fragmentation pattern of the compound **4a** is shown in Scheme 5.

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