Pure Appl. Chem., Vol. 76, No. 3, pp. 557–564, 2004.

Stereochemistry of epoxide carbonylation using bimetallic Lewis acid/metal carbonyl complexes*

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Abstract: The stereochemistry of epoxide carbonylation using bimetallic [Lewis acid]$^+$[Co(CO)$_4$]$^-$ complexes is reported. The achiral complex [(salph)Al(THF)$_2$][Co(CO)$_4$] stereospecifically carbonylates *cis-* and *trans*-2-butene oxide to the *trans-* and *cis*-β-lactones, respectively. Preliminary experiments regarding the carbonylative kinetic resolution of racemic *trans*-2-butene oxide using the enantiomerically pure complex [(*R,R*-salcy)Al(THF)$_2$][Co(CO)$_4$] are also reported.

INTRODUCTION

β-Lactones are highly attractive synthetic targets due to their versatility in organic synthesis [1] as well as their presence in natural products with biological activity [2]. They are also useful monomers for the synthesis of poly(β-hydroxyalkanoate)s, a naturally occurring class of biodegradable polyesters [3]. One route to β-lactones which is drawing considerable recent interest, is the selective carbonylation of epoxides [4–14]. An early important advance in this field was the report that $Co_2(CO)_8$ in combination with 3-hydroxypyridine formed an active catalyst for the carbonylation of epoxides of ethylene and propylene; depending on the reaction conditions, either β-lactones [7] or poly(β-hydroxyalkanoate)s [9,15] were formed. Recently, Alper and Lee reported the regioselective carbonylation of epoxides and aziridines using a catalyst system consisting of a mixture of $[Ph_3P{=}N{=}PPh_3][Co(CO)_4]$ and $BF_3{\cdot}Et_2O$ [9]. Our research has focused on the development of a class of discrete bimetallic catalysts of the general formula [Lewis acid]$^+$[Co(CO)$_4$]$^-$ [10–12], catalysts which exhibit high selectivities as well as excellent activity for a range of epoxide and aziridine carbonylations.

In developing these bimetallic Lewis acid/metal carbonyl catalysts, we envisioned a mechanism (Scheme 1) whereby the cationic Lewis acid coordinates and activates the substrate for attack by an anionic metal carbonyl. Following migratory insertion of CO into the metal alkyl bond and recoordination of CO, an intramolecular attack of the metal alkoxide on the metal acyl forms the β-lactone [10,11]. Rieger and coworkers have recently reported density functional theory (DFT) calculations which support this mechanism [14]. In our search for further experimental evidence in support of this mechanism, we noted the stereochemistry of epoxide carbonylation could serve as a mechanistic probe. Based on the mechanism in Scheme 1, *cis*-epoxide should be converted to a *trans*-β-lactone upon carbonylation. We therefore initiated research regarding the carbonylation of epoxides of 2-butene, and the preliminary results of these studies employing $[Cp_2Ti][Co(CO)_4]$ were recently published [11], supporting our pro-

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*Plenary and invited lectures presented at the 12th IUPAC International Symposium on Organometallic Chemistry Directed Towards Organic Synthesis (OMCOS-12), Toronto, Ontario, Canada, 6–10 July 2003. Other presentations are published in this issue, pp. 453–695.

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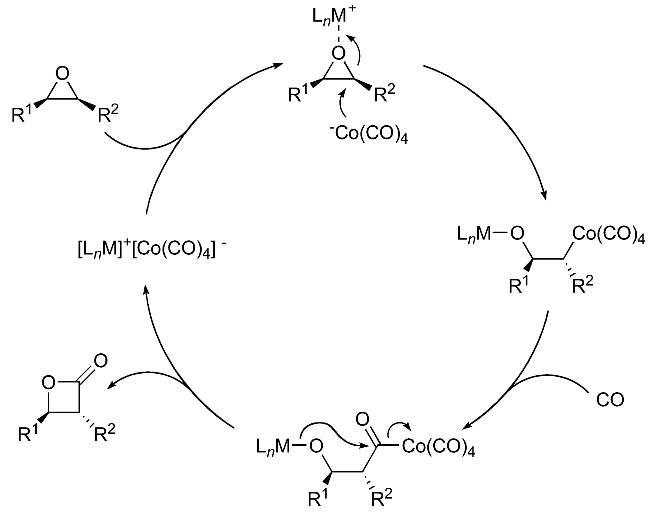
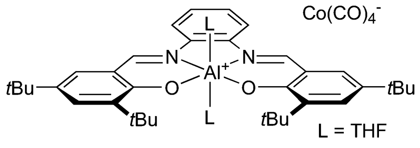


Scheme 1 Proposed mechanism of epoxide carbonylation using bimetallic [Lewis acid][$Co(CO)_4$] complexes; inversion occurs at the carbon adjacent to CO insertion.

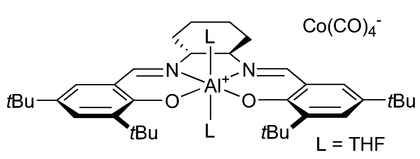
posed mechanism. In addition, we have discovered chiral catalysts capable of kinetically resolving racemic epoxides. Herein, we report a full account of the stereochemistry of the carbonylation of 2-butene oxides using achiral and chiral [(salen)Al][$Co(CO)_4$] complexes.

RESULTS AND DISCUSSION

[(Salen)Al][$Co(CO)_4$] complexes are readily synthesized by the reaction of $NaCo(CO)_4$ and (salen)AlCl. The steric and electronic nature of the salen ligand can be readily modified, allowing the Lewis acidic aluminum center to be optimized for the carbonylation [16]. We therefore chose to study the stereochemistry of epoxide carbonylation using achiral [(salph)Al$(THF)_2$][$Co(CO)_4$] (**1**) and enantiomerically pure [(*R*,*R*-salcy)Al$(THF)_2$][$Co(CO)_4$] (**2**) (Fig. 1).



[(salph)Al$(THF)_2$][$Co(CO)_4$]; **1**



[(*R*, *R*-salcy)Al$(THF)_2$][$Co(CO)_4$]; **2**

Fig. 1 Bimetallic carbonylation catalysts [(salph)Al$(THF)_2$][$Co(CO)_4$] (**1**) and [(*R*,*R*-salcy)Al$(THF)_2$][$Co(CO)_4$] (**2**).

Carbonylation employing [(salph)Al(THF)$_2$][Co(CO)$_4$] (1)

Neat *cis*- and *trans*-2-butene oxide were separately carbonylated using 1 mol % [(salph)Al(THF)$_2$][Co(CO)$_4$] (**1**) at 800 psi of CO (Fig. 2). The *trans*-isomer proved to react faster and with higher selectivity than the *cis*-isomer (100 vs. 40 % lactone formation). The *cis*-2-butene oxide reaction also produced oligomeric materials and 2-butanone. The β-lactones were isolated by vacuum distillation and subjected to NMR spectroscopy. By comparing the spectral data to those in the literature, it was determined that **1** stereospecifically converts *cis*-2-butene oxide to *trans*-2,3-dimethyloxetan-2-one and *trans*-2-butene oxide to *cis*-2,3-dimethyloxetan-2-one [17,18]. Given that there are conflicting literature reports regarding the NMR spectra of the epimeric 2,3-dimethyloxetan-2-ones, we chose to further confirm the stereochemistry by *syn*-decarboxylation of the β-lactones. Thermolysis of β-lactones produces CO_2 and an alkene; the reaction has been shown to proceed with retention of stereochemistry of the carbon framework [19,20]. By comparing the ^1H NMR spectra (Fig. 3) (as well as the ^{13}C NMR spectra) of the 2-butenes formed to those of known compounds, the assignment of the relative configurations shown in Fig. 2 was confirmed [11].

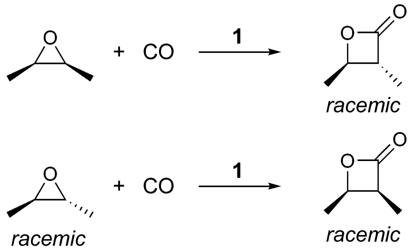


Fig. 2 Stereochemistry of the carbonylation of *cis*- and *trans*-2-butene oxide using [(salph)Al(THF)$_2$][Co(CO)$_4$] (**1**).

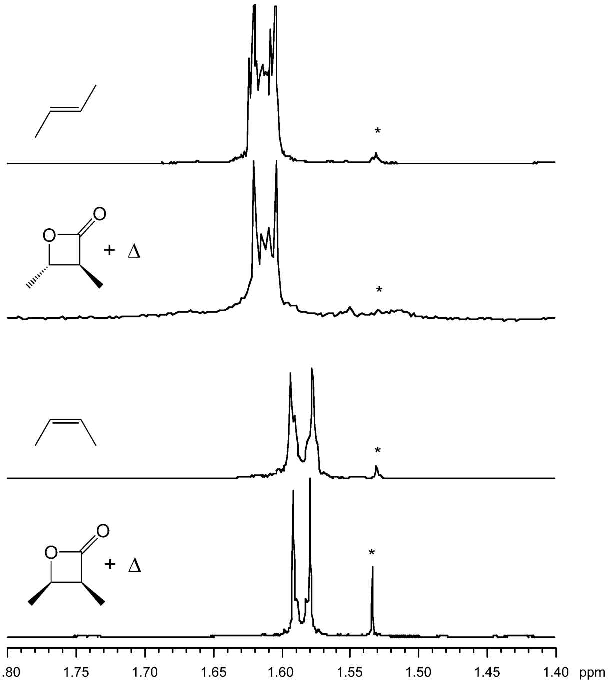


Fig. 3 Methyl regions of the ^1H NMR spectra (300 MHz, $CDCl_3$) of the volatile products resulting from the thermolysis of 3,4-dimethyloxetan-2-ones in comparison with known 2-butene samples. The peaks marked with asterisks are due to water.

Carbonylation employing [(*R,R*-salcy)Al(THF)$_2$][Co(CO)$_4$] (2)

The synthetic value of β-lactones in both organic as well as polymer chemistry is largely determined by the availability of these building blocks in their enantiomerically pure forms [2,21]. We have previously shown that optically active epoxides such as (*R*)-propylene oxide are carbonylated to (*R*)-β-butyrolactone with complete retention of configuration [10,11]. Given that enantiopure epoxides are readily available by a range of synthetic methods, catalytic carbonylation of optically active epoxides with discrete complexes provides a reliable route to a wide range of chiral β-lactones. Despite the fact that enantioselective catalysts for β-lactones have been developed [22], to the best of our knowledge enantioselective catalysts for epoxide carbonylation have not been reported. We initially chose to investigate [(salen)Al][Co(CO)$_4$] complexes given the great successes of related chiral salen complexes in asymmetric catalysis [23]. Following the successful discovery of achiral catalyst **1**, we decided to explore the synthesis and utility of enantiopure **2** in epoxide carbonylation. [(*R,R*-salcy)Al(THF)$_2$][Co(CO)$_4$] (**2**) is synthesized in the same manner as **1**. Crystals of **2** were examined by X-ray diffraction. The molecular structure of **2** is virtually isostructural to that of **1** (Fig. 4; see Experimental Section for refinement data) [10]. Complex **2** was investigated for the carbonylation of racemic *trans*-2-butene oxide (Fig. 5), and was found to have comparable activity to complex **1**. The carbonylation of racemic

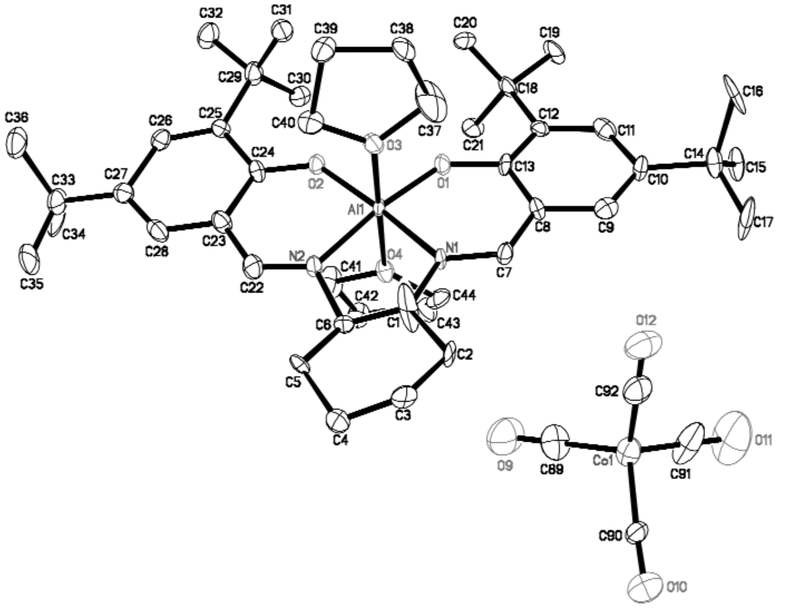
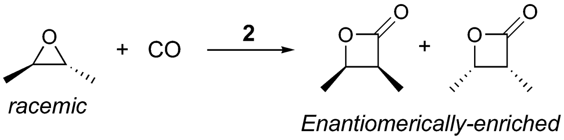


Fig. 4 Molecular structure of [(*R,R*-salcy)Al(THF)$_2$][Co(CO)$_4$] (**2**) with displacement ellipsoids drawn at 40 % probability.



T_{rxn}(°C)	k_{rel}
30	3.8
0	4.1

Fig. 5 Kinetic resolution in the carbonylation of *trans*-2-butene oxide using [(*R,R*-salcy)Al(THF)$_2$][Co(CO)$_4$] (**2**).

trans-2-butene oxide was then carried out at 30 °C for 4 h to give *cis*-2,3-dimethyloxetan-2-one; ^{1}H NMR revealed a clean 49 % conversion. Using chiral GC (see Experimental Section for conditions), a percent enantiomeric excess (% ee) of 44 % for the lactone was measured. Since the correlation between optical rotation and absolute configuration of *cis*-2,3-dimethyloxetan-2-one has not been reported, we do not know the absolute configuration of the major enantiomer. However, assuming that only one molecule of propylene oxide is involved in the step determining enantioselectivity, we calculate the relative ratio of the rate constants (k_{rel}) for consumption of the two enantiomers using the equation [24]:

$$k_{\mathrm{rel}} = \frac{\ln[1 - C(1+\mathrm{ee})]}{\ln[1 - C(1-\mathrm{ee})]} \tag{1}$$

where C is the reaction conversion and ee is the enantiomeric excess of the β-lactone product. At 30 °C, we calculate $k_{\mathrm{rel}} = 3.8$, whereas at 0 °C, $k_{\mathrm{rel}} = 4.1$. Although these selectivities are not synthetically efficient, they provide important mechanistic evidence that the enantiomerically pure cationic aluminum Lewis acid is intimately involved in the reaction, possibly as depicted in Scheme 1. We are confident that further empirical modifications to the [Lewis acid][$Co(CO)_4$] catalyst framework will yield much higher stereoselectivities.

CONCLUSION

The stereochemistry of epoxide carbonylation using bimetallic [Lewis acid][$Co(CO)_4$] complexes is reported. The achiral complex [(salph)Al$(THF)_2$][$Co(CO)_4$] (**1**) carbonylates *cis*- and *trans*-2-butene oxide to the corresponding *trans*- and *cis*-β-lactones, respectively. Catalyst **1** also has significant potential utility for the synthesis of optically active β-lactones by the carbonylation of optically active epoxides. Preliminary experiments regarding the kinetic resolution of racemic, *trans*-2-butene oxide using the enantiomerically pure complex [(*R,R*-salcy)Al$(THF)_2$][$Co(CO)_4$] (**2**) revealed k_{rel} values of 3.8–4.1. These results support the mechanism originally proposed for this class of complexes. Future work will center on the development of chiral catalysts that exhibit higher selectivity for the carbonylation of small molecules.

EXPERIMENTAL SECTION

General considerations

All manipulations of air- and/or water-sensitive compounds were carried out under dry nitrogen using a Braun Unilab drybox or standard Schlenk line techniques. NMR spectra were recorded on Bruker AF300 (^{1}H, 300 MHz; ^{13}C, 75 MHz), Varian Gemini (^{1}H, 300 MHz; ^{13}C, 75 MHz) or Varian Inova (^{1}H, 400 MHz; ^{13}C, 100 MHz) spectrometers and referenced versus residual nondeuterated solvent shifts ($\delta = 7.24$ for $C\mathit{H}Cl_3$; $\delta = 77.0$ for $\mathit{C}DCl_3$). X-ray crystallographic data were collected using a SMART CCD Area Detector System (Mo K_α, $\lambda = 0.71073$ Å), and frames were integrated with the Siemens SAINT program. The enantiomeric excess of *cis*-3,4-dimethyloxetan-2-one was measured on an HP 6890 Series GC equipped with a Supelco 2-4318 beta-DEX 225 column (0.25 mm × 30 m) employing helium as the carrier gas. Following injection, the oven temperature was increased at 2 °C/min from 120 °C to 160 °C, then 40 °C/min to 200 °C, where it was held for 5 min.

Materials

Tetrahydrofuran and hexanes were dried and degassed over solvent purification columns. Epoxides were distilled from CaH_2 under nitrogen and degassed. All other chemicals were commercially available and used as received. $NaCo(CO)_4$ was prepared by standard procedures [25]. The synthesis of $[(salph)Al(THF)_2][Co(CO)_4]$ (**1**) was previously reported [10].

Synthesis of [(*R,R*-salcy)Al(THF)$_2$][Co(CO)$_4$] (2)

All manipulations were performed with strict air-free techniques. All reagents and solvent were dried and degassed prior to use. In a drybox, (*R,R*)-*N,N′*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamine (1.0 g, 1.8 mmol) was placed in a Schlenk tube equipped with a stir-bar, and an air-free addition funnel was charged with diethyl aluminum chloride (Aldrich, 1.8 M in toluene, 1.0 ml, 1.8 mmol). Upon removal to the bench top the ligand was dissolved in CH_2Cl_2, giving a pale yellow solution. Dropwise addition of diethyl aluminum chloride solution resulted in the yellowing of the solution and a considerable evolution of ethane gas. After rinsing the addition funnel several times with CH_2Cl_2 the solution was stirred for 2.5 h. In vacuo, solvent removal gave a yellow solid that was rinsed 3 times with hexanes (10–20 ml) and then dried under vacuum. The Schlenk tube was brought into a drybox where white sodium cobalt tetracarbonyl powder (0.35 g, 1.8 mmol), stored at –35 °C under nitrogen, was added. Upon removal to the bench, tetrahydrofuran was added. The solution was stirred for two days in the foil wrapped tube and was concentrated to 5–10 ml, layered with hexanes (50 ml) and left to sit until well-formed bright yellow X-ray quality crystals appeared. Impurities were washed away with repeated rinses of hexanes allowing isolation of pure catalyst (1.4 g, 88 % yield). ^1H NMR (C_6D_6, 300 MHz): δ 1.14 (8H, br s), 1.38 (18H, br s), 1.68 (18H, br s), 1.91 (2H, br s), 2.31 (4H, br s), 2.79 (4H, br s), 3.37 (8H, dd, J_1 = 6.0 Hz, J_2 = 28.1 Hz), 7.66 (br s, 2H), 7.85 (br s, 2h) 8.62 (br s, 2H). ^{13}C NMR (C_6D_6, 100 MHz): δ 24.2, 24.9, 27.6, 29.8, 31.6, 34.4, 35.8, 64.3, 71.0, 119.3, 130.1, 131.7, 139.7, 139.9, 162.3, 167.5. Crystal data for [(*R,R*-salcy)Al(THF)$_2$][Co(CO)$_4$] (**2**): $(C_{48}H_{67}AlCoN_2O_8)\cdot(C_4H_8O)_2$, M = 885.95, triclinic, a = 12.1629(7), b = 13.1027(7), c = 15.7384(9) Å, α = 101.5810(10), β = 90.4660(10), γ = 90.0100(10)°, U = 2457.0(2) Å^3, T = 173(2) K, space group P1, Z = 2, μ(Mo-Kα) = 0.418 mm^{-1}, 19377 reflections measured, 14024 unique (R_{int} = 0.0300) which were used in all calculations. The final R1 was 0.0460 [$I > 2\sigma(I)$].

General procedure for the carbonylation of epoxides with [(salph)Al(THF)$_2$][Co(CO)$_4$] (1) or [(*R,R*-salcy)Al(THF)$_2$][Co(CO)$_4$] (2)

A 100-ml Parr reactor was heated at 90 °C overnight, under vacuum. In a dry-box, the reactor equipped with a test-tube and magnetic stir bar were cooled in a –35 °C freezer for at least 2 h. The test-tube was charged with precooled (–35 °C) epoxides (0.50 ml) and catalyst (1 mol %). Upon removal from the drybox, the reactor was pressured to ~800 psi with carbon monoxide (Matheson, Research Grade) and warmed to the desired temperature with stirring for the amount of time indicated. Finally, the reactor was cooled in a bath of dry ice/acetone until the pressure reached a minimum and the reactor was slowly vented. The resulting reaction mixture was analyzed by chiral GC and ^1H NMR for yield, then by $^1H/^{13}C$ NMR following vacuum distillation.

*Carbonylation of trans-2-butene oxide using [(salph)Al(THF)$_2$][Co(CO)$_4$] (**1**)*

T_{rxn} = 50 °C for 20 h; 100 % conversion to *cis*-3,4-dimethyloxetan-2-one: ^1H NMR ($CDCl_3$, 300 MHz): δ 1.25 (3H, d, J = 7.7 Hz), 1.43 (3H, d, J = 6.3 Hz), 3.72 (1H, m), 4.77 (1H, m). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 8.28, 15.59, 47.61, 71.99, 172.80.

*Carbonylation of cis-2-butene oxide using [(salph)Al(THF)$_2$][Co(CO)$_4$] (**1**)*

T_{rxn} = 75 °C for 7.5 h; 40 % conversion to *trans*-3,4-dimethyloxetan-2-one: ^1H NMR ($CDCl_3$, 300 MHz): δ 1.36 (3H, d, J = 7.5 Hz), 1.52 (3H, d, J = 6.6 Hz), 3.19 (1H, m), 4.32 (1H, m). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 12.53, 20.20, 52.38, 76.34, 172.10.

Carbonylation of trans-2-butene oxide using [(R,R-salcy)Al(THF)$_2$][Co(CO)$_4$] (2)

T_{rxn} = 30 °C for 4 h; 49 % conversion to *cis*-3,4-dimethyloxetan-2-one with the same spectroscopic data as reported above. Peaks in the chiral GC chromatograph due to the lactones were found at 16.6 and 17.6 min with areas corresponding to a 43.8 % ee.

T_{rxn} = 0 °C for 10 h; 17 % conversion to *cis*-3,4-dimethyloxetan-2-one with the same spectroscopic data as reported above. Peaks in the chiral GC chromatograph due to the lactones were found at 16.6 and 17.6 min with areas corresponding to a 56.6 % ee.

Thermolysis of 3,4-dimethyloxetan-2-ones

The lactone was purified by vacuum distillation, and placed in a thick-walled Pyrex tube equipped with a Kontes valve. The tube was frozen in N_2 and evacuated. The tube was heated to 171 °C in an oil bath for 2 h. The thermolysis tube was connected, via a short-path distillation head, to a $CDCl_3$-filled NMR tube fitted with a J-Young valve. The $CDCl_3$ was frozen in liquid N_2, the tube was evacuated, and the apparatus isolated from vacuum. The thermolysis tube was cooled to –78 °C and opened to the apparatus, warming of the thermolysis tube resulted in transfer of the volatile compounds into the NMR tube for analysis. The nonvolatile compounds were analyzed by NMR as well and revealed primarily residual lactone.

Thermolysis of cis-3,4-dimethyloxetan-2-one

Cis-2-butene: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.58 (6H, m), 5.44 (2H, m). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 12.35, 124.70. These spectral data were identical to the data of a commercial sample.

Thermolysis of trans-3,4-dimethyloxetan-2-one

Trans-2-butene: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.61 (6H, m), 5.41 (2H, m). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.05, 126.05. These spectral data were identical to the data of a commercial sample.

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