# Preparation of Binaphthyldiamine Derived Chiral Stationary Phases†

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1,1'-Binaphthyl-2,2'-diamine and its derivatives have been used as a very powerful chiral catalyst for asymmetric synthesis.[1,2] The preparative separation of racemic 1,1'-binaphthyl-2,2'-diamine has been reported recently,[3] but very few results by using this compound as a chiral selector have been reported. Miyano and co-workers reported on the many uses of chiral binaphthalene derivatives as a chiral derivatizing agent,[4] a chiral catalyst,[5] and chiral stationary phases. (CSPs)[6-10] In their work, the CSPs were prepared with binaphthyl dicarboxylic acids and the separated samples were limited to the derivatives of few chiral compounds as the overall selectivity was not good. Uray *et al.* also reported on the use of diphenylethanediamine derivatives, including 3,5-dinitrobenzoyl group, as chiral selectors, and tried to separate different enantiomeric compounds. He succeeded in separating some derivatized chiral compound and a few underivatized chiral samples with generally low selectivity levels.[11-14]

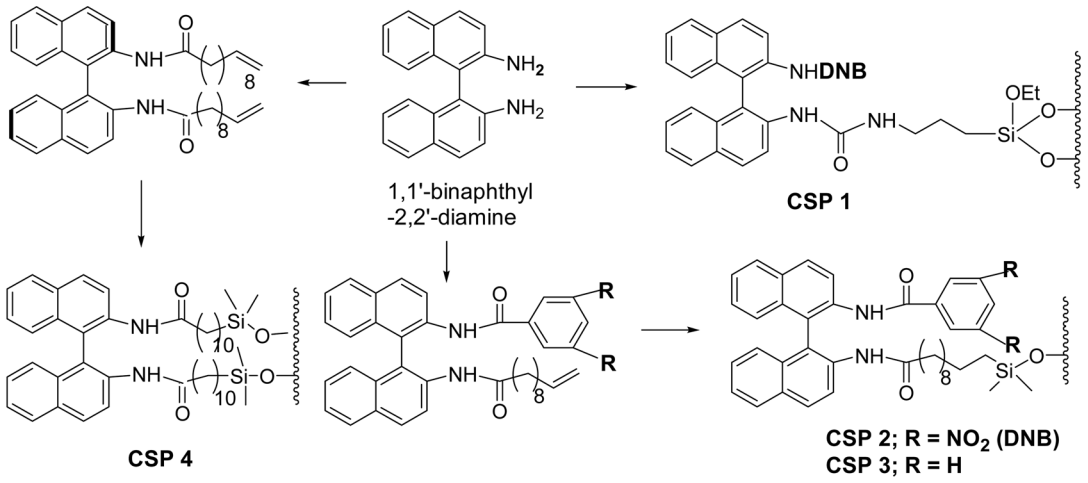
In this study, we report on the preparation of four different 1,1'-binaphthyl-2,2'-diamine derived chiral stationary phases (CSPs 1-4), and showed the separation results of randomly selected commercially available chiral compounds on these columns.

## Experimental

The HPLC system consisted of a Shimadzu (Tokyo, Japan) LC-10AD HPLC pump, a Rheodyne (Cotati, CA, USA) Model 7125 injector with a 20 $\mu$L sample loop, a Shimadzu Model 710 absorbance detector with a 254 nm UV filter and a Shimadzu integrator. analysis. All chromatographic data were obtained using 2.5-20% 2-propanol(IPA) in heptane, as a mobile phase at a flow rate of 1.2 mL/min. Dead time ($t_0$) was checked by injecting 1,3,5-tri-tert-butylbenzene, a presumed unretained solute obtained from Aldrich Chemical Co.

The number of tested racemic samples was 45. All chiral samples were commercially available and underivatized samples except for **S9**. The names of the 15 separated compounds and their structures are shown in Figure 1: methyl-2-naphthalene methanol (**S1**), 2,2,2-trifluoro-1-(9-anthryl)ethanol (**S2**), 2,2'-diamino-1,1'-binaphthalene (**S3**), *cis*-2,3-dihydro-*7a*-methyl-3-phenylpyrollolo [2,1-*b*]-oxazol-5 (7*aH*)-one (**S4**, a mixure of 3*S*-*cis* and 3*R*-*cis*), 1,5-dimethyl-4-phenyl-2-imidazolidinone (**S5**, a mixure of 4*S*,5*R* and 4*R*,5*S*), 5,5-dimethyl-4-phenyl-2-oxazolidinone (**S6**), $\alpha,\alpha$-dimethyl-$\beta$-methyl-succinimide (**S7**), *cis*-4,5-diphenyl-2-oxazolidinone (**S8**, a mixure of 4*S*,5*R* and 4*R*,5*S*), (R,S)-**7** (**S9**, a mixture of *R* and *S*-**7** synthesized from synthetic procedure of Scheme 4), furoin (**S10**), *N*-3,5-dinitrobenzoyl-DL-phenylglycine (**S11**), bis-*a*-ethylbenzyl-sulfamide (**S12**), 5-chloro-1,3-dihydro-1,3,3-trimethylspiro-[2H-indole-2,3'-(*3H*)-naphth[2,1-*b*](1,4)oxazine] (**S13**), and 1-aminoindane (**S14**).

In addition, the racemic samples in this study that could not be separated are as follows: *p*-fluorophenylalanine, 2-fluorophenylalanine, N-acetyl-*o*-fluorophenylalanine, N-acetylphenylalanine, *p*-nitrophenylalanine, N-formylphenyl-




† This paper is dedicated to Professor Sang Chul Shim on the occasion of his honorable retirement.

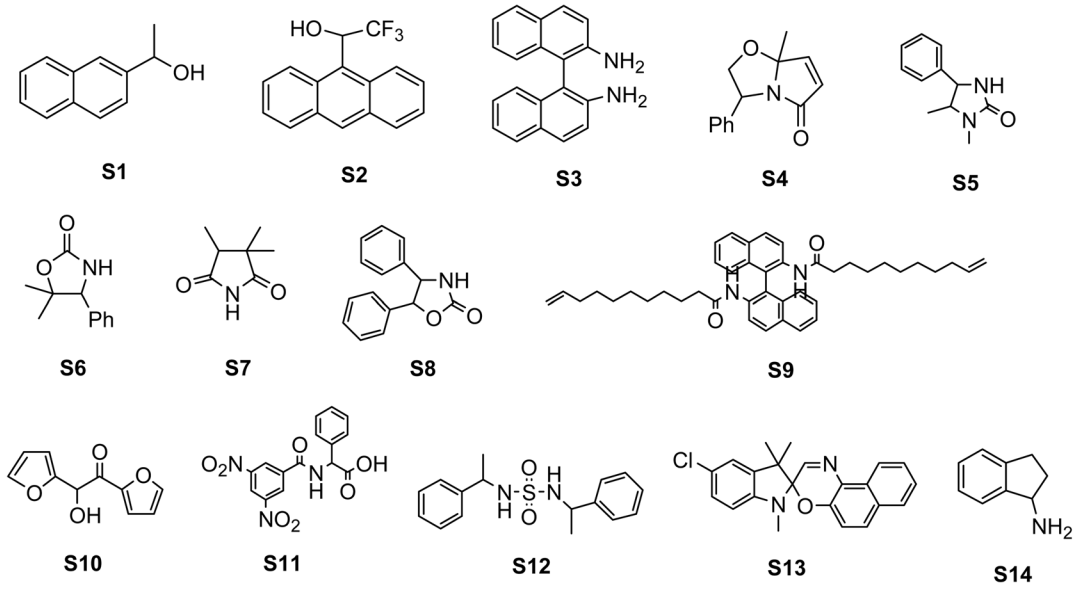



**Figure 1**. Structures of the separated chiral samples.

alanine, $\alpha$-methyltryptophan, 4-methyltryptophan, N-2,4-dinitrophenylnorleucine, N-phthalylvaline, N$\alpha$-benzoylalanine, 3-(1-naphthyl)alanine, 4-benzyl-2-oxazolidinone, 4-benzyl-3-propionyl-2-oxazolidinone, 4-benzyl-5,5-dimethyl-2-oxazolidinone, benzylphthalide, binaphthol-bis(trifluoromethane sulfonate), 2-(4-biphenyl)-5-phenyloxazole, 3-bromo-2-coumaranone, 2-bromo-1-indanol, 2-bromo-3-methylbutyric acid, $\alpha$-carbethoxy-$\gamma$-phenyl-$\gamma$-butyrolactone, 4-chloro-3-hydroxybutyronitrile, *p*-chloromandelic acid, 2-(3-chlorophenoxy)propionamide, $\alpha$-cyclopropylbenzylalcohol, 1',3'-dihydro-1',3',3'-trimethyl-6-nitrospiro[2H-1-benzopyran-2,2'-(2H)-indole], dihydro-5-phenyl-5-propyl-4,6-(1H,5H)-pyrimidinedione, $\alpha$,4-dimethylbenzylamine, epinephrine, and 2,3-epoxypropylbenzene.

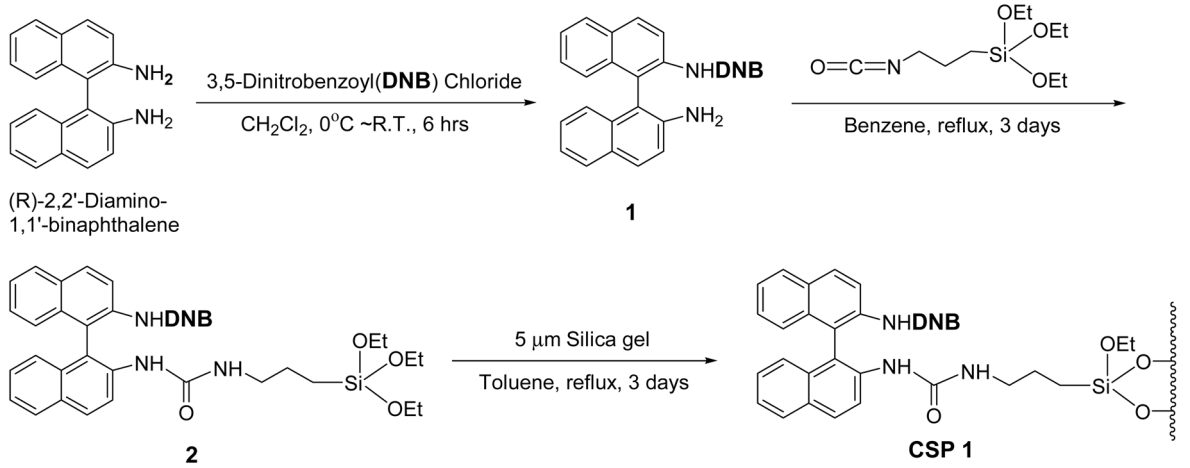
## Results and Discussion

The preparation of CSP 1 is summarized in Scheme 1. First, the mono-amidated compound was a major product at low temperatures, but a di-amidated product also appeared. The di-amidated one could be cleanly removed by classical extraction by varying the pH of aqueous solution. The synthetic procedures outlined in Schemes 1-4 involved only three major steps: Amidation, silylation and bonding to silica gel. These simple reactions have been reported in literature previously.[11-15] The covalently modified silica gels were packed into 250 × 4.6 mm I.D stainless steel columns using conventional methods.[15-17]

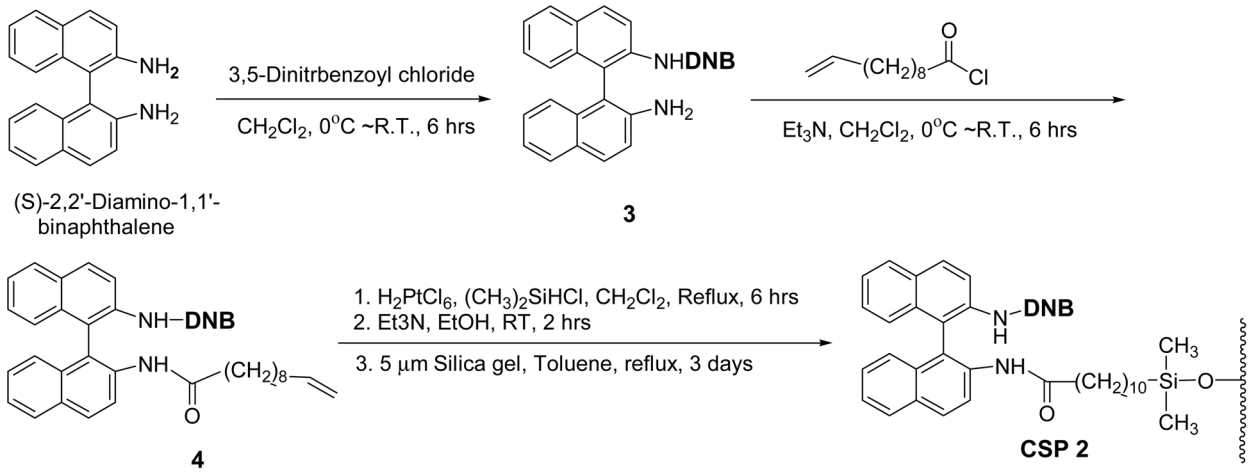
All CSPs have two $\pi$-basic naphthyl moieties, in addition to them, CSP 1 (with a short linkage arm) and CSP 2 (with a long linkage arm) have an additional $\pi$-acidic 3,5-dinitrobenzoyl group, while CSP 3 has a phenyl group and CSP 4 does not have any additional functional groups.

An example of the enantiomeric separation of 2,2,2-trifluoro-1-(9-anthryl)ethanol (**S2**) on CSP 1, and the effect of altering the composition of 2-propanol in heptane is shown in Figure 2.

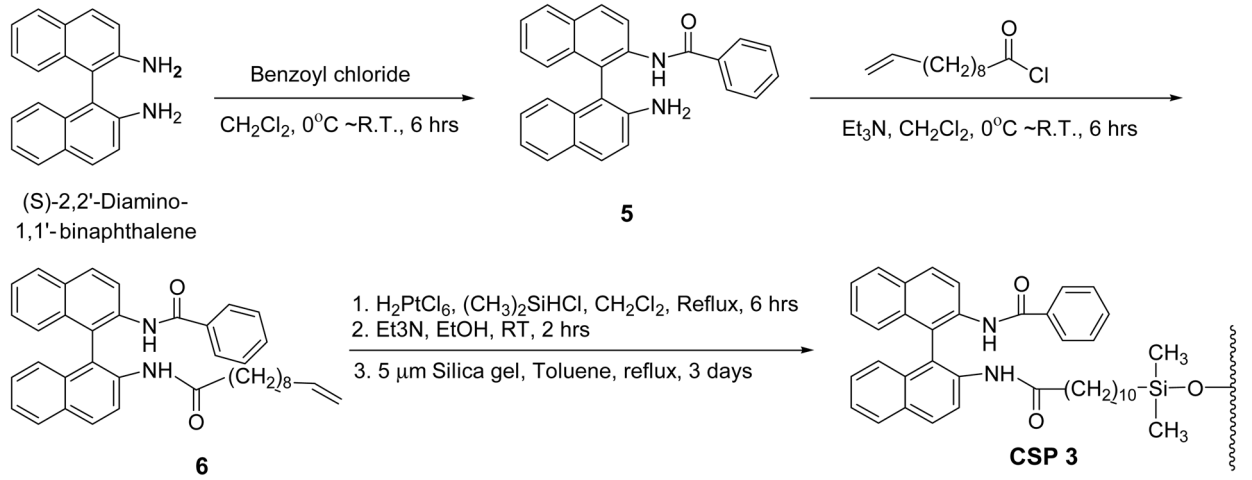
The chromatographic separation data of the 11 racemic



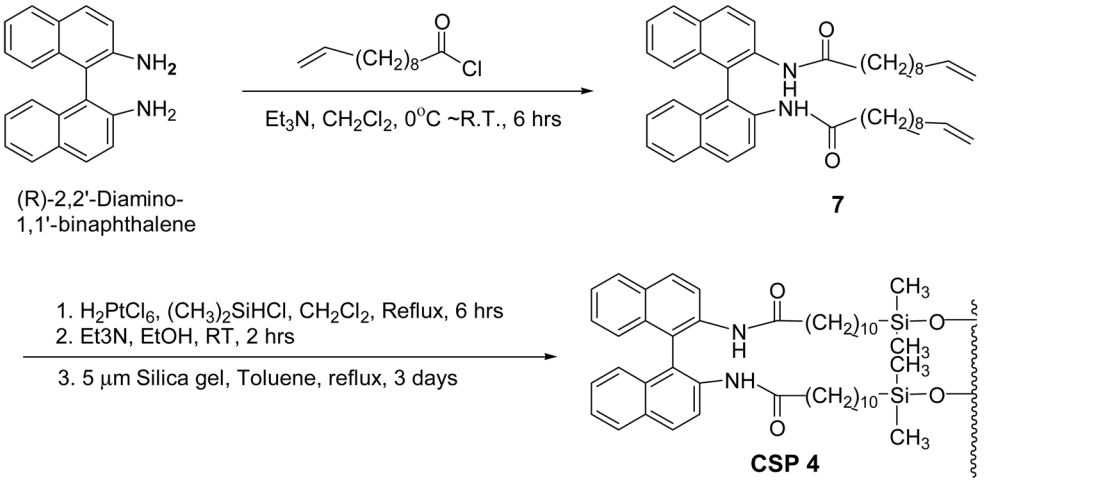

**Scheme 1**




**Scheme 2**




**Scheme 3**




**Scheme 4**

samples on CSP 1 are summarized in Table 1.

As shown in Table 1, better resolution was shown at low composition of IPA in heptane, therefore, the enantiomeric separation on CSPs 1-4 were performed by using 2.5% 2-propanol (IPA) in heptane as a mobile phase at a flow rate of 1.2 mL/min. The chromatographic separation data for 14 racemic samples on CSP 1-4 are summarized in Table 2. Thirteen racemic compounds were separated on CSP 1 and CSP 2, while only five and four chiral compounds were separated on CSP 3 and CSP 4, respectively. The dinitro-

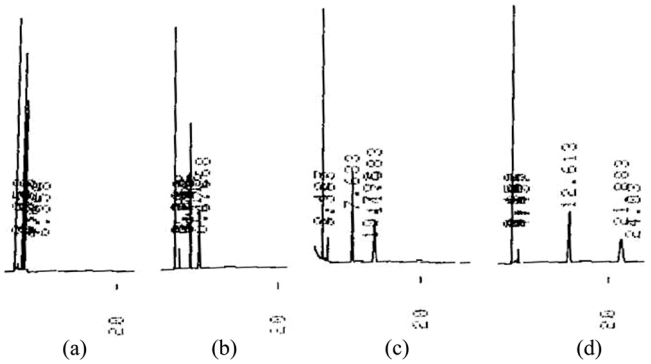



**Figure 2**. Separation of 2,2,2-trifluoro-1-(9-anthryl)ethanol (S2) enantiomers on CSP 1. Flow rate; 1.2 mL/min. Mobile phase (a) 20% isopropylalcohol (IPA) in heptane (b) 10% IPA in heptane (c) 5% IPA in heptane (d) 2.5% IPA in heptane.

**Table 1**. Separation data for eleven racemic compounds on CSP 1 as a function of different mobile phase compositions[a]

| Sample | Eluent (percent of IPA in heptane) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 2.5% | | 5% | | 10% | | 20% | |
| | $t_0$; 2.46 min | | $t_0$; 2.43 min | | $t_0$; 2.38 min | | $t_0$; 2.35 min | |
| | $k_1$ | $\alpha$ | $k_1$ | $\alpha$ | $k_1$ | $\alpha$ | $k_1$ | $\alpha$ |
| **S1** | 4.81 | 1.04 | 2.51 | 1.04 | 1.33 | 1.00 | 0.73 | 1.00 |
| **S2** | 4.13 | 1.91 | 2.14 | 1.76 | 1.15 | 1.57 | 0.53 | 1.35 |
| **S3** | 7.02 | 1.02 | 5.02 | 1.01 | 2.63 | 1.00 | 1.08 | 1.00 |
| **S4** | 4.34 | 1.07 | 3.16 | 1.05 | 1.85 | 1.00 | 0.97 | 1.00 |
| **S5** | 21.8 | 1.04 | 10.1 | 1.05 | 3.79 | 1.04 | 1.96 | 1.04 |
| **S6** | 9.85 | 1.06 | 4.74 | 1.06 | 2.01 | 1.05 | 1.03 | 1.00 |
| **S7** | 4.46 | 1.04 | 2.40 | 1.04 | 1.17 | 1.00 | 0.62 | 1.00 |
| **S8** | 14.5 | 1.04 | 6.98 | 1.04 | 2.77 | 1.04 | 1.33 | 1.00 |
| **S9** | 4.03 | 1.24 | 2.11 | 1.20 | 1.16 | 1.18 | 0.55 | 1.17 |
| **S10** | 5.50 | 1.03 | 3.76 | 1.04 | 2.29 | 1.04 | 1.27 | 1.00 |
| **S11** | 8.23 | 1.07 | 5.24 | 1.06 | 2.77 | 1.04 | 1.33 | 1.00 |

[a]Flow rate; 1.2 mL/min. detection 254 nm UV.

benzoyl (DNB) group containing CSPs (CSP 1 and CSP 2) showed much broader selectivity than the previously reported binaphthalene or diphenylethanediamine derived CSPs.[6-14] There are some interesting points in this resolution. For example, sample 13 (S13) was separated on both CSP 2 and CSP 3, but not on CSP 1. Also samples 9 and 14 were separated on all four CSPs with moderate separation factors.

In conclusion, four different binaphthyldiamine derived chiral stationary phases were easily prepared and used to study the separation of 45 commercially available chiral compounds. The numbers of separated samples on each CSP are as follows; CSP 1 (12/45), CSP 2 (12/45), CSP 3 (4/45), CSP 4 (3/45). The two dinitrobenzoyl (DNB) group containing CSPs (CSP 1 and CSP 2) showed much better results than the previously reported binaphthalene or diphenylethanediamine derived CSPs.

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**Table 2**. Resolution of fourteen chiral compounds on CSP 1-4[a]

| Sample | CSP 1 | | CSP 2 | | CSP 3 | | CSP 4 | |
|---|---|---|---|---|---|---|---|---|
| | $t_0$; 2.46 min | | $t_0$; 2.34 min | | $t_0$; 2.38 min | | $t_0$; 2.34 min | |
| | $k_1$ | $\alpha$ | $k_1$ | $\alpha$ | $k_1$ | $\alpha$ | $k_1$ | $\alpha$ |
| **S1** | 4.81 | 1.04 | 6.62 | 1.03 | 2.68 | 1.00 | 2.47 | 1.00 |
| **S2** | 4.13 | 1.91 | 7.90 | 1.04 | 1.88 | 1.00 | 2.30 | 1.00 |
| **S3** | 7.02 | 1.02 | 12.19 | 1.03 | 6.95 | 1.00 | 6.28 | 1.00 |
| **S4** | 4.34 | 1.07 | 6.93 | 1.06 | 3.83 | 1.00 | 3.51 | 1.00 |
| **S5** | 21.75 | 1.04 | 2.42 | 1.00 | 3.80 | 1.00 | 3.67 | 1.00 |
| **S6** | 9.85 | 1.06 | 13.40 | 1.06 | 8.06 | 1.00 | 7.09 | 1.00 |
| **S7** | 4.46 | 1.04 | 5.58 | 1.00 | 4.53 | 1.00 | 4.02 | 1.00 |
| **S8** | 14.49 | 1.04 | 17.63 | 1.03 | 11.29 | 1.00 | 10.54 | 1.00 |
| **S9** | 4.03 | 1.24 | 8.51 | 1.38 | 3.20 | 1.14 | 2.02 | 1.19 |
| | (R) | | (R) | | (S) | | (R) | |
| **S10** | 5.50 | 1.03 | 7.09 | 1.03 | 3.70 | 1.00 | 3.37 | 1.00 |
| **S11** | 8.23 | 1.07 | 17.10 | 1.17 | 4.88 | 1.06 | 3.71 | 1.04 |
| **S12** | 4.78 | 1.00 | 6.34 | 1.02 | 2.65 | 1.00 | 2.27 | 1.00 |
| **S13** | 2.20 | 1.00 | 3.78 | 1.05 | 1.66 | 1.14 | 1.45 | 1.00 |
| **S14** | 1.76 | 1.35 | 2.76 | 1.19 | 1.43 | 1.22 | 1.31 | 1.24 |

[a]Eluent; 2.5% IPA/Heptane. Flow rate; 1.2 mL/min. detection 254 nm UV.

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