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On the Mechanism of the Photochemical Reaction between 1,4-Dicyanobenzene and 2,3-Dimethylbutene in the Presence of Nucleophiles.

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Abstract. The irradiation of 1,4-dicyanobenzene (DCB) in the presence of 2,3-dimethyl-2-butene (DMB) leads to allylation of the aromatic. In the presence of nucleophiles (MeOH, H_2O, CF_3CH_2OH) this reaction is substituted by the nucleophile olefin combination - aromatic substitution (NOCAS) process. The quantum yield increases from 0.006 in the absence to a limiting value of ca 0.02 in the presence of the nucleophiles. The reaction involves competing deprotonation and nucleophile addition to the olefin radical cation, followed by coupling of the thus formed radical with $DCB^{-\cdot}$. Minor processes are hydrogen abstraction from the solvent by the allyl radical, revealed by isolation of the phenylpentanonitrile **3** and coupling of the radical ions before separation, revealed by a small amount of the cyclohexadiene **6**.
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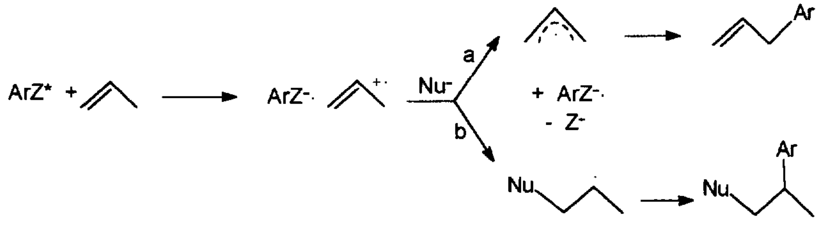
Aromatic nitriles are strong acceptors in the singlet excited state, and their interaction with alkenes mostly involves electron transfer (SET).[1] The radical cation of alkenes is thus formed, and its characteristic reactions are dimerization[2-6] and nucleophile addition.[5,6] Further reactions involve coupling between the arenenitrile radical anion and an alkyl radical. In turn, this arises from the alkene radical cation either by deprotonation, and then the end result is substitution of a cyano by an allyl group (path a in Scheme 1), or by nucleophile addition, and then the overall process is nucleophile olefin addition - aromatic substitution, known with the acronym NOCAS (path b).[7-14] The two last reactions offer a new path for aromatic functionalization.

Scheme 1



The NOCAS process has been thoroughly characterized and its synthetic potential is significant since a complex and regioselective functionalization is obtained in a single step often in a good chemical yield. This reaction has been extended also to alkenes rearranging at the radical ion stage,[9,14] conjugated[11] and non conjugated dienes,[12a-c] and alkenols (for intramolecular trapping).[12c,d]

Obviously, consideration for synthetic planning benefits from a clear knowledge of the mechanism, in particular the relation of the NOCAS reaction with competing processes, e.g. simple alkylation. At the moment, some detailed mechanistic issues have not yet been clarified. As an example, at which stage is the C-C bond formed, viz, does alkylation involve addition between the radical ions, or previous deprotonation of the alkene radical cation and neutral radical - radical anion addition? Is the alkene arylation regioselective? Does nucleophile addition precede or follow the C-C bond formation? Therefore, we decided to further examine the prototype system, the photochemistry of DCB in the presence of 2,3-dimethylbutene (DMB) under various conditions.

Results

All the reactions were carried out in the presence of phenanthrene (Phen) under conditions where only this additive absorbed the light. There is ample previous evidence[7] that this is advantageous, due both to the better matching of the Phen absorption with the emission of commonly available mercury arcs and to the increased efficiency of SET photoinduced reactions when secondary electron transfer takes place.

Irradiation of DCB - DMB in the presence of Phen in acetonitrile gave, as previously reported, the two allylbenzonitriles **1** and **2**, but a small amount of a further alkylated benzonitrile was isolated. The last compound was identified as the pentanonitrile **3** on the basis of analytical and spectroscopic properties (Scheme 2, Table 1).

Likewise, irradiation of the same system in MeCN-MeOH 3:1 gave, again as reported, the ether **4** as the main product. The pentanonitrile **3** was again present, and minor products were the alcohol **5** as well as a non aromatic derivative which was identified as the 1,4-cyclohexadiene-1,4-dinitrile **6** on the basis of the spectroscopic properties (see in particular the ABX system for the methylene group in position 6 and the small H-3 H-6 coupling in ^{1}H Nnmr and the ^{13}C nmr spectra in the Experimental). When the reaction was repeated using MeOD, no ring deuteration occurred in product **4**, while in the dihydroaromatic derivative **6** selective monodeuteration in position 5 took place.

The effect of different nucleophiles was explored. Thus, irradiation of the same system as above in MeCN containing 2% water gave the alcohol **5** as the main product, along with a minor amount of the nitrile **3**. Similar irradiation adding 0.05% trifluoroacetic acid greatly reduced the amount of **5**.

Finally, irradiation in MeCN containing 10% trifluoroethanol could not be led to completion, since the solution underwent rapid yellowing due to the formation of new absorptions in the 300-400 nm region, and the the reaction was stopped at virtually 25% DCB conversion. The only products identified under these conditions were the allyl derivative **2** and a new compound recognized as the trifluoroethyl ether **7**.

Quantum yields were measured in low conversion experiments. The measured values are reported in Table 2. These experiments were carried out at low (≤25%) DCB conversions. Under this condition the proportion of the allylated derivatives **1** and **2** is higher than in the preparative runs, which is understandable since these compounds are known to be themselves photoreactive.[7]

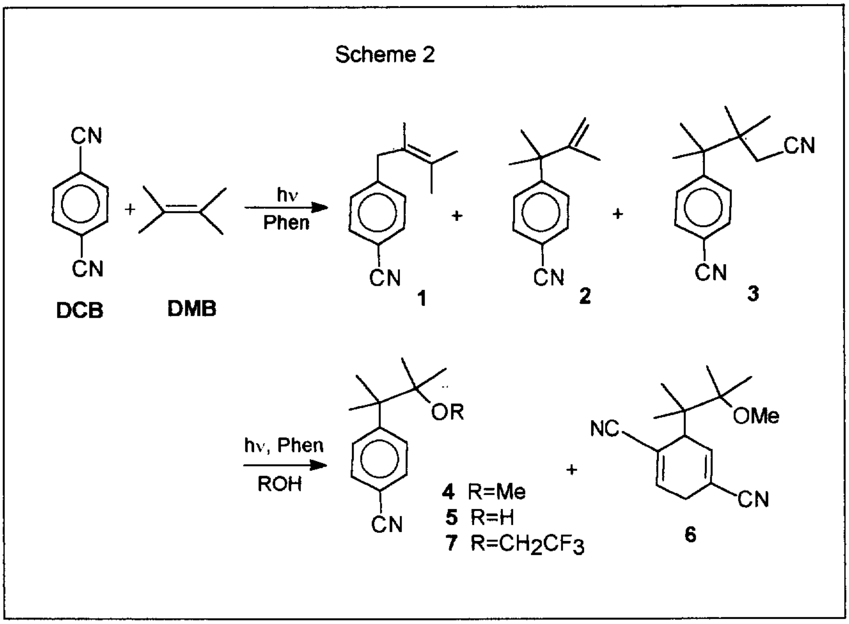


Table 1. Chromatographic isolated yield from the photoreaction of DCB in the presence of DMB

Solvent	Products (%)Yield
MeCN	**1**(20), **2**(22), **3**(6)
MeCN-MeOH 3:1	**3**(3), **4**(68), **5**(3), **6**(9)
MeCN-2% H_2O	**3**(3), **5**(46)
MeCN-10% $CF_3CH_2OH^a$	**1**(2), **2**(2), **7**(15)

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a. the reaction stopped at 25% DCB conversion, due to the formation of coloured by-products

Table 2. Quantum yield for the photoreaction of DCB in the presence of DMB (low conversion experiments).

Solvent	Φ(-DCB)	Φ(Products)
MeCN	0.006	**1**(0.002), **2**(0.0035)
MeCN-MeOH 3:1	0.017	**1**(0.0016), **2**(0.003), **4**(0.011)
MeCN-2% H_2O	0.017	**1**(0.001), **2**(0.0015), **5**(0.01)
MeCN-10% CF_3CH_2OH	0.012	**1**(0.001), **2**(0.0015), **7**(0.002)

In order to determine the amount of methanol required to divert the DCB alkylation from the formation of products **1** and **2** to the formation of ether **4**, irradiations in different MeCN-MeOH mixtures as the solvent were performed under the low conversion conditions mentioned above. As it appears in Fig.1, the quantum yield for DCB conversion grew and attained a limiting value at ca 5% MeOH, but the product distribution changed in favour of product **4** at a larger MeOH content.

Irradiation in the presence of 2,6-lutidine was performed both in neat, anhydrous MeCN and in 3:1 MeCN-MeOH . In the first case the quantum yield of the reaction increased for base concentration in the 0.001-0.1 M range, doubling at 0.005 M, while in the latter one no change was observed in this region.

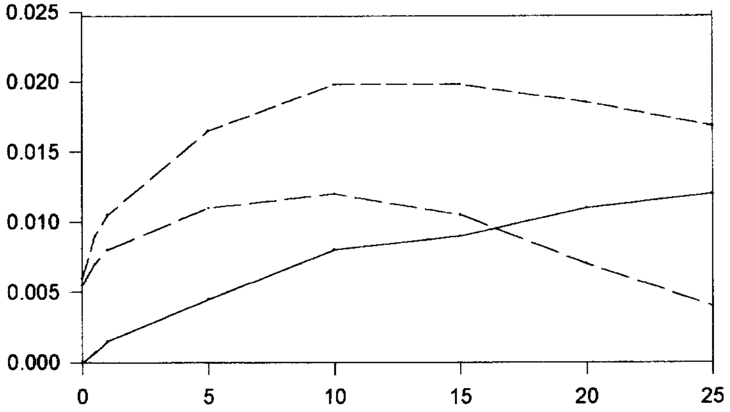


Figure 1. Quantum yield for reaction of DCB (----) and for formation of products **1+2** (_ _ _ _) and **4** (_______) as a function of the solvent composition (% MeOH in MeCN vol/vol).

Discussion

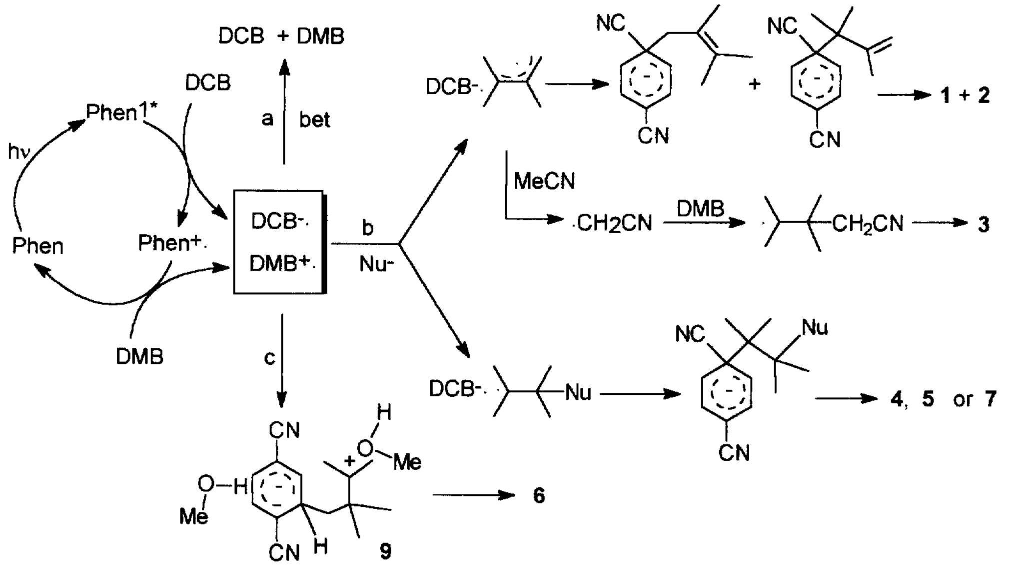
The present results can be satisfactorily discussed in the frame of the known SET photochemistry of arenenitriles in the presence of alkenes. Under the conditions of the experiments Phen absorbs the light, and quenching of Phen^{1*} by DCB followed by secondary electron transfer from DMB to Phen$^{+\cdot}$ leads to the reactive radical ions (Scheme 3).

Similarly to what observed in previous cases, the end products depend on the reactions of the alkene radical cation under the conditions chosen. Thus, allylation of arenenitriles occurs in inert solvents (in this case leading to the arylalkenes **1** and **2** from DCB and DMB in acetonitrile) and is substituted by the NOCAS process in the presence of a nucleophile. The results show that the latter reaction is quite general: addition of water gives alcohol **5** under conditions similar to those leading to the ether **4** with methanol, and even with the poorly nucleophilic trifluoroethanol this process (giving ether **7** in this case) is observed, although with a lower quantum yield.

Discussing first the allylation, we note that the quantum yield of this process in neat acetonitrile is rather low (0.006). This is no exception, since all reported reactions involving the SET deprotonation sequence occur with a quantum yield <<0.1.[1,15] This is due to the predominance of back electron transfer (path a in Scheme 3) over all chemical reactions, in the present case deprotonation. The base is here the solvent, since previous experiments with dicyano benzenes[7] and other evidence[15] show that the proton is not transferred to the acceptor radical anion, a very poor nucleophile. Addition of methanol increases the yield of both allylation and NOCAS reaction. The overall quantum yield increases by a factor of 3 reaching a plateau value of ca 0.015-0.02 with >5% v/v (1.3M) alcohol content (Fig.1).

The ratio between the two alkylation products does not change significantly over the observed range, while the NOCAS process overcomes alkylation at >15% alcohol content. The yield of alkylation is increased also by addition of lutidine. This doubles the quantum yield at 0.001 M level, again with no change in the **1**/**2** isomer ratio. However, lutidine does not affect the reaction in methanol. The invariance of the **1**/**2** ratio suggests that both alkylated products are formed, at least predominantly, through the same intermediate, and thus that C-C bond formation takes place after deprotonation, rather than the reverse.

Scheme 3



The determining step is deprotonation of the radical cation. The thermodynamic acidity can be calculated by means of the Nicholas-Arnold equation[16]:

$$pK_a(\text{R-H}^{+\cdot}) = 1/2.303\ RT \cdot (-FE^\circ_{\text{R-H}} + \Delta G^\circ_{\text{tr(H}^+\text{)solv}} - \Delta G^\circ_{\text{f(H)g}} + \Delta G^\circ_{\text{BDE(R-H)}})$$

Introducing the appropriate values and with the usual approximation that $\Delta H^\circ_{\text{BDE(R-H)}}$ is substituted for $\Delta G^\circ_{\text{BDE(R-H)}}$, the equation is reduced to

$$pK_a(R\text{-}H^{+\cdot}) = -16.91E(R\text{-}H) - 27.55 + BDE(R\text{-}H)/1.36$$

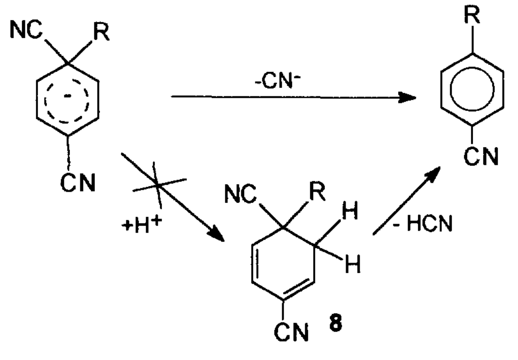
as a function of the oxidation potential (vs NHE) of the substrate and of the BDE (kcal mol^{-1}) of the substrate. For $DMB^{+\cdot}$ one obtains pK_a -1.5. Even more negative values have been evaluated for other radical cations,[16] but this certainly suggests that deprotonation of this intermediate will occur fast enough to compete with back electron transfer at least in the presence of cosolvents more nucleophilic than acetonitrile, such as methanol.

Consistently with the limited acidity of the radical cation, a better nucleophile such as lutidine is active at a much lower concentration, although also in this case the quantum yield increase obtained is moderate. Conversely, addition of a small amount of an acid (0.05% CF_3CO_2H in 2% water containing MeCN) prevents the increase of the quantum yield and the occurring of the NOCAS reaction.

The thus formed allyl radical couples with DCB radical anion to yield an anion and final cyanide loss leads to the observed products. Noteworthy, coupling between $DCB^{-\cdot}$ and the allyl radical occurs at a comparable rates both at the primary and at the tertiary position. This coupling appears to be sensitive to polar effects, since we previously observed that with the more stabilized radical anion of 1,2,4,5-tetracyanobenzene attack at the primary position is by far the major reaction.[13] The allyl radical has at any rate a significative lifetime, since some hydrogen abstraction from the solvent occurs. This is somewhat unexpected, in view of the stability of the allyl radical, and is certainly a minor process, as indicated by the fact that the cyanomethyl radicals generated are less than 10% of the initial radicals, as judged from the final alkylation products. Addition of this nucleophilic radical to DMB and coupling of the adduct radicals with $DCB^{-\cdot}$ (similarly to the key step of the NOCAS reaction) lead to product **3**, thus revealing the radicalic sequence. In the meantime, Roth has also found products revealing the $\cdot CH_2CN$ radical in the reaction of DCB with norbornadiene.[14a]

The NOCAS process depends on the competition between deprotonation and addition of the nucleophile on the alkene radical cation. As Fig.1 shows, methanol at a relatively low concentration (<1M) acts essentially as proton acceptor, and only at a higher level the product ratio shifts towards the NOCAS product with no change of the total quantum yield. This seems well accountable by assuming that at >1M MeOH the radical ions have unitary probability of being (statically) complexed by one molecule of the alcohol, and there the deprotonation probability (and the overall quantum yield) reachs the maximum value. Increasing the number of methanol molecules in the solvation sphere of the radical cation favours nucleophile addition over proton transfer but does not affect the chemical reaction vs back electron transfer (the latter largely dominating) ratio.

Scheme 4



Just as for the allylation case, the NOCAS reaction involves radical - radical anion coupling, and this takes place, as in the previous case, at the position of highest spin in the acceptor radical anion.[7,17,18] Cyanide loss from the anion then leads directly to the aromatic derivative, while protonation of the anion followed by dehydrocyanation of a dihydroaromatic derivative (see formula **8**, Scheme 4) is unimportant, as shown by the lack of deuterium incorporation in product **4** in the methanol -d_1 experiments.

The minor product **6** is an exception to this mechanism both because a dihydro rather than a rearomatized derivative is obtained and because alkylation takes place at position 2 rather than 1. This suggests that a different path is involved (see path c in Scheme 3). This can be explained by admitting that direct C-C bond formation in the initial radical ion pair occurs as a minor process, and leads to the zwitterion **9**, which may receive some stabilization from charge-pairing. Nucleophile and proton addition then occur in such a way as to form the most stable cyclohexadienedinitrile **6**. No analogous dihydro derivatives have been previously isolated for 1,2- and 1,4-dicyanobenzene, but some tetrahydro derivatives were detected in the NOCAS reaction of *m*-dicyanobenzene - DMB in the presence of methanol (which occurs in position 3).[7] It is relevant to note that minor products involving alkylation of the aromatic at a position different form that of the highest spin have been previously rationalized as arising from a geminate radical ion pair rather than free radical ions.[18,19]

Of the three process from the radical ion pair in Scheme 3, under the best condition for reaction (presence of a nucleophile), back electron transfer (path a) accounts for ca 98%, reaction of the free radical cation (path b, either proton transfer or nucleophile addition) for slightly over 1%, and direct C-C bond formation (path c) to yield a zwitterion for less than 0.1%.

Summing up, this work has given some new evidence about the sequence followed in aromatic alkylation and the NOCAS process, photochemical processes in which initial SET is followed by several steps. The main path involves either proton transfer to or addition of a nucleophile from the radical cation, and recombination of the alkyl radicals with DCB$^{-\cdot}$ (for a part the radicals diffuse and abstract a hydrogen atom from the solvent). A minor path involves radical ion coupling before diffusion and is revealed by the formation of product **6**. The relatively low rate of reaction of alkene radical cations makes this reaction inefficient, but modification of the medium offers some opportunity for controlling the follow up reactions.

Experimental

Photochemical reactions. Solutions (80 mL) of DCB (1.3x10^{-2}M), phenanthrene (3.1x10^{-3}) and DMB (0.25M) were subdivided in three qurtz tubes, flushed with argon, serum capped and irradiated by means of six phosphor-coated 15W lamps (centre of emission, 320 nm). The solution was analysed by gpc and the products separated as oils by silica gel column chromatography eluting with cyclohexane - ethyl acetate 8 to 2 mixture. Quantum yields were determined with reference to a benzophenone (0.05M) - benzhydrol (0.1M) solution with vpc determination.

Products **1**, **2**, and **4** had been previously reported.[7] The main characteristics of the new products are as follows.

4-(4-Cyanophenyl)-3,3,4-trimethylpentanonitrile (**3**) ^{1}H nmr ($CDCl_3$, 300 MHz) δ: 1.05 (s, 6H), 1.4 (s, 6H), 2.2(s, 2H), 7.45 and 7.6 (AA'BB' system, 4H); ^{13}C nmr δ: 22.9 (CH_2), 23.8 (CH_3), 27.2 (CH_2), 38.2, 43.3, 110.1, 118.4 (CN), 118.5 (CN), 128.6 (CH), 131.1 (CH), 150.73. ms 226 (M^+). Anal. C, 79.5;.H, 8.3; N, 12.2. Calcd for $C_{15}H_{18}N_2$: C, 79.90; H, 8.02; N, 12.38.

2-(4-Cyanophenyl)-1,1,2-trimethylpropanol (**5**) ^{1}H nmr [$(CD_3)_2CO$] δ: 1.1 (s, 6H), 1.45 (s, 6H), 3.4 (s, 1H, exch), 7.7 (AA'BB' system, 4H). ^{13}C nmr 24.0 (CH_3), 25.8 CH_3), 45.4, 74.3, 109.5, 118.9 (CN), 128.9 (CH), 131.0 (CH), 152.3. Anal. C, 76.5;.H, 8.5; N, 6.6. Calcd for $C_{13}H_{17}N_2O$: C, 76.81; H, 8.43; N, 6.89.

3-(2-Methoxy-1,1,2,2-tetramethylethyl)-cyclohexa-1,4-diene-1,4-dicarbonitrile (**6**) ^{1}H nmr ($CDCl_3$) δ: 0.9 (s, 3H), 1.1 (s, 3H), 1.15 (s, 3H), 1.2 (s, 3H), 2.98 (AB part of an ABX system, 2H, H-6), 3.2 (s, 3H, OMe), 3.35 (X part, dt, $J_{2,3}$ = 6Hz, $J_{3,6}$ = 4.5Hz, H-3), 6.8 (t, $J_{2,6}$ = 4Hz, H-5), 6.9 (dt, $J_{2,3}$ = 6Hz, $J_{2,6}$ = 1 Hz, H-2), the appropriate double irradiation experiments were in accord with the suggested structure; ^{13}C nmr δ: 19.6 (CH_3), 19.7 (CH_3), 19.8 (CH_3), 22.4 (CH_3), 28.7 (CH_2), 44.1 (CH), 48.5 (OMe), 50.6, 79.9, 107.8, 115.1, 118.3 CN), 119.6 (CN), 142.4 (CH), 147.5 (CH). Anal. C, 73.9;.H, 8.3; N, 11.2. Calcd for $C_{15}H_{20}N_2O$: C, 73.73; H, 8.25; N, 11.43. In the presence of MeOH-d_1 a single derivative was obtained. This showed the following differences: ^{1}H nmr δ: 2.98 (1H), 3.35 (dd, J = 6 and 4.5 Hz, 1H), 6.68 (d, J = 6 Hz, 1H), 6.9 (dd, J = 6 and 1 Hz, 1H); ^{13}C nmr δ: 28.7 (t).

2-(4-Cyanophenyl)-1,1,2-trimethylpropyl 2,2,2-trifluoroethyl ether (7) ^{1}H nmr ($CDCl_3$) δ: 1.05 (s, 6H), 1.45 (s, 6H), 3.6 (q, $J_{H\text{-}F}$ = 6Hz, 2H), 7.6 (s, 4H). Anal. C, 63.2;.H, 6.4; N, 4.8. Calcd for $C_{15}H_{18}N_3F_3O$: C, 63.14; H, 6.36; N, 4.91.

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