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Oxidation–Reduction ofMethionine Sulfoxide Induced by anArgon–Hydrogen Plasma Jet

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ABSTRACT

Formation of hydroxyl and hydrogen radicals from water molecules has explained the mechanism of plasma-induced reactionsin aqueous solutions. Oxidation–reductionofthe carbon–carbon double bond using an argon–hydrogen plasma jet hasdemonstrated the action of hydrogen radicals.This paper describes the action of hydrogen radicals onmethionine sulfoxide induced byan argon–hydrogen plasma jet. Methionine sulfoxide gave 2-amino-1-butanoic acid with a yield of 33%. Carbon radical formation from methionine sulfoxide may explain the mechanism.

Keywords: Plasmajet, Methionine sulfoxide,Oxidation–Reduction, Argon–Hydrogen

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INTRODUCTION

Fundamental research and industrial applications [1–4] of plasma-induced reactionshave beenperformed to clarify the mechanism of several types of reactions [1–4]. The gaseous, solution, and phase-boundary reactions induced by a plasma have been reported in relation toorganic syntheses [1–4]and simulation of prebiotic reactions [5–20]. Hickling et al. had originally investigated[21–23] a glow discharge electrolysis in the solution phase and the boundary between gaseous and solution phases.Haradaand co-workershave developedthis type of glow discharge [5–8, 12, 14–18, 20] electrolysis of organic compounds as well as other types ofplasma-induced reactions,such as flame [11] and plasma jet [9–11, 13, 19, 20] in the solution phase and at the boundary between gas and solution phases.These plasma sources havebeen appliedto oxidation, reduction, amination, carboxylation, and other reactions.The triggerfor these reactions seemed to bethe dissociation of water molecules to form hydroxyl and hydrogen radicals [18], as shown in Scheme 1. These radical species abstract hydrogen from carbon–hydrogen bonds to form carbon radicals, which undergo hydroxylation, hydrogenation, carboxylation, and other reactions[11]. Reduction of the carbon–carbon double bond in maleic acid [19], acrylic acid, crotonic acid, vinylacetic acid, and allylamine gave the corresponding aliphatic compounds [24].

$$, H_2O \longrightarrow \cdot OH + \cdot H$$

Scheme 1

Although the carbon–carbon double bond described above proved to be a good acceptor of hydrogen and hydroxyl radicals, the sulfur atom composing organic compounds also suggestsa good indicator to look at the oxidation–reduction induced by a plasma jet blowing into aqueous solutions. This is because the compound is easily oxidized and reduced. In the case of an argon plasma jet blowing into methionine (**1**), the compound diminishedin only 5 min to give methionine sulfoxide (**2**)(60%, 5 min), methionine sulfone (**3**) (24%, 8 min), homocysteic acid (**4**)(4%, 30 min), homoserine (**6**)(2%, 20 min), 2-formyl-alanine (**7**) (3%, 20 min), aspartic acid(**8**) (14%, 30 min)and glycine (**9**)(2%, 30 min).Scheme 2 shows the pathway for degradation of methionine induced by an argon plasma jet. The plain arrows give the same pathway as in the literature [10].Formation of homoserine (**6**) from methionine (**1**) strongly suggests the existence of intermediate (**5**), which reacts with hydroxyl radicals to afford homoserine (**6**). Therefore, intermediate (**5**) may react with hydrogen radicalsproduced by a hydrogen plasma jet, but the reactions indicated by dashed lines are not clear.

This paper describes the reactions of methionine sulfoxide with hydrogen radicals generated by an argon–hydrogen plasma jet.
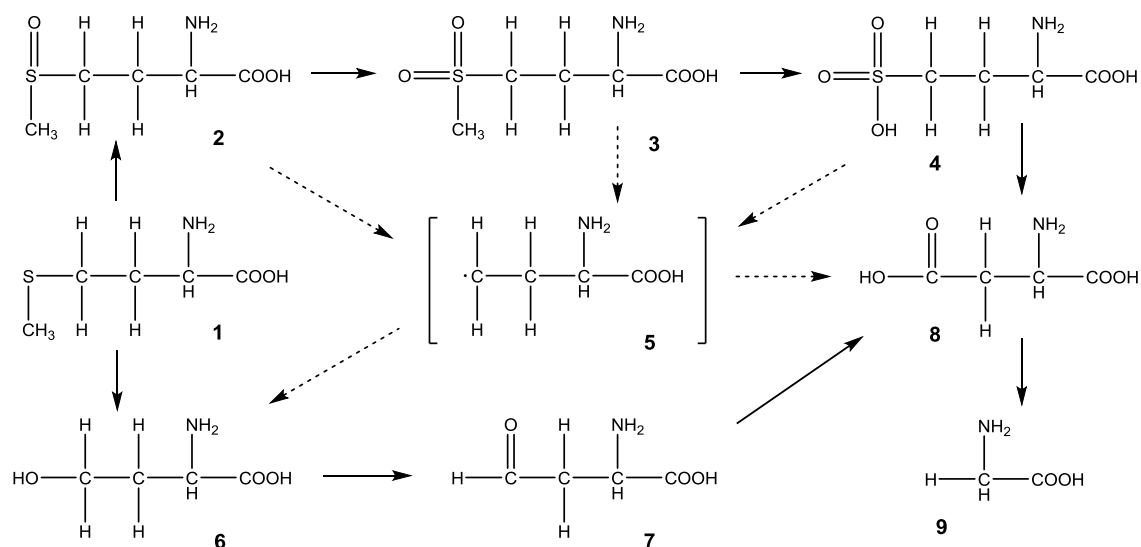
Scheme 2

EXPERIMENTAL

Methionine sulfoxideand the standard compoundsof the reaction productswerepurchased from Tokyo Chemical Industry Co., Ltd.The apparatus for the reactions induced by an argon–hydrogen plasmajet has been reportedpreviously [24].A Well Pen NP-7 (Nippon Welding Co.) was used as the plasmajet generator through a flow of an argon–hydrogen gas mixture. A plasma torch incorporating a tungsten rod cathode (100 mm × 2.5mmI.D.) and a copper nozzle anode (1.8mmI.D.) was immersed from the central vent into a reaction solution (300 mL) containing a substrate compound in a cylindrical reaction vessel. The reaction vessel was a double-walled structure in which the inner chambercontained the reaction solution and the outer chambercontained circulating water to cool the reaction solution. A Liebig condenser was connected to another vent of the reaction vessel. The reaction temperature was maintainedat 30°C by this cooling system. The total flow rate of the argon–hydrogen mixturewas controlledat 2.0L/min.

Argon gas was bubbled through the torch into the reaction solution, and thenthe plasmajet at the torch was introduced into the reaction solution. A part of the reaction solution was removedat a constant period for analysis.

The removed reaction solutionwas analyzed with a Hitachi 835 amino acid analyzer.

RESULTS AND DISCUSSION

Formation of 2-amino-1-butanoic acid

Figure 1 shows the time course of hydrogenation of methionine sulfoxide (**2**) by the argon–hydrogen plasma jet. Methionine sulfoxide (**2**) rapidly decreased and the recovery decreased to 10% at 90 min. The product 2-amino-1-butanoic acid (**10**) formed gradually up to 33% at 60min. Oxidation products, methionine sulfone (**3**) and homocysteic acid (**4**); reduction products, methionine (**1**) and homoserine(**6**),were detected ata lower yield than 10%.Formation of 2-amino-1-butanoic acid (**10**) suggests radical–radical coupling between the carbon radical intermediate (**5**) and hydrogen radical, as shown in Scheme 3. However, the formation pathway of the carbon radical intermediate (**5**) has to beclear as well as further evidence of the formation.
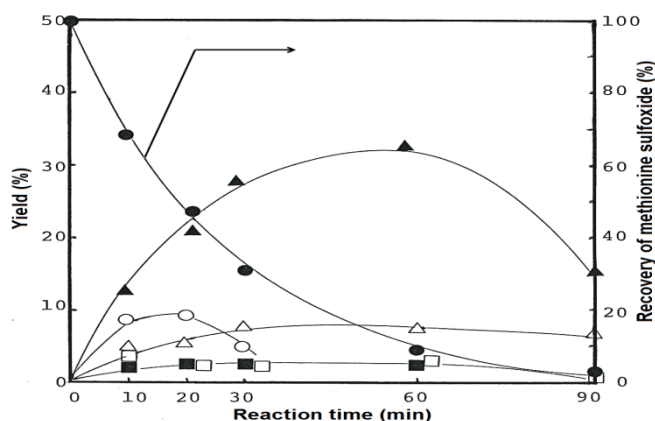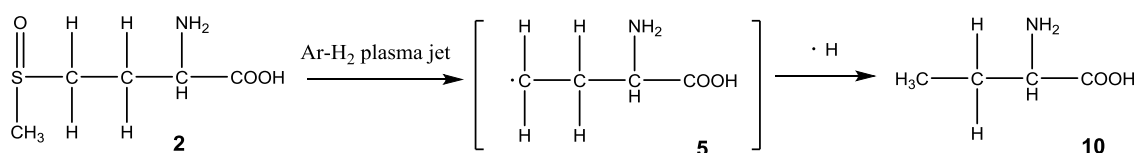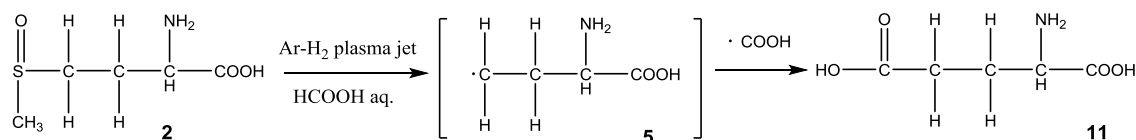

Fig. 1. Formation of 2-amino-1-butanoic acid (**10**)from an aqueous solution of methionine sulfoxide (**2**) (0.50mM) at 30°C induced by an argon–hydrogen plasma jet blowing at the gas flow rates of 1.5 L/min (argon) and 0.5 L/min (hydrogen). Electric current and voltage were maintained at 20 A and 15V, respectively.□: methionine (**1**); ●: methionine sulfoxide (**2**); ○: methionine sulfone (**3**); △: homocysteic acid (**4**); ■: homoserine (**6**); ▲: 2-amino-1-butanoic acid (**10**)

Scheme 3

Trapping of carbon radical using formic acid

First, trapping the carboxyl radical using formic acid may prove the formation of carbon radical intermediates. This method has afforded carboxylic acids to clarify the mechanism of reactions induced by plasma jets[11,14,16].
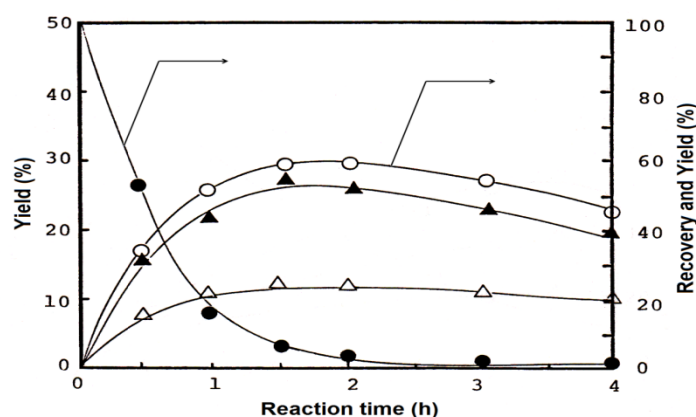
Scheme 4

Fig. 2.Reaction of methionine sulfoxide (**2**) (0.50mM) in 5% formic acid aqueous solution at 30°C induced by an argon–hydrogen plasma jet blowing at the gas flow rates of2.0 L/min (argon) and 0.0 L/min (hydrogen). Electric current and voltage were maintained at 20 A and 15V, respectively.

●: methionine sulfoxide (**2**); ○: methionine sulfone (**3**); △: 2-amino-1-butanoic acid (**10**); ▲: glutamic acid (**11**)

Figure 2 shows the time course of the reaction of methionine sulfoxide (**2**) in 5% formic acid induced by the argon plasma jet.Methionine sulfoxide (**2**) decreased rapidly and diminished after 4 h reaction to yield methionine sulfone (**3**) up to 60% at 2 h, glutamic acid (**11**) (27%, 1.5 h), and 2-amino-1-butanoic acid (**10**) (12%, 1.5 h).It seems reasonable for methionine sulfoxide (**2**) to yield its sulfone (**3**) rapidly, because the argon plasma jet produces more hydroxyl radicals than the argon–hydrogen plasma jet does [23] and methionine sulfoxide (**2**) is very labile to hydroxyl radicals. Formation of glutamic acid (**11**) strongly suggests that a coupling reaction occurred between intermediate (**5**) and a carboxyl radical (Scheme 4).

Figure 3 shows the time course of the reaction of methionine sulfoxide (**2**) in 20% formic acid induced by the argon plasma jet.Degradation of methionine sulfoxide (**2**) was depressed to give 18% recovery at 4 h because of the scavenger effect of formic acid on the hydroxyl radical. Yields of the other products werelower than those in the reaction using 5%formic acid.
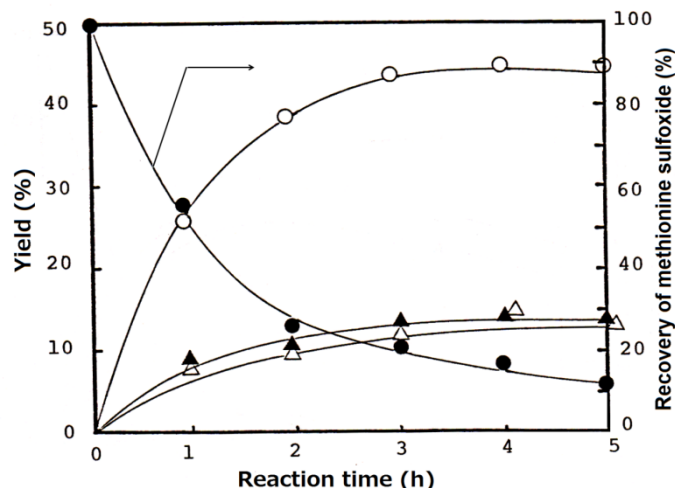
Fig. 3. Reaction of methionine sulfoxide (**2**) (0.50mM) in 20% formic acid aqueous solution at 30°C induced by an argon–hydrogen plasma jet blowing at the gas flow ratesof2.0 L/min (argon) and 0.0 L/min (hydrogen). Electric current and voltage were maintained at 20 A and 15V, respectively.

●: methionine sulfoxide (**2**); ○: methionine sulfone (**3**); △: 2-amino-1-butanoic acid (**10**); ▲: glutamic acid (**11**)
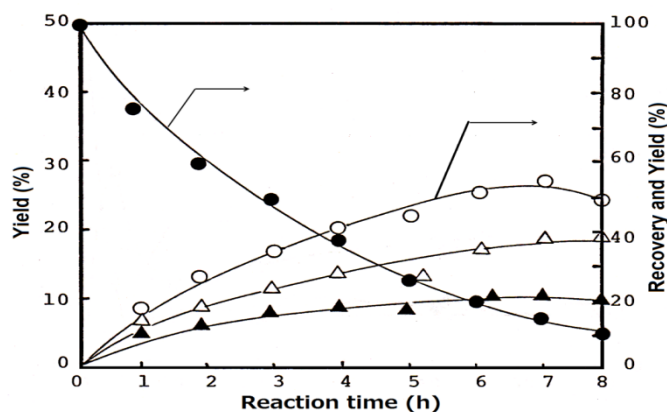

Fig. 4. Reaction of methionine sulfoxide (**2**) (0.50mM) in 40% formic acid aqueous solution at 30°C induced by an argon–hydrogen plasma jet blowing at the gas flow rates of 2.0 L/min (argon) and 0.0 L/min (hydrogen). Electric current and voltage were maintained at 20 A and 15V, respectively.

●: methionine sulfoxide (**2**); ○: methionine sulfone (**3**);△: 2-amino-1-butanoic acid (**10**); ▲: glutamic acid (**11**)

Figure 4 shows the time course of the reaction of methionine sulfoxide (**2**) in 40% formic acid induced by the argon plasma jet. Degradation of methionine sulfoxide (**2**) was depressed to give 40% recovery at 4 h. Yields of the other products, except for 2-amino-1-butanoic acid (**10**), were lower thanthose in the reaction using 20% formic acid.

Reaction of methionine (1) and methionine sulfone (3)

Figure 5 shows the time course of the reaction of methionine (**1**) in 20% formic acid

induced by the argon plasma jet. Methionine (**1**) rapidly decomposed with the rapid formation of methionine sulfoxide (**2**). After that, methionine sulfone (**3**) formed with the decrease of methionine sulfoxide (**2**). However, before methionine sulfone (**3**) emerged, 2-amino-1-butanoic acid (**10**) and glutamic acid (**11**) started to form. This result suggests that methionine sulfone (**3**) did not yield 2-amino-1-butanoic acid (**10**) and glutamic acid (**11**).

Figure 6 shows the time course of the reaction of methionine sulfone (**3**) in 20% formic acid induced by the argon plasma jet. Methionine sulfone (**3**) decomposed very slowly to give 92% recovery at 4 h;however, the amino acid analyzer could not detectthe products. This result shows that methionine sulfone (**3**) did not give the carbon radical intermediate (**5**).
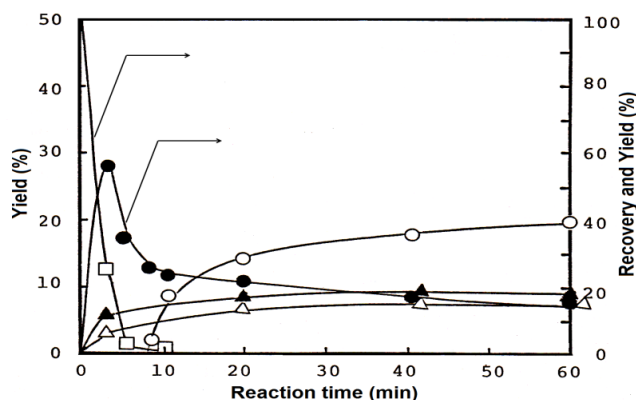

Fig. 5. Reaction of methionine (**1**) (0.50mM) in 20% formic acid aqueous solution at 30°C induced by an argon–hydrogen plasma jet blowing at the gas flow rates of 2.0 L/min (argon) and 0.0 L/min (hydrogen). Electric current and voltage were maintained at 20 A and 15V, respectively.

□: methionine (**1**); ●: methionine sulfoxide (**2**); ○: methionine sulfone (**3**); △: 2-amino-1-butanoic acid (**10**); ▲: glutamic acid (**11**)
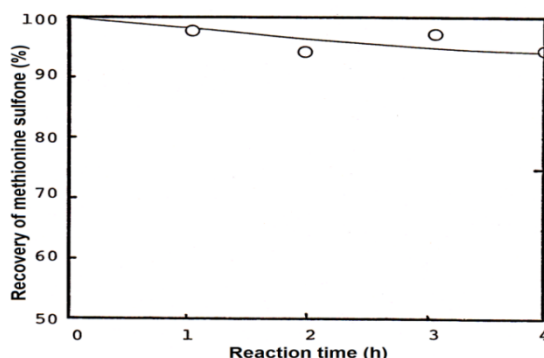

Fig. 6. Reaction of methionine sulfone (**2**) (0.50mM) in 20% formic acid aqueous solution at 30°C induced by an argon–hydrogen plasma jet blowing at the gas flow rates of 2.0 L/min (argon) and 0.0 L/min (hydrogen). Electric current and voltage were maintained at 20 A and 15V, respectively.

○: methionine sulfone (**3**)

Plausible reaction pathway from the results

Table 1 shows a summary of the plasma-induced reactions of methionine-related compounds.

The yield of 2-amino-1-butanoic acid(**10**) in the reaction using the argon–hydrogen plasma jet had the highest value (33%). The reactions using formic acid aqueous solutions gave 2-amino-1-butanoic acid (**10**) and glutamic acid (**11**).From this summary and the discussion in the abovesection, we can suggestthe plausible reaction pathway shown in Scheme 5.

Methionine sulfoxide (**2**) easily forms methionine sulfone (**3**). This reaction is common in all of the reactions carried out in this research. However, the formation of homocysteic acid (**4**) depends on the reaction conditions. Hydroxyl radicals accelerate the oxidation of methionine sulfone (**3**) to homocysteic acid (**4**), while formic acid depresses the oxidation of methionine sulfone (**3**).The carbon radical intermediate (**5**) seemed to form in the reactions. The primary evidence is the results that 2-amino-1-butanoic acid (**10**) formed using the argon–hydrogen plasma in water and argon plasma in formic acid solution, as well as the formation of glutamic acid (**11**) using the argon plasma in formic acid solutions.The secondary evidence is that homoserine (**6**) formed in the conditions without formic acid. In the formic acid case, glutamic acid (**11**) formed instead of homoserine (**6**).
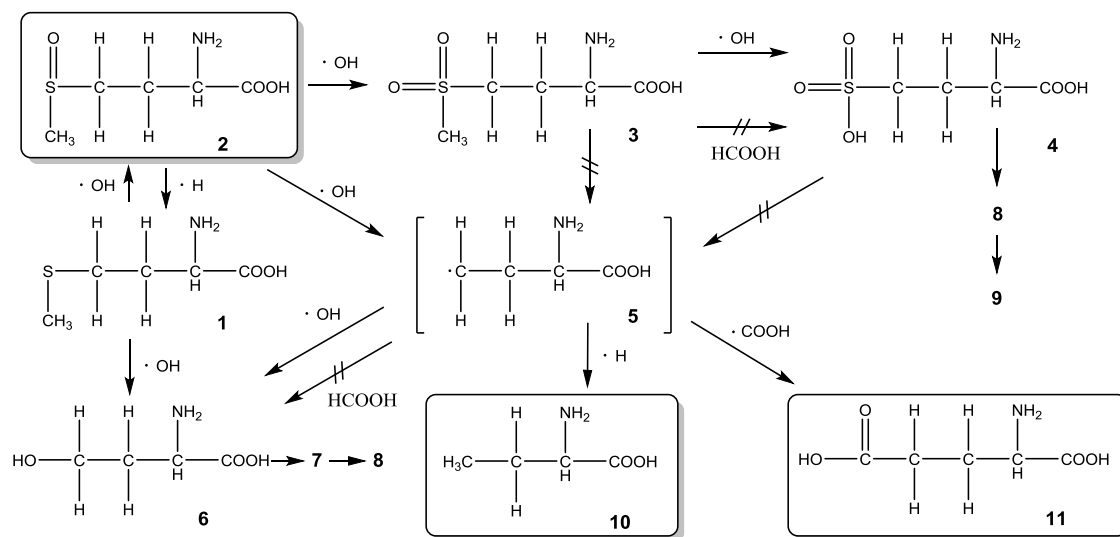
Scheme 5

Table 1 Summary of optimum yield of products by plasma jet

Substrate	Plasma gas*	Solvent	Optimum yield of products (%)									
			1	2	3	4	6	7	8	9	10	11
Methionine (1)**	Ar	H_2O	–	60	24	4	2	3	14	2	–	–
Methionine sulfoxide (2)	Ar–H_2	H_2O	4	–	9	8	3	–	–	–	33	–
Methionine sulfoxide (2)	Ar	5% HCOOH	–	–	58	–	–	–	–	–	13	27
Methionine sulfoxide (2)	Ar	20% HCOOH	–	–	45	–	–	–	–	–	13	15
Methionine sulfoxide (2)	Ar	40% HCOOH	–	–	55	–	–	–	–	–	19	12
Methionine (1)	Ar	20% HCOOH	–	57	15	–	–	–	–	–	6	6
Methionine sulfone (3)	Ar	20% HCOOH	–	–	–	–	–	–	–	–	–	–
* Ar (2.0 L/min); Ar–H_2 (1.5–0.5 L/min)												
** Data were extracted from the literature [11].												

The formation path of intermediate (5) from methionine sulfoxide (2) was clear because plasma jet blowing into the solution containing methionine sulfone (3) and formic acid did not give any of the predicted coupling products(10) and (11). Therefore, intermediate (5) comes from methionine sulfoxide (2).

CONCLUSIONS

Methionine sulfoxide (2) gave 2-amino-1-butanoic acid (10) with a yield of 33% by the action of an argon–hydrogen plasma jet. The reactions of methionine sulfoxide (2) and its related compounds in formic acid induced by an argon plasma jet suggested the formation of carbon radical intermediate (5). The formation of 2-amino-1-butanoic acid (10) and glutamic acid (11) proved the formation of the intermediate, which was supported by the formation of homoserine (6) depending on formic acid concentration.This research demonstrated that methionine-related compounds react to yield amino acids induced by argon–hydrogen and argon plasma jets.

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