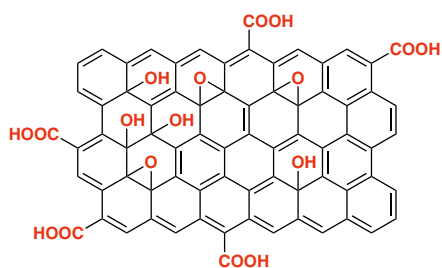


# TCIMAIL

number **167**



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### 2 Chemistry Chat –Focusing on the Elements– - Compounds Composed of Two Elements (3)

Kentaro Sato

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- Cyclin-Dependent Kinases Inhibitor
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## Compounds Composed of Two Elements (3)

Kentaro Sato

### Compounds Composed of Carbon and Sulfur

This column covered compounds composed of just carbon and oxygen previously. This time, let us start off with the combination of carbon and sulfur, the element positioned directly below oxygen in the periodic table.

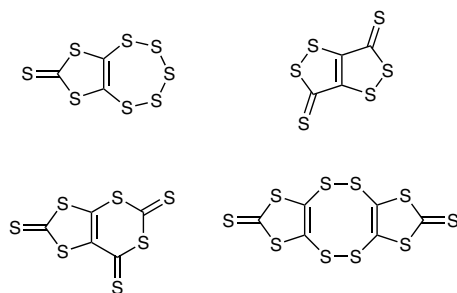
From this combination, one would probably think of carbon disulfide ( $\text{CS}_2$ ) first. Carbon disulfide is isoelectronic to carbon dioxide, but unlike  $\text{CO}_2$  this compound exists as a liquid at room temperature, melting at  $-111\text{ }^\circ\text{C}$  and boiling at  $46\text{ }^\circ\text{C}$ . Although you might expect it to have an unpleasant smell characteristic of sulfur compounds, the smell actually originates from its decomposition impurities and pure  $\text{CS}_2$  is supposed to have an ether-like odor.

$\text{CS}_2$  has been used as a solvent for the manufacture of rubber and cellophane products. However, it is being used less and less frequently these days due to its high toxicity. It is a neurotoxin that is even an ingredient of some insecticides, so it has to be used with appropriate caution.

Carbon monosulfide ( $\text{CS}$ ), the compound isoelectronic to carbon monoxide, is also known. It has been detected in outer space and is also formed by the decomposition of carbon disulfide mediated by light or electric discharge. Monomeric  $\text{CS}$ , however, is extremely unstable and easily polymerize to form  $(\text{CS})_n$ .

More than 10 other examples of low molecular weight compounds composed of just carbon and sulfur are known, some of which are shown below. Since organic sulfur compounds often exhibit unique electronic properties and constitute an actively studied field, the list is only expected to grow.

In 2006, a new member of carbon sulfide family entered the scene boasting a beautiful, unprecedented structure. The structure is shown below and the compound was named Sulflower after sulfur and flower. Aside from functioning as an organic semiconductor, it has been suggested computationally that it may have hydrogen storage ability by adsorbing hydrogen molecules within its crystal structure, which is a remarkable potential.



Organic sulfur compounds

As you can see, Sulflower has a structure composed of 8 thiophene units fused in circular fashion. According to the theoretical calculation, the molecule is planar when the number of thiophene units is 8 or 9. The molecule takes a crown-like shape and a saddle-like shape when the thiophene units are less than 8 and more than 9, respectively. It will be exciting to learn about the properties of these non-planar Sulflowers, as well as those of variants containing other heteroatoms, that could potentially be useful materials.

## Compounds Composed of Carbon and Nitrogen

### (1) Cyano Compounds

Nitrogen sits on the right side of carbon in the periodic table and is an element found widely in a number of natural organic compounds such as amino acids and alkaloids. Like hydrogen and oxygen are, nitrogen is a great partner of carbon in organic chemistry. Yet, compounds composed of only carbon and nitrogen might be comparatively harder to imagine.

The simplest example is cyanogen, which has a molecular formula of  $(\text{CN})_2$  and was first synthesized in 1815 by the renowned French chemist Joseph Gay-Lussac. It is a gas with a pungent odor and is highly toxic similar to other cyano compounds.

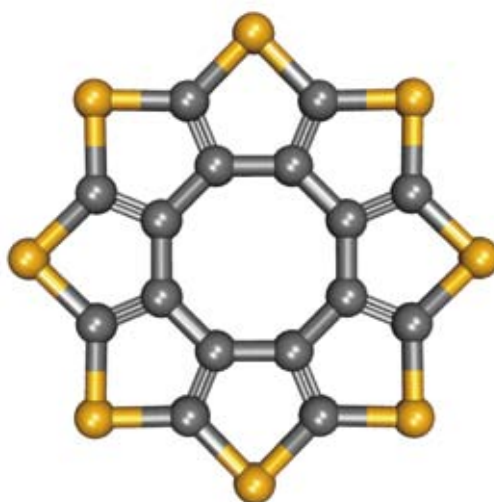
When Halley's Comet approached the earth in 1910, this cyanogen was detected spectroscopically in the tail of the comet. Since it was expected that the earth would pass

through the tail of the comet, it spread a false rumor that the poisonous gas would exterminate all life forms on the earth, creating a wave of panic around the world. But of course, the concentration of the gas in the tail of the comet turned out to be so dilute that nothing happened to the earth.

Dicyanoacetylene ( $\text{N}\equiv\text{C}-\text{C}\equiv\text{C}-\text{C}\equiv\text{N}$ ) is obtained by passing nitrogen gas through graphite at around 3000 K. It is a clear and colorless liquid that is known to burn with the hottest flame among all substances (ca. 5260 K).

In outer space, it is known that compounds called cyanopolynes ( $\text{H}-(\text{C}\equiv\text{C})_n-\text{C}\equiv\text{N}$ ) exist. Dicyanoacetylene is also considered to exist with them, but it has no rotational spectrum because of its molecular symmetry, therefore there is no effective way to detect it. It is known to exist in the atmosphere of Titan, the satellite of Saturn, so chances are that it could be a building block of other complex molecules.

In this way, one could imagine compounds based on only carbon and nitrogen by replacing the hydrogen atoms of hydrocarbons with cyano groups. Compounds such as tetracyanomethane ( $\text{C}(\text{CN})_4$ ) and hexacyanobenzene ( $\text{C}_6(\text{CN})_6$ ) have been actually synthesized. Among them, the most famous one is probably tetracyanoethylene (TCNE). With the four electron-withdrawing cyano groups attached on a small carbon scaffold, this molecule serves as an excellent electron acceptor in the research of organic semiconductors and organic superconductors.



Sulflower

## (2) Azide Compounds

Metal complexes containing multiple azide ligands have been synthesized in recent years. Tetraazidomethane ( $C(N_3)_4$ ), which has four azide groups bonded to one carbon atom, was also synthesized surprisingly recently in 2007. After many attempts, the only successful way to prepare it has been the reaction between trichloroacetonitrile ( $Cl_3CCN$ ) and sodium azide ( $NaN_3$ ). The ratio of carbon to nitrogen is 1 to 12 for this molecule, which is somewhat astonishing.

As is well known, azide compounds have explosive properties and their handling requires great care. Tetraazidomethane, with the four azide groups crowded within a small molecule, is something of an ultimate high-energy substance and extremely dangerous. The author of the report says that, "Tetraazidomethane is extremely dangerous as a pure substance. It can explode at any time—without a recognizable cause. Less than a drop of this compound isolated by gas chromatography is able to destroy completely not only the glass trap but also the vacuum Dewar flask of the cooling bath." Personally, I would never like to try this experiment regardless of the quality of lab environment!

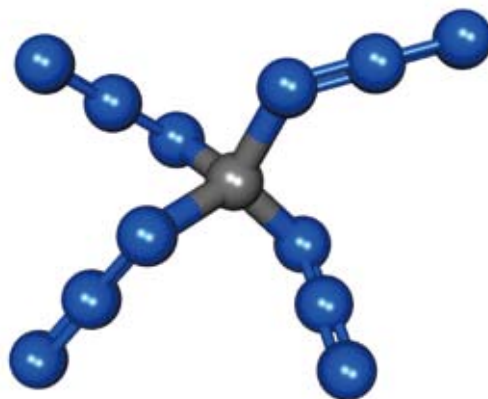
## (3) Azafullerenes

If the compound having the highest N to C ratio is tetraazidomethane, then the compound with very high C to N ratios would be these azafullerenes. Azafullerenes have been synthesized from  $C_{60}$  fullerene in multiple steps by incorporating nitrogen atom(s) into the original skeleton to produce such compounds as  $C_{59}N^+$  cation and the dimeric  $(C_{59}N)_2$ , in which two buckyballs are connected at the carbons adjacent to the nitrogens. There is also a report of the synthesis of  $C_{69}N^+$  cation starting from  $C_{70}$ .

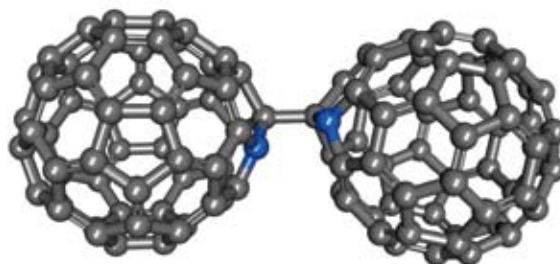
In addition to these examples, the molecule of fullerene in which a nitrogen atom is trapped inside the fullerene structure ( $N@C_{60}$ ) has been isolated. This "endohedral fullerene" compound was synthesized by irradiating ordinary fullerene with nitrogen plasma, which enables the "implantation" of nitrogen. Various derivatives have been actively synthesized in recent years and they could be developed into useful applications.

## (4) Polymeric Carbon Nitrides

"Photocatalysts" which are capable of decomposing substances such as water with the assist of light have been applied to various areas ranging from environmental



Tetraazidomethane



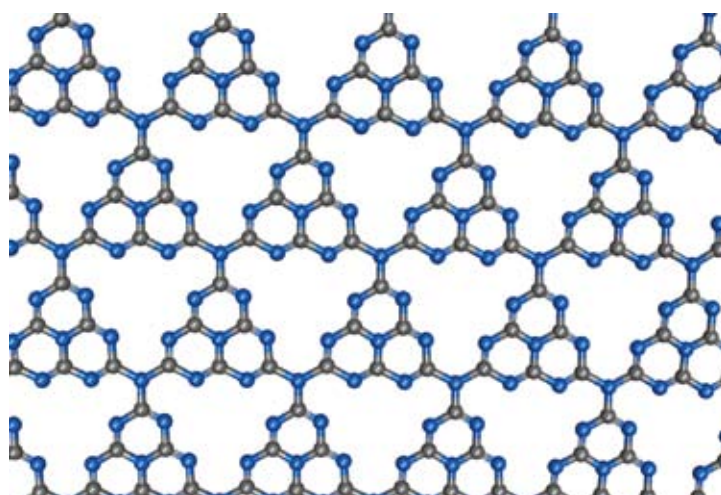
$(C_{59}N)_2$

purification to energy creation, and are one of the innovations that emerged from Japan. Whereas the development of this field has centered on inorganic materials such as titanium dioxide, recent years have seen the advent of organic materials with promising properties. One of them is called graphitic carbon nitride ( $g\text{-C}_3\text{N}_4$ ).

Graphitic carbon nitrides are obtained by heating nitrogen-rich compounds such as melamine, and by depositing a small amount of co-catalysts (e.g. platinum), these materials can decompose water under visible light. And more recently, synthetic improvement has led to the introduction of a new version of  $g\text{-C}_3\text{N}_4$  having a larger surface area, which enables more efficient decomposition of harmful substances such as nitrogen monoxide. These polymers can certainly be counted as one of the promising groups of carbon materials.

Furthermore, there is a substance called “hexagonal crystalline carbon nitride” ( $\beta\text{-C}_3\text{N}_4$ ), which has a structure consisting of three-dimensional network of carbon and nitrogen and is predicted to be harder than diamond. At present, only nano-scale crystal preparation has been successful, but it sure would have a wide range of applications if it could be prepared on practical scales.

The chemical space of carbon nitrides can be just as deep as other substances, as it encompasses explosives, organic electronic devices, and super-hard materials. There seems to be a room for further developments and discoveries of fascinating compounds.



Graphitic carbon nitride

#### Introduction of the author :

##### Kentaro Sato

[Brief career history] He was born in Ibaraki, Japan, in 1970. 1995 M. Sc. Graduate School of Science and Engineering, Tokyo Institute of Technology. 1995-2007 Researcher in a pharmaceutical company. 2008-Present Freelance science writer. 2009-2012 Project assistant professor of the graduate school of Science, the University of Tokyo. 2014-present Publicist for  $\pi$ -system figuration, scientific research on innovative areas.

[Specialty] Organic chemistry

[Website] The Museum of Organic Chemistry <<http://www.org-chem.org/yuuki/MOC.html>>

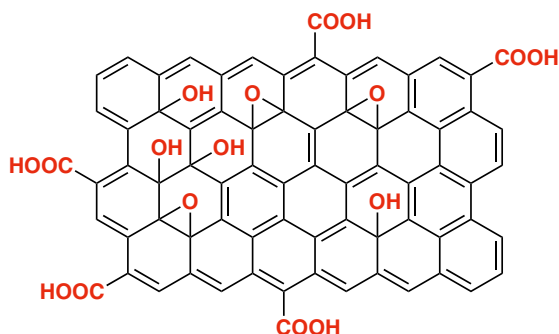
## Graphene Oxide

G0443 Graphene Oxide (1)

100mg

G0444 Graphene Oxide (10mg/mL, Dispersion in Water) (2)

5mL 25mL



Graphene oxide (1)

Graphene oxide, Dispersion in Water (2)

Graphene oxide (GO, 1) has a structure of an oxidized graphene having hydroxy, carboxy and epoxy groups. Accordingly, GO can be dispersed in water and several polar solvents. A water dispersion of GO (2) is used as a lubricant to reduce friction on metal surfaces.<sup>1)</sup> Although graphene consists of only  $sp^2$  carbons, GO consists of some  $sp^3$  carbons and structural defects giving insulating properties. On the other hand, the reduction of GO provides a reduced graphene oxide (rGO) which is conductive. Therefore the rGO is expected to be an electrode material.

There are various synthetic methods of manufacturing GO, and the properties and applications depend on the degree of oxidation. A characteristic feature of our GO (1) is having a high degree of oxidation (50-55%). Highly oxidized GO supports a metal catalyst to drastically enhance its catalytic activity. Nishina *et al.* reported that GO-supported palladium prepared *in situ* catalyzes a cross-coupling reaction and hydrogenation even if there is very small amount of the catalyst.<sup>2,3)</sup> A silica-assisted rGO-Pt catalyst showed high catalytic activity and durability, compared with conventional catalysts.<sup>4)</sup> We can introduce several functional groups on GO because there are oxygen-based groups. These GO derivatives may be useful for luminescent materials and biosensors.<sup>5,6)</sup>

### References

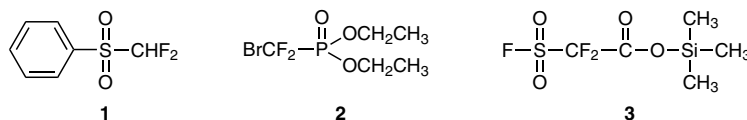
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- 2) Facile preparation of Pd nanoparticles supported on single-layer graphene oxide and application for the Suzuki–Miyaura cross-coupling reaction  
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### Related Products

G0441	Graphene Nanoplatelets 6-8nm(thick), 5 $\mu$ m(wide)	5g 25g
G0442	Graphene Nanoplatelets 6-8nm(thick), 15 $\mu$ m(wide)	5g 25g
G0438	Graphene Nanoplatelets 6-8nm(thick), 25 $\mu$ m(wide)	5g 25g

## Difluoromethylating Reagents

D4764	Difluoromethyl Phenyl Sulfone (1)	1g	5g
D3071	Diethyl (Bromodifluoromethyl)phosphonate (2)	5g	25g
T3022	Trimethylsilyl Difluoro(fluorosulfonyl)acetate (3)	5g	25g

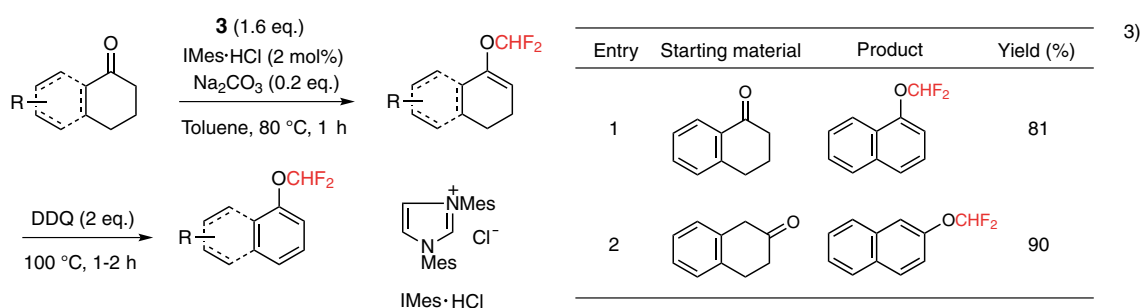
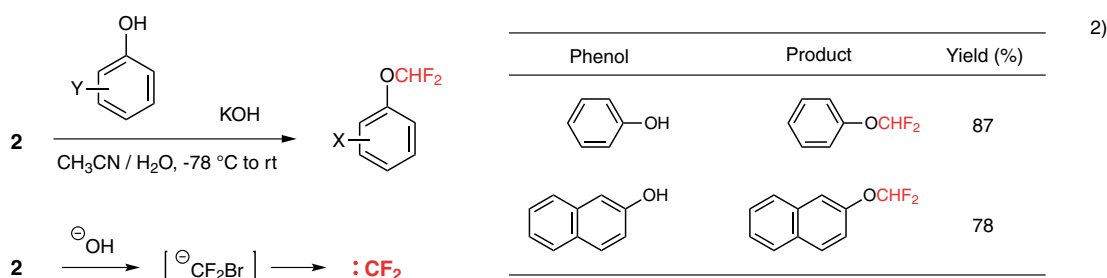


Difluoromethylated compounds have been widely used as building blocks for pharmaceuticals or agrochemicals, thus, various kinds of difluoromethylating reagents have been developed. For example, difluoromethyl phenyl sulfone (1), a difluoromethyl anion equivalent, reacts with primary alkyl halides to afford the corresponding difluoromethylated products through a nucleophilic substitution – reductive desulfonylation.<sup>1)</sup>

1	$\xrightarrow[\text{DMF, -50 } ^\circ\text{C, 1 h}]{\text{RCH}_2\text{I, t-BuOK}}$	$\text{RCH}_2\text{CF}_2\text{SO}_2\text{Ph}$ <b>(A)</b>		
	$\xrightarrow[\text{MeOH, -20 } ^\circ\text{C to 0 } ^\circ\text{C, 1 h}]{\text{Na(Hg), Na}_2\text{HPO}_4}$	$\text{RCH}_2\text{CF}_2\text{H}$ <b>(B)</b>		
<b>Desulfonylation</b>				

RCH <sub>2</sub> I		(A) (Yield %)	(B) (Yield %)
Ph(CH <sub>2</sub> ) <sub>4</sub> I	Ph(CH <sub>2</sub> ) <sub>4</sub> CF <sub>2</sub> SO <sub>2</sub> Ph	52	Ph(CH <sub>2</sub> ) <sub>4</sub> CF <sub>2</sub> H 87
Ph(CH <sub>2</sub> ) <sub>5</sub> I	Ph(CH <sub>2</sub> ) <sub>5</sub> CF <sub>2</sub> SO <sub>2</sub> Ph	59	Ph(CH <sub>2</sub> ) <sub>5</sub> CF <sub>2</sub> H 90
PhO(CH <sub>2</sub> ) <sub>3</sub> I	PhO(CH <sub>2</sub> ) <sub>3</sub> CF <sub>2</sub> SO <sub>2</sub> Ph	71	PhO(CH <sub>2</sub> ) <sub>3</sub> CF <sub>2</sub> H 91

Moreover, the difluoromethylation methods using diethyl (bromodifluoromethyl)phosphonate (2) or trimethylsilyl difluoro(fluorosulfonyl)acetate (3) as difluorocarbene (:CF<sub>2</sub>) precursors also have been reported. 2 and 3 generate :CF<sub>2</sub> in the presence of KOH and NHC catalysts, respectively, to afford the corresponding aryl difluoromethyl ethers.



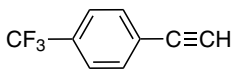
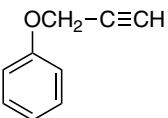
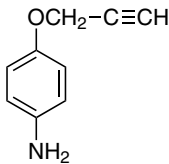
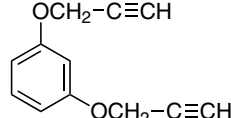
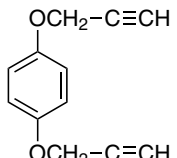
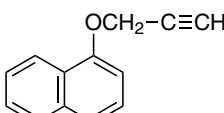
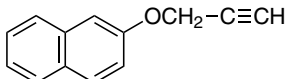
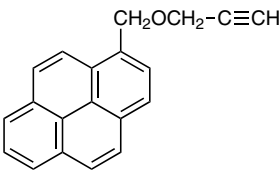
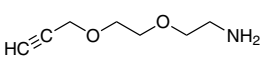
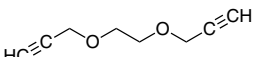
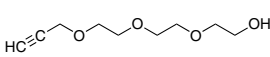
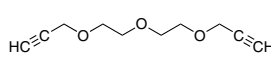
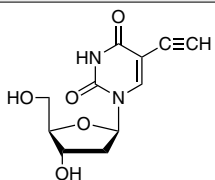
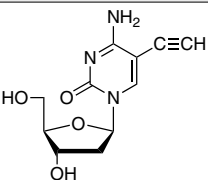
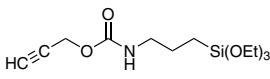
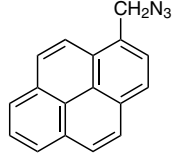
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## Building Blocks for Click Chemistry

E0626	1-Ethynyl-4-(trifluoromethyl)benzene (1)	1g	5g
P2222	Phenyl Propargyl Ether (2)	5g	25g
P2224	4-(2-Propynyloxy)aniline (3)	1g	5g
B4521	1,3-Bis(2-propynyloxy)benzene (4)	200mg	1g
B4607	1,4-Bis(2-propynyloxy)benzene (5)	1g	5g
P2227	1-(2-Propynyloxy)naphthalene (6)	1g	5g
P2190	2-(2-Propynyloxy)naphthalene (7)	200mg	1g
P2226	1-[(2-Propynyloxy)methyl]pyrene (8)	200mg	1g
P2225	2-[2-(2-Propynyloxy)ethoxy]ethylamine (9)	1g	5g
E1054	Ethylene Glycol 1,2-Bis(2-propynyl) Ether (10)	5g	25g
T3114	Triethylene Glycol Mono(2-propynyl) Ether (11)	1g	5g
D4581	Diethylene Glycol Bis(2-propynyl) Ether (12)	5g	25g
E1057	5-Ethynyl-2'-deoxyuridine (= EdU) (13)	50mg	200mg
E1093	5-Ethynyl-2'-deoxycytidine (= EdC) (14)	50mg	200mg
P2258	2-Propynyl [3-(Triethoxysilyl)propyl]carbamate (15)	1g	5g
A2791	1-(Azidomethyl)pyrene (16)	200mg	1g

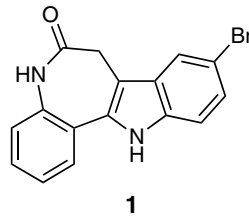
Terminal Acetylenes			
Aryls			
			
1	2	3	4
			
5	6	7	8
PEG			
			
9	10	11	12
Nucleosides		Silane coupling reagent	Organic azide
			
13	14	15	16



## Cyclin-Dependent Kinases Inhibitor

K0052 Kenpaullone (1)

10mg 50mg



Kenpaullone (**1**) is a cell-permeable inhibitor of several cyclin-dependent kinases, CDK1/cyclin B, CDK2/cyclin A, CDK2/cyclin E and CDK5/p35, as shown in the Table.<sup>1)</sup> **1** also inhibits GSK3 $\beta$ .<sup>1,2)</sup>

**1** is also utilized for establishing induced pluripotent stem cells (iPSCs) as one of the chemical “substitutes” of Klf4, which is one of four transcription factors (Oct4, Klf4, Sox2, and c-Myc).<sup>3)</sup>

ALS (amyotrophic lateral sclerosis) is a neurodegenerative disease caused by motor neuron death. Rubin *et al.* found that **1** promoted the survival of motor neurons by using human ALS iPSCs and ES Cells derived from an ALS model mouse.<sup>4)</sup>

**Table.** Inhibition of selected protein kinases by kenpaullone<sup>1)</sup>

Protein kinase	IC <sub>50</sub> ( $\mu$ M)
cdk1/cyclin B	0.4
cdk2/cyclin A	0.68
cdk2/cyclin E	7.5
cdk4/cyclin D1	>100
cdk5/p35	0.85
erk1	20
erk2	9
c-raf	38
MAPKK	>100
c-Jun NH <sub>2</sub> -terminal kinase	>100
Protein kinase C $\alpha$	>100
Protein kinase C $\beta$ 1	>100
Protein kinase C $\beta$ 2	>100
Protein kinase C $\gamma$	>100
Protein kinase C $\delta$	>100
Protein kinase C $\epsilon$	>100
Protein kinase C $\eta$	>100
Protein kinase C $\xi$	>100
cAMP-dependent PK	>1000
cGMP-dependent PK	>1000
Casein kinase 1	>100
Casein kinase 2	20
Insulin receptor tyrosine kinase	>1000
c-src	15
v-abl	350

This product is for research purpose only.

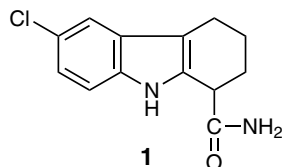
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## SIRT1 Inhibitor

C2739 6-Chloro-2,3,4,9-tetrahydro-1H-carbazole-1-carboxamide (= Ex-527) (1)

25mg



SIRT1 is a member of the sirtuin family of enzymes that catalyze the deacetylation of acetyl-lysine residues in histones and other proteins.<sup>1)</sup> SIRT1 plays an important role in a variety of processes including stress resistance, metabolism, differentiation, and aging.<sup>1)</sup> Sirtuins are the mammalian orthologues of the yeast Sir2 (silent information regulator 2).<sup>1,2)</sup> In the catalytic process of SIRT1, NAD<sup>+</sup> is cleaved and O-acetyl ADP-ribose is generated.<sup>1,3,4)</sup>

Ex-527 (**1**) is a small molecule inhibitor of SIRT1 and possesses much higher selectivity for SIRT1 than others as shown below (Table).<sup>5)</sup> **1** also does not inhibit class I/II HDACs at concentrations up to 100 μM.<sup>6)</sup>

\*Class I/II HDACs are histone deacetylases and remove acetyl groups without hydrolysis of NAD<sup>+</sup>.

**Table.** Sirtuin inhibitory activity of Ex-527<sup>5)</sup>

Sirtuins	inhibitory activity
SIRT1	IC <sub>50</sub> = 98 nM
SIRT2	IC <sub>50</sub> = 19.6 μM
SIRT3	IC <sub>50</sub> = 48.7 μM
SIRT4	— <sup>a</sup>
SIRT5	Not inhibited at >50 μM
SIRT6	— <sup>a</sup>
SIRT7	— <sup>a</sup>

<sup>a</sup> No deacetylase activity was detected for these sirtuins.

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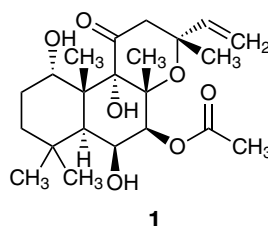
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## Adenylate Cyclase Activator

F0855 Forskolin (1)

10mg 50mg



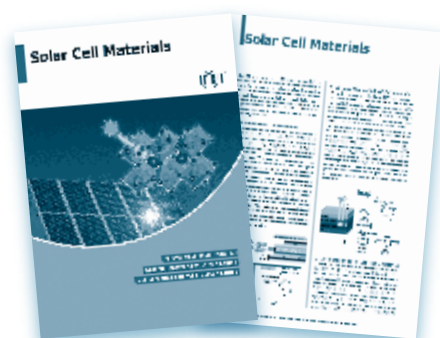
Forskolin (**1**) is a diterpenoid from the Indian plant, *Coleus forskohlii*.<sup>1)</sup> **1** activates adenylate cyclase.<sup>2,3)</sup> **1** induces differentiation of mesenchymal stem cells into neuron-like cells.<sup>4)</sup> Recently, **1** was utilized for establishing chemically induced pluripotent stem cells (iPSCs) as one of the chemical “substitutes” of Oct4, which is one of four transcription factors (Oct4, Klf4, Sox2, and c-Myc or Oct4, Sox2, Nanog, and Lin28).<sup>5)</sup>

This product is for research purpose only.

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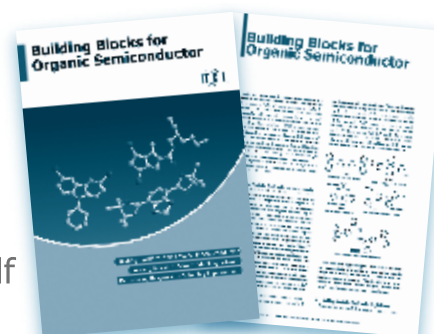
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