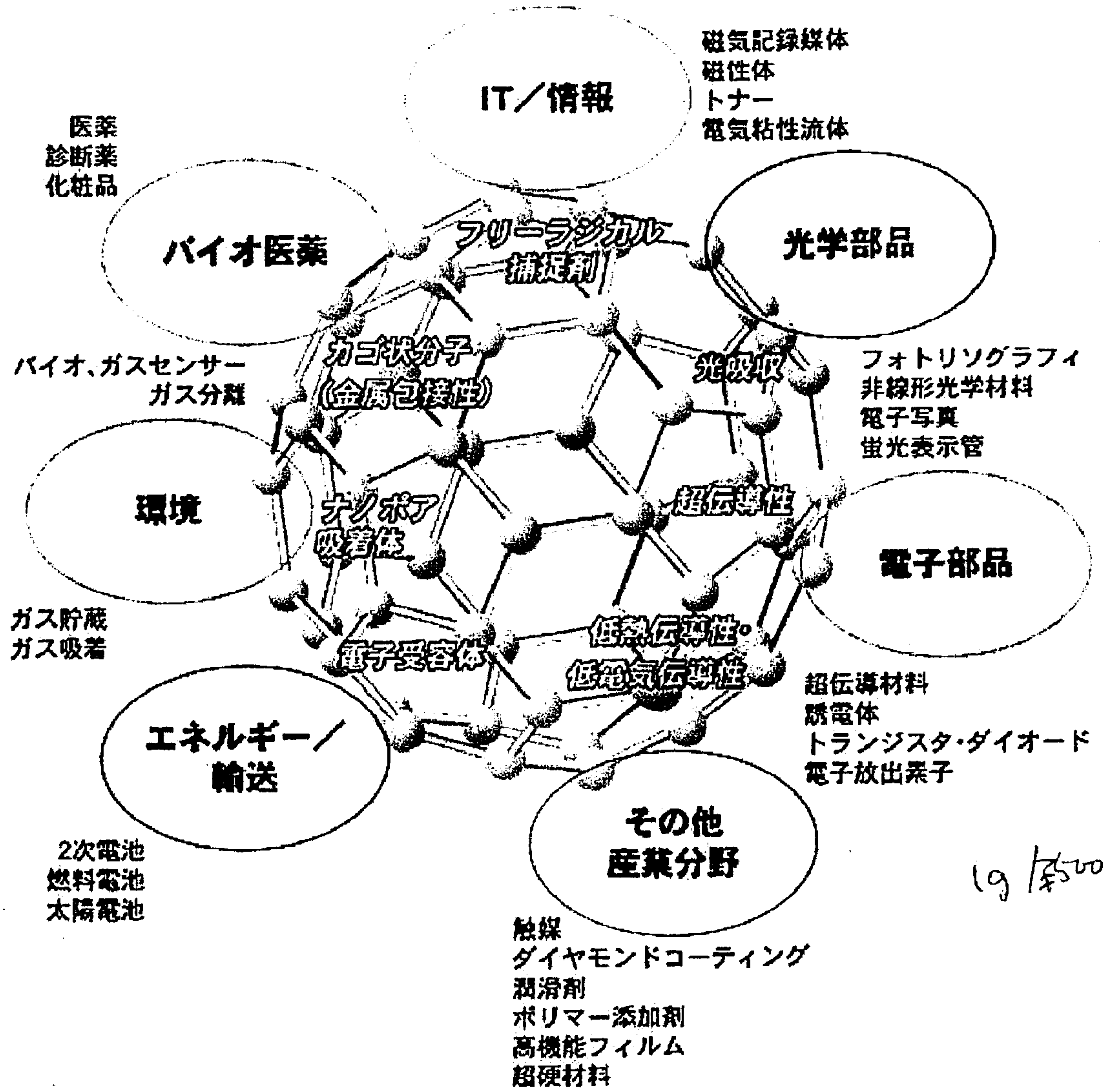
Fullerene Chemistry

2006/07/ Lit.(M1) M1 K.Hara



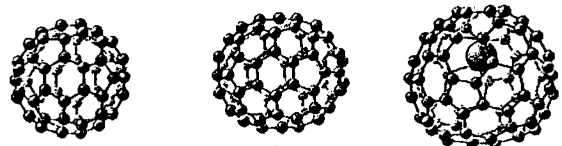
Contents

1. Introduction

The fullerenes are a recently-discovered family of carbon allotropes. They are molecules composed entirely of carbon. Spherical fullerenes are sometimes called buckyballs, and cylindrical fullerenes are called buckytubes.

Discovery

In 1985, Harold Kroto (of the University of Sussex), Robert Curl and Richard Smalley, from Rice University, discovered C_{60}, and shortly after came to discover the fullerenes. Kroto, Curl, and Smalley were awarded the 1996 Nobel Prize in Chemistry for their roles in the discovery of this class of compounds.



C_{60} C_{70} La@C_{82}

C_{70} etc…

Structural Determination

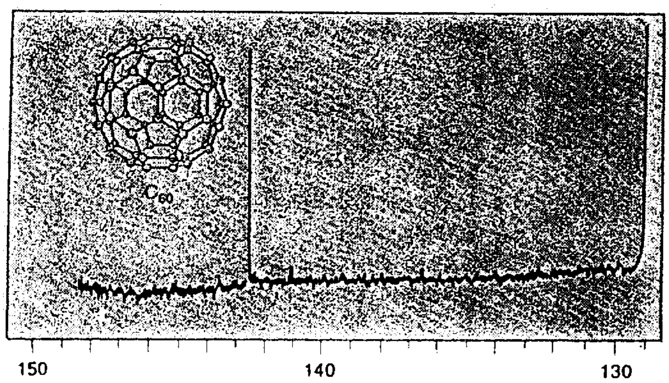
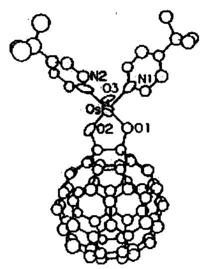


Fig 1.

H. W. Kroto et al. J. Chem. Soc. Chem. Com 1990. 1423.



J. M. Hawkins et al. SCIENCE. 1990. 252. 312.

Fig 2. $C_{60}(OsO_4)$(4-tert-butyl pyridine$)_2$

Reactivity

Fullerenes are stable, but not totally unreactive.

Low LUMO energy

- Easy to react with Nucleophile or radical species.
- Diels-Alder or 1,3dispolar rxn.

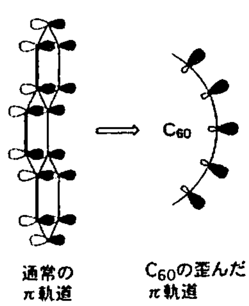
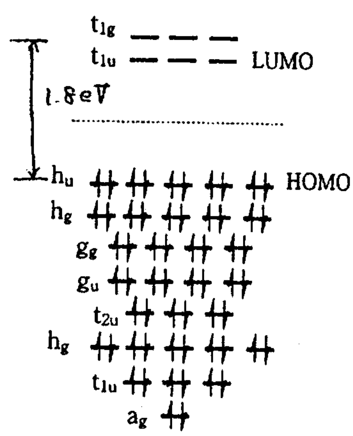


Fig 3

Low LUMO Energy.



π orbital of C_{60}

Fig 4.

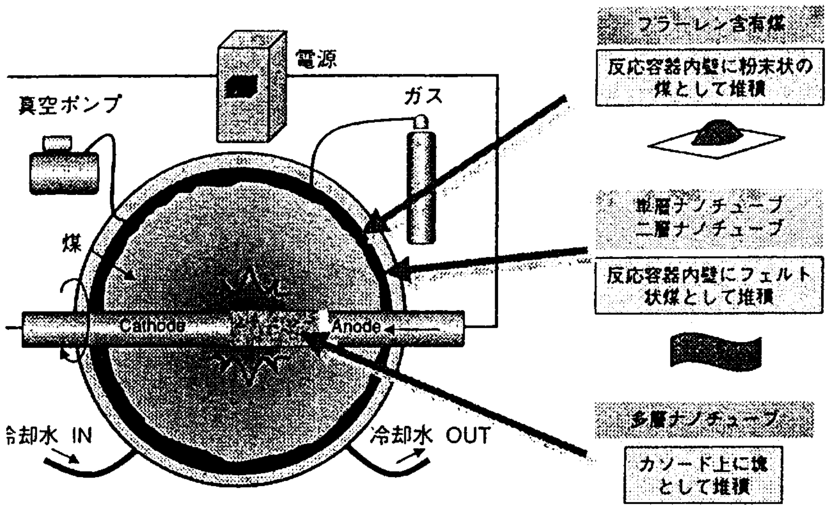
Solubility

1,2,4-tri.chlorobenzene (20 mg/ml), carbon disulfide (12 mg/ml), toluene (3.2 mg/ml), chloroform (0.5 mg/ml), n-hexane (0.046 mg/ml), tetrahydrofuran (0.037 mg/ml)

2. Large amount of supply of fullerenes

2-1. Large scale synthesis of fullerenes

Ark dischange method (アーク放電法、1990 , Krätschmer et al)



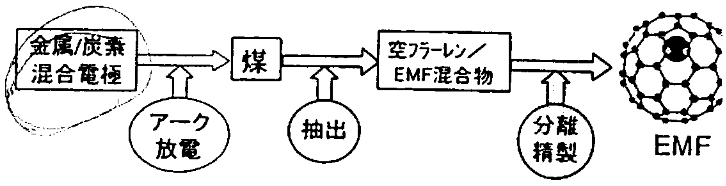
アーク放電法の生成物

Fig 5.

Radiation and Sublime

Graphite → soot (すす) { $C_{60} + C_{70} > 90\%$; $C_{70} < 10\%$ }

(scheme 1.)



金属内包フラーレン製造工程

Fig 6.

The cost of graphite is high and large current is needed.

Not suitable for large-scale synthesis of fullerenes.

Combustion method (燃焼法 , 1991, J.B Howard et al.)

Benzen or Toluene —(不完全燃焼, 1000 ℃, 減圧下)→ Soot —(20 % ~ 50%)→ ミックスフラーレン(MF) → { C_{60} 60 % ; C_{70} 25 % ; $C_{>70}$ 15 % }

(scheme 2.)

The cost of raw material is low.

The assemblyline operation

In JAPAN, FCC company

40 tons/year

500 yens/g

The detailed generation mechanism of fullerenes is unknown.

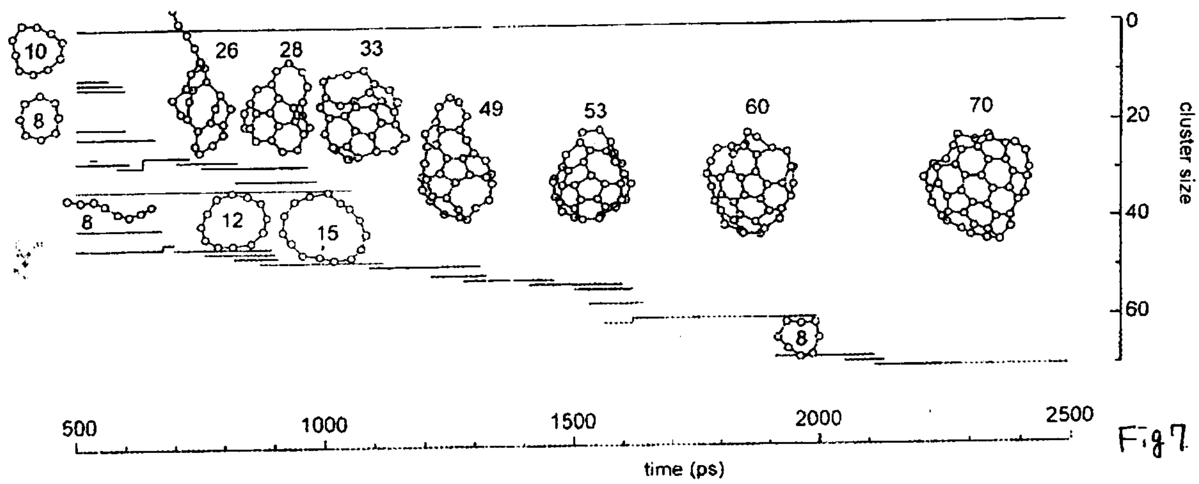


Fig 7

2-2. Development of practical purification methods

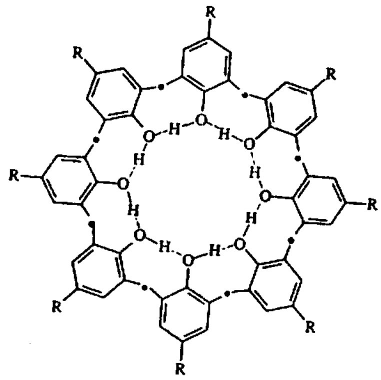
・Typical method (column chromatography / HPLC) ⟹ not suitable for large-scale purification

selective complexation

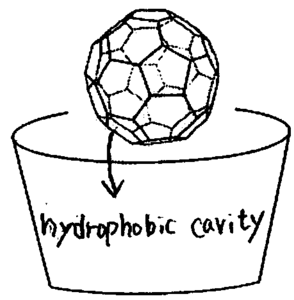
J. L. Atwood et al. Nature 1994. 368. 229

Fullerene mixture —(a1, Toluene)→ C_{60}-a1 complex —(recry with Tol × 2, 90%)→ pure C_{60}-a1 complex —($CHCl_3$)→ recover C₆₀ calixarene; ↓ 92% recig. C_{60} (>99.5% purity)

(scheme 3)



a1. R = tBu



host-guest complexes

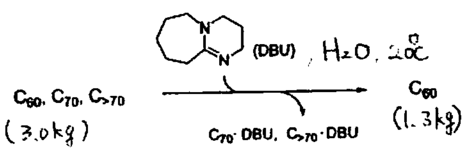
The cavity of the calixarene is too small for favourable binding of higer fullerenes.

Efficient and Scalable Method for [60]Fullerene Separation from a Fullerene Mixture: Selective Complexation of Fullerenes with DBU in the Presence of Water

K. Nagata et al. (Engineering and Development Center, FCC)

Organic Process Research & Development. 2005. 9. 660.

Scheme 1



(scheme 4)

Table 1. **Complexation of fullerenes and various amines without water at 0°C**

entry	amine[a]	component (%) C_{60}	C_{70}	$C_{>70}$	C_{60} yield[b] (%)
1	DBU	>99	<1	0	72
2	DBN	>99	<1	0	70
3	2-Me-2-imidazolene	>99	<1	0	68
4	DABCO	57	24	19	100
5	TMEDA	57	24	19	99
6	Et_3N	57	24	19	100

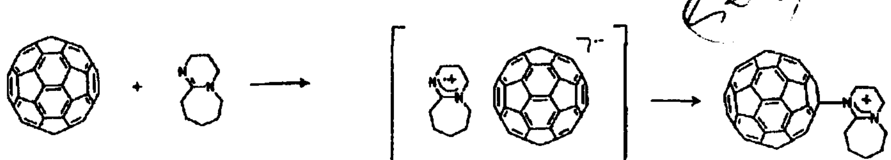
[a] 6.9 mmol of amine was used for 1.0 g of fullerene mixture (C_{60}: 57%, C_{70}: 24%, $C_{>70}$: 19%). [b] Based on the quantity of [60]fullerene in the starting fullerene mixture.

Table 2. **Complexation of fullerenes and DBU in the presence of a small amount of water at 20 °C**[a]

entry	amount of H_2O (equiv of DBU)	component (%) C_{60}	C_{70}	$C_{>70}$	C_{60} yield[b] (%)
1	0	88	11	1	86
2	0.16	>99	<1	0	73
3	0.32	>99	<1	0	77
4	0.64	99	1	0	78
5	1.61	89	10	1	88

[a] 6.9 mmol of DBU was used for 1.0 g of fullerene mixture (C_{60}: 57%, C_{70}: 24%, $C_{>70}$: 19%). [b] Based on the quantity of [60]fullerene in the starting fullerene mixture.

Hirsch et al. Chem. Phys. Lett. 1994. 220. 138



(scheme 5)

H₂O stabilized the polar transition state or the zwitterion complex ?

Boltalina et al. Chem. Phys. Lett.

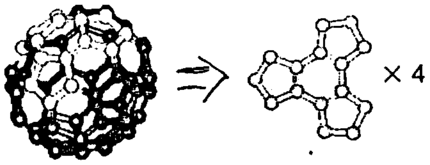
Electron affinity of fullerenes.

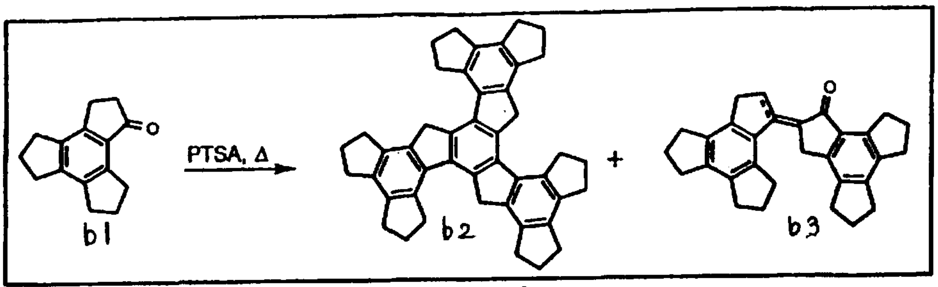
C_{60} 2.65 (eV)
C_{70} 2.73 (eV)
C_{72} 3.09 (eV)

3. Chemical synthesis of C_{60}

SYNTHETIC EFFORTS TOWARDS C60 FRAGMENTS

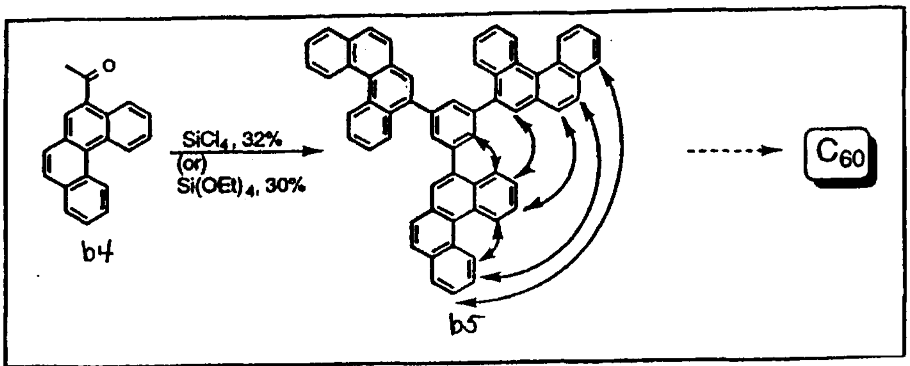
◦ Rassat et al. (1989)





Scheme 6

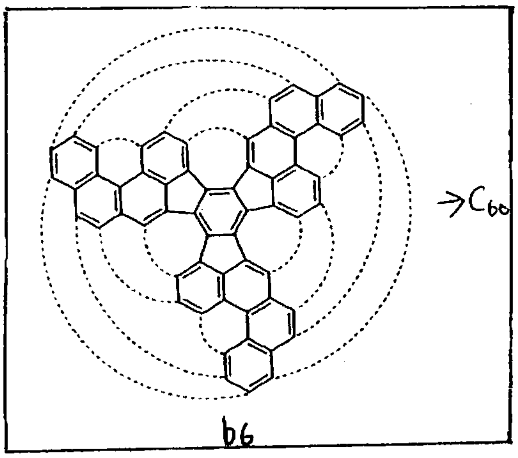
◦ Plater et al. (Synlett. 1993. 405)

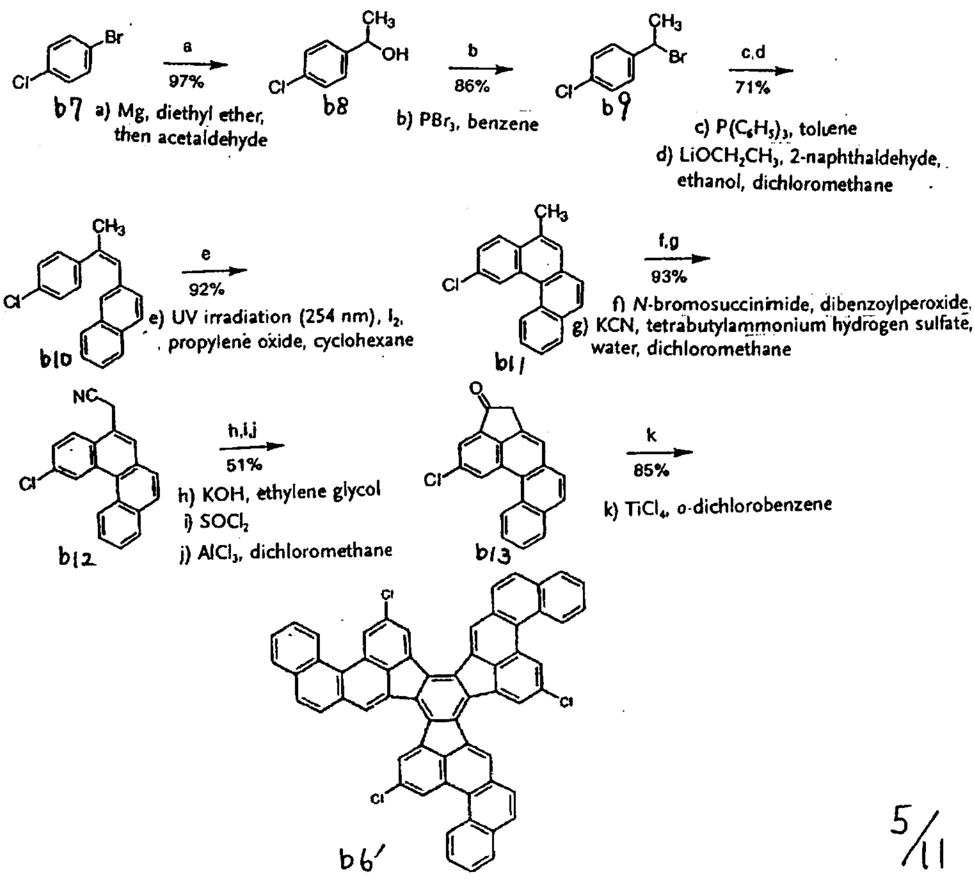


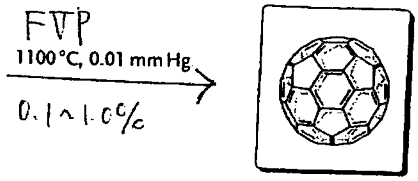
Scheme 7, ***Plater's strategy for C60***

A Rational Chemical Synthesis of C_{60}

L.T. Scott et al. SCIENCE 2002. 295. 1500.
Angew. Chem. Int. Ed 2004. 43 4994





b6' 

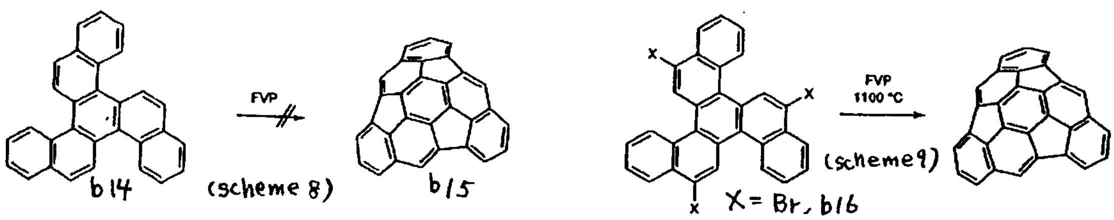
C_{60} Buckminsterfullerene

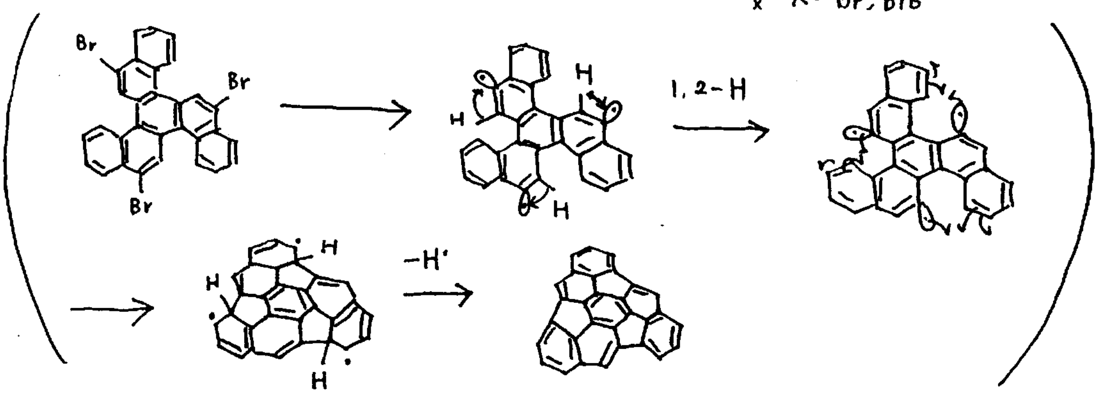
FVP (Flash Vacuum Pyrolysis).

化合物を水晶の管に閉じ込めて真空状態にし、瞬間的に1000℃前後の高温をかける手法。この熱で一部の炭素－水素結合などを開裂させる。

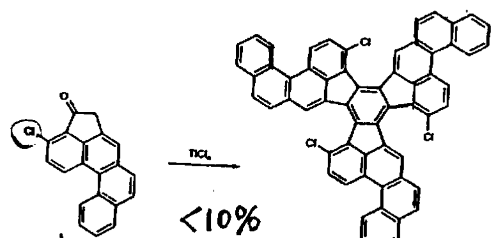
- Curvanture can be introduced in polyarenes by flash vacuum pyrolysis (FVP).
- Even a yield in the range 0.1-1.0%, however, means that the 15 new C-C bond must have been formed with an average yield od greaer than 60% each. $(0.60)^{15} = 0.05\%$
- Introductioon of halogen atoms is very important. (Ar−X < Ar−H)

ex)



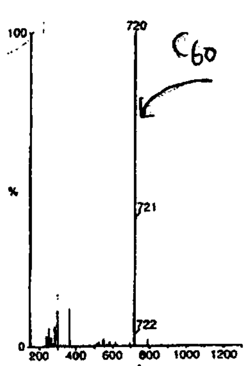


- The extra steric strain affects the yield of aldol cyclotrimerization.



b17 b18

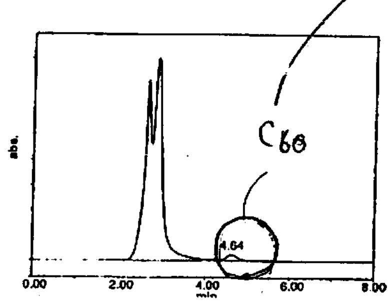
Structural characterization.



(Mass analysis of crude)

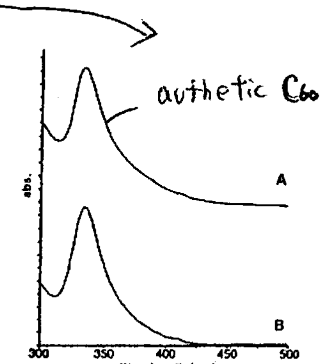
Fig 8.

. HPLC analysis of the product obtained from the reaction in Fig. 1. The peak at 4.64 min appears at the same retention time as the peak given by authentic C_{60}. The identities of the other products that elute faster than C_{60} have not yet been determined. abs., absorbance.



(HPLC analysis of crude)

Fig 9.



Diode array UV-VIS absorption spectra of the HPLC peak at 4.64 min

Fig 10

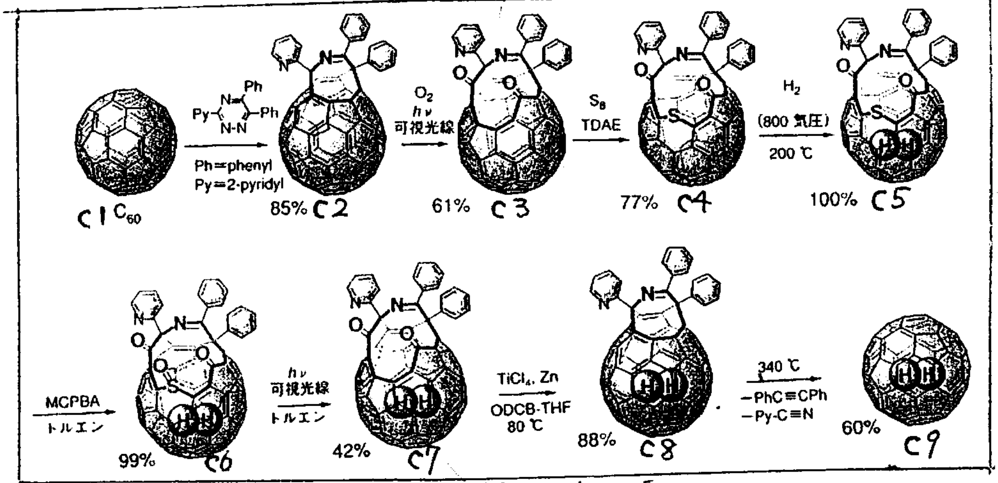
4. Chemical synthesis of $H_2@C_{60}$

* Encapsulation of Molecular Hydrogen in Fullerene C_{60} by Organic Synthesis

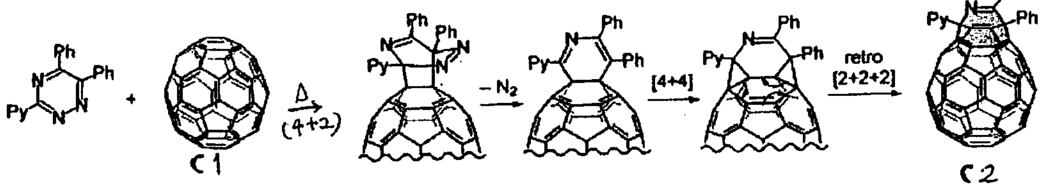
Koichi Komatsu,* Michihisa Murata, Yasujiro Murata

Science 2005, 307, 238 / J. Am. Chem. Soc 2003, 125, 7152

- The success in 100% hydrogen introduction to open-cage fullerene.
- The first chemical synthesis of H_2-encapsulated fullerene C_{60}.

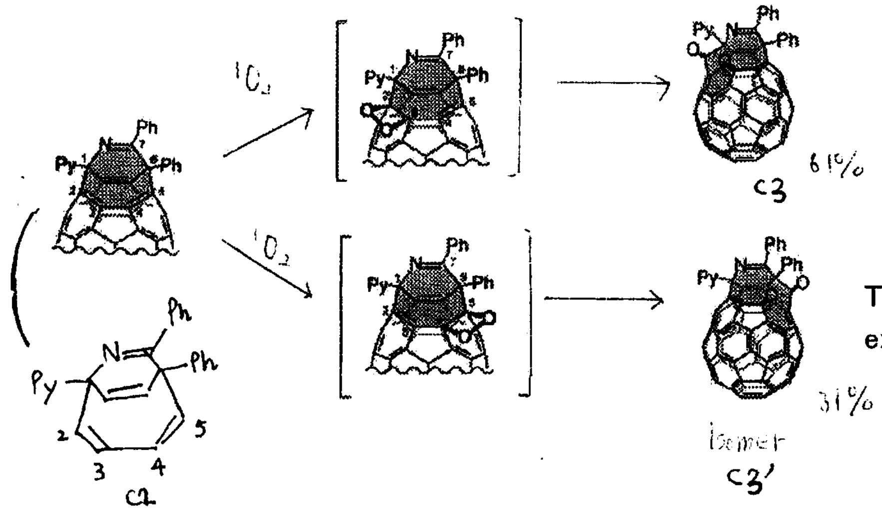


Reaction C1 → C2



C60-M-θ (X ray analysis)

Reaction C2 → C3



The HOMO was found to be localized primarily at the two double bonds, C2–C3 and C4–C5, whereas the LUMO was found to be spread over almost all the sp^2 carbon atoms.

⇓

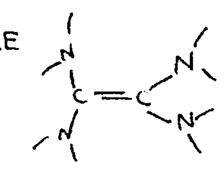
The electrophilic addition of the singlet oxygen was expected to take place on these double bonds.

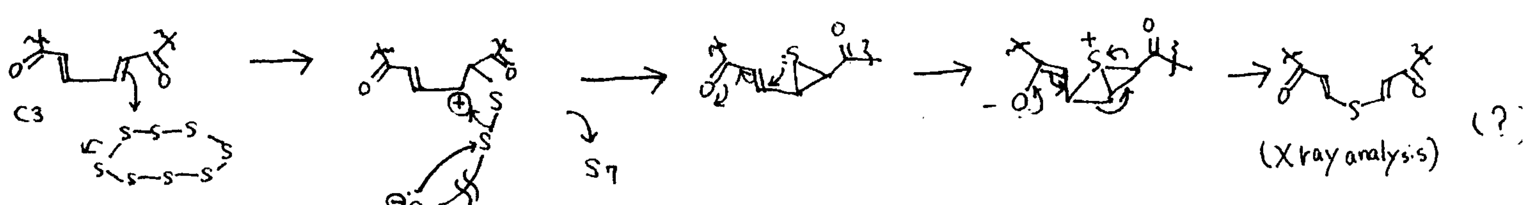
Reaction C3 → C4

TDAE (π-electron donor)

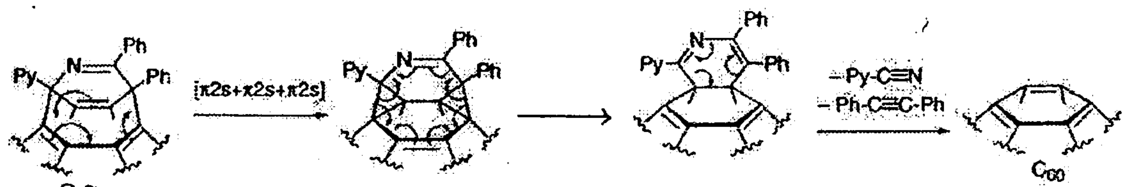
↓ activate

The electrophilic addition of S_8 to C3





Reaction C8 → C9



C8 C9

Structural characterization

- MALDI-TOF mass analysis
- X-ray analysis (C2, C5) etc…
- NMR spectrum

Table 1. Experimental and Calculated NMR Chemical Shifts for Encapsulated Hydrogen of a Series of Open-Cage Fullerene Derivatives and $H_2@C_{60}$

	$H_2@5$ (C)	$H_2@6$ (C)	$H_2@7$ (C)	$H_2@8$ (C)	$H_2@C_{60}$ (C9)
exp[a]	−7.25	−6.33	−5.80	−2.95	−1.45
calcd[b]	−5.87	−4.72	−3.85	−0.17	+1.79
Δ	1.38	1.61	1.95	2.78	3.24

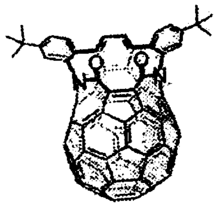
[a] At 300 MHz, in ODCB-d_4. [b] Calculated at the GIAO−B3LYP/6-311G**//B3LYP/6-31G* level of theory.

C4 —(H_2, high pressure)→ H_2@C4 0%

C5 —(H_2, high pressure)→ H_2@C5 100%

Another example

Rubin et al. Angew. Chem. Int. Ed 2001. 40. 1543



C10

He or H_2 → (< 5%) H_2 or He @ C10

5. Application of fullerenes

5-1. MRI contrast agents

Metallofullerens.

$M@C_{82} \equiv M^{n+}@C_{82}^{n-}$

unpaired electron

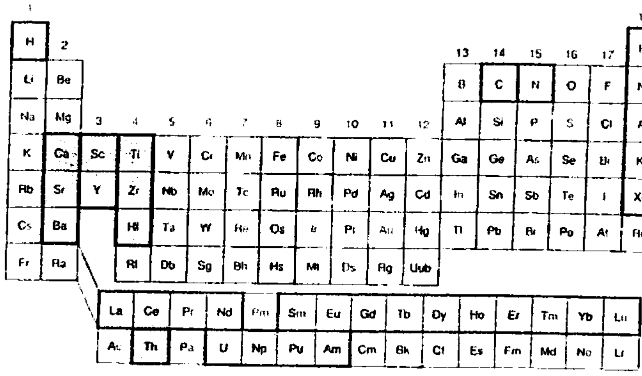
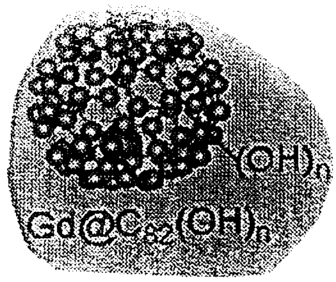


図1　フラーレンに内包される元素
枠に囲まれた元素はフラーレンに内包される。黒い枠は金属，アミの枠は非金属.

Paramagnetic Water-Soluble Metallofullerenes Having the Highest Relaxivity for MRI Contrast Agents

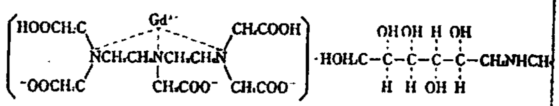
H. Shinohara et al. *Bioconjugate Chem.* **2001**, *12*, 510



- Water soluble Gd endohedral fullerenes' s paramagnetic properties are evaluated MRI contrast agents for next generation.
- Gd-fullerenols is significantly higher than the commercial MRI contrast agent Gd-DTPA (20-folds).

  ⇒ 1/20 of the clinical dose
- The strong signal was confirmed in vivo MRI at lung, liver, spleen, and kidney.
- Gd^{3+} is enshrouded to fullerene. ⇒ More stable complex

構造式:



Gd-DTPA（マグネビスト）
Commercial MRI contrast agent.

$$\text{signal intensity} \propto \rho\,(1 - e^{-TR/T_1})\,e^{-TE/T_2}$$

ρ：プロトン密度
TR：くり返し時間
TE：エコー時間
T_1, T_2：緩和時間

$T_1, T_2 \rightarrow 0$, signal intensity → 大
($1/R_1$, $1/R_2$)

Table 1. Proton Relaxivities, R_1 and R_2 of $Gd@C_{82}(OH)_{40}$ and Gd-DTPA at 0.47, 1.0, and 4.7 T, 25 °C and pH 7.5

	$Gd@C_{82}(OH)_{40}$[a]			Gd-DTPA[b]		
[$mM^{-1}\,s^{-1}$]	0.47 T	1.0 T	4.7 T	0.47 T	1.0 T	4.7 T
R_1	67	81	31	3.8	3.9	3.8
R_2	79	108	131	4.2	6.2	5.9

[a] The proton relaxivities R_1 and R_2 (the effect on $1/T_1$ and $1/T_2$) of $Gd@C_{82}(OH)_{40}$ were determined at 0.47 T (Minispec, Bruker), 1.0 T (MAGNETOM Harmony, Siemens), and 4.7 T (Unity INOVA, Varian) at 25 °C. [b] The values of the conventional MRI contrast agent, Gd-DTPA (Magnevist), were also determined for comparison.

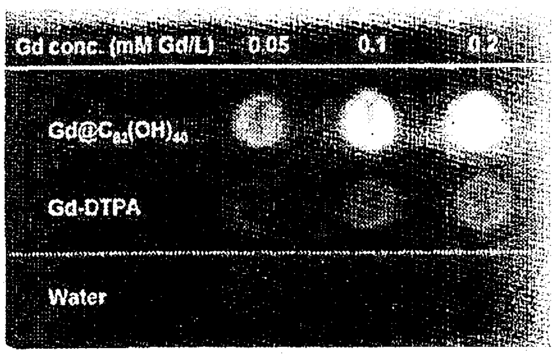


fig 11.

MRI（磁気共鳴画像法）とは
原子核を構成する核子（陽子および中性子）スピンを持っている。水素原子核としてのスピン状態は、ばらばらの場合と、そろっている場合とがあるが、通常は同じエネルギー準位をもっている。これに外部磁場を存在させると、スピン状態そろい方によってエネルギー準位の値が違うようになる。その結果、原子核はラジオ波を吸収して高いエネルギー状態になり、あるいは低いエネルギー状態になるときラジオ波を放出することができるようになる。静磁場中でラジオ波をあて、全ての原子核のエネルギー状態をそろえるとスピンの状態もそろえられる。その後放置すると、原子核は電波を出しながら低いエネルギー準位（とスピン状態）に戻ってくる。この現象を緩和と呼ぶ。緩和の速度は、組織により、また病変により異なる。これらの信号を記録し、コンピュータによって処理する事で生体組織の画像を作り出す。
医療用 MRI では特に、水素原子 ^1H の信号を見る。これらの信号を距離に比例した勾配をかけた磁場中で取ることにより、^1H の共鳴周波数が距離に比例するようにして、得られた信号の強度を白黒に変換してやる事で生体組織の画像を作り出す。造影剤を生体組織に吸収させることにより、化合物中の不対電子のつくる強磁場によりプロトン緩和が促進され、その結果信号強度が大きくなり造影能がます。

5-2. HIV-protease inhibitor (Application of fullerenes)

hydrophobic interaction

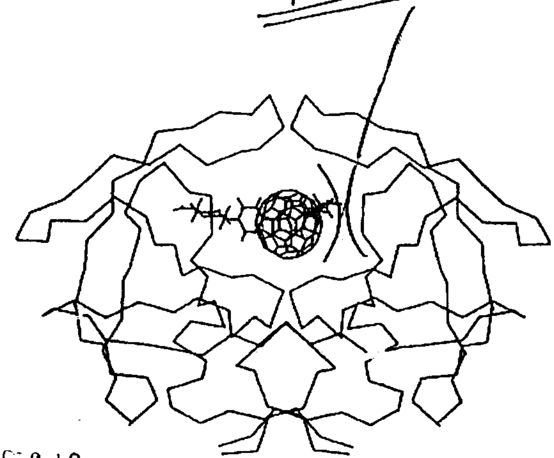
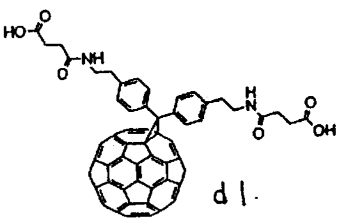


fig 12.
hydrophobic surface of HIVP's activesite.
(hydrophobic amino acids except for two Asp)

Inhibition of the HIV-1 Protease by Fullerene Derivatives: Model Building Studies and Experimental Verification

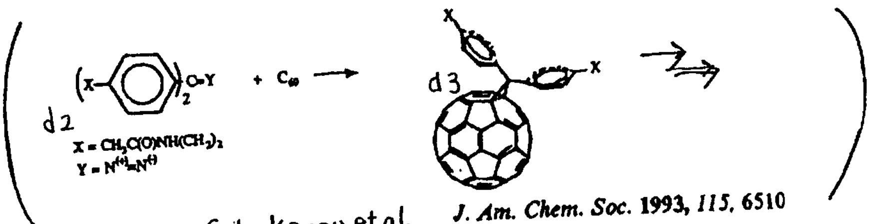
George L. Kenyon et al. *J. Am. Chem. Soc.* **1993**, *115*, 6506

- C_{60}'s steric and chemical (hydrophobic interaction) complementary with the active site of HIVP.
- Possibility of recognition of fullerene derivatives to the mutant that acquired a tolerance ?
- The fullerene derivatives recognize the shape of the entire actice site of HIVP.



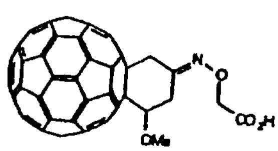
d1.

Activity EC_{50} = = 7 μM
(PBMC)
Toxiaty: EC_{50} > 100 μM
(PBMC, Verocell)



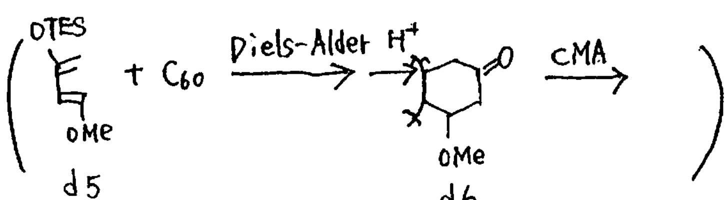
G.L. Kenyon et al. *J. Am. Chem. Soc.* **1993**, *115*, 6510

D. I. SCHUSTER *et al.* Bio. Med. Chem. Lett. 1996. 6. 1253



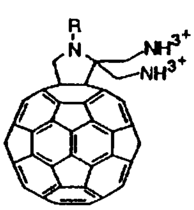
d4.

Activity : EC_{50} = 0.9 μM
Toxicity: EC_{50} > 100 μM

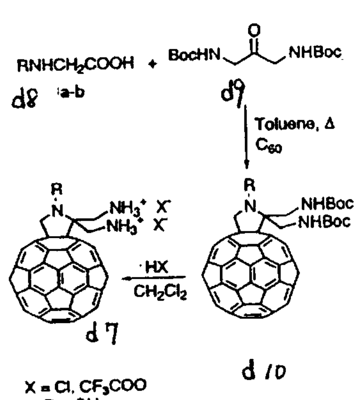


CMA; carboxy methoxyamine

M. Prato et al.
(Org. Lett 2000. 2. 3955)



d7



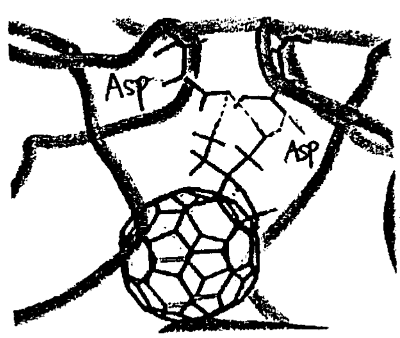
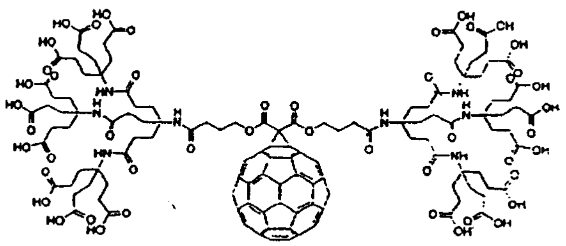


fig 13.

electrostatic interaction with Asp25 and Asp125. should increase the binding constant.

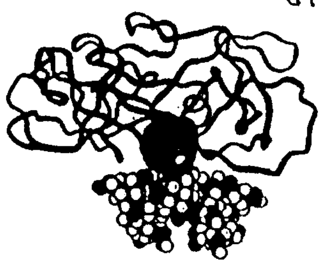
Water-soluble dendrimeric fullerene as anti-HIV therapeutic

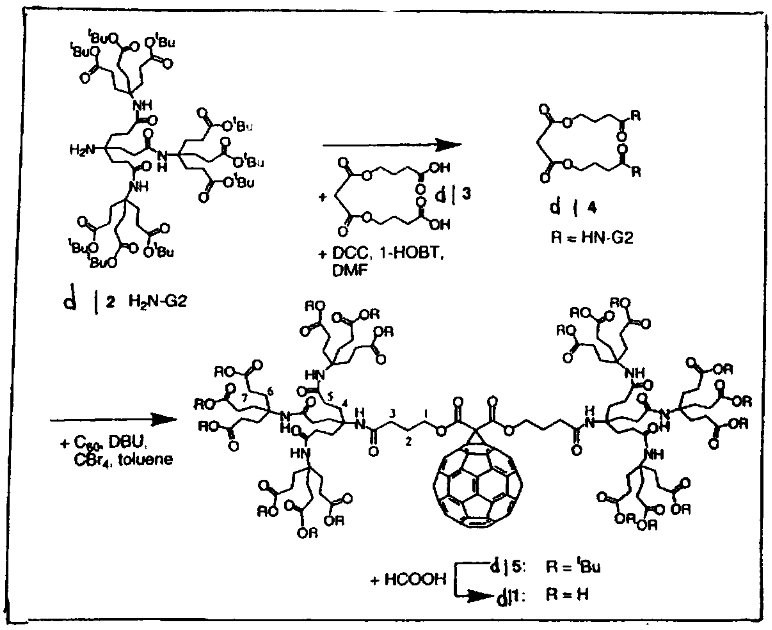
Hirsch et al. U.S. Pat. Appl. Publ., 2003, 23 pp



d11

Activity: EC_{50} = 0.22 μM
Toxicity: EC_{50} > 100 μM





- A highly water-soluble dendrimeric derivative of C_{60} with 18 carboxylic acid groups was found to be active in primary human lymphocytes acutely infected with HIV-1LAI with an EC50 of 0.22 μM (most active anti-HIV fullerene derivative), and showed no toxicity up to 100 μM in human PBM, Vero and CEM cells.
- The fullerene dendrimer was also active against mutant mol. infectious clones of HIV-1 which are resistant to AZT. and/or 3TC, drugs that are widely used in AIDS therapy.

5-3.

A non-metal system for nitrogen fixation

(Zen-ichi Yoshida et al. Nature 2004. 428. 280)

- Haber-Bosch process (1906)

$$N_2 + 3H_2 \xrightarrow[200\,atm.\ 500^\circ C]{Fe\ cat.} 2NH_3$$ (very hard condition)

C_{60} $\xrightarrow{h\nu}$ C_{60}^{*} $\xrightarrow[H^+]{N_2}$ NH_3

$$N_2 + 3H_2 \xrightarrow[visible\ light]{C_{60}:\gamma\text{-}CD\ (1:2)\ complex,\ Na_2S_2O_4,\ H_2O} 2NH_3$$ (up to 45%)

normal temperature, normal pressure
(very soft condition)

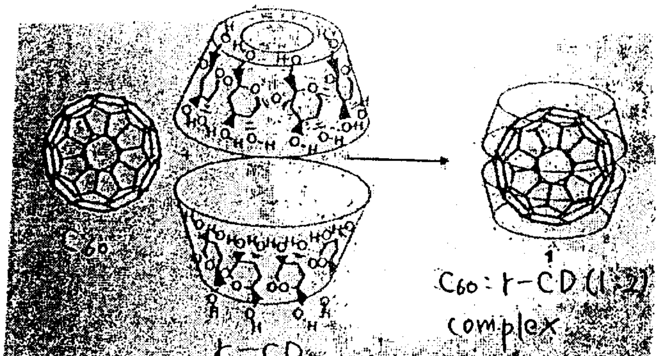


fig 14.

Zen-ichi Yoshida et al. Angew. Chem. Int. Ed 1994. 33 1597