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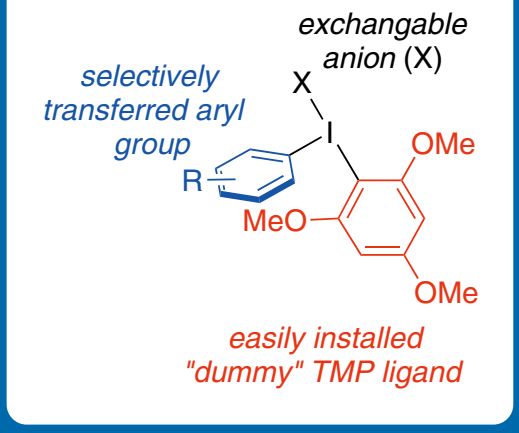

CONTENTS

Research Article

Aryl(2,4,6-trimethoxyphenyl)iodonium Salts as Reagents for Metal-Free Arylation of Carbon and Heteroatom Nucleophiles

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Abstract: The use of aryl(2,4,6-trimethoxyphenyl)iodonium salts as novel arylation reagents is discussed. The reaction mechanism of diaryliodonium salts and nucleophiles is outlined and the advantage of using unsymmetrical aryl(auxiliary)iodonium electrophiles is highlighted. Auxiliaries (dummy ligands) that are derived from 1,3,5-trimethoxybenzene are a specific focus and general synthetic approaches to and synthetic applications of these compounds are detailed.

Keywords: hypervalent iodine, diaryliodonium, arylation, metal-free

1. Introduction

Diaryliodonium salts, also referred to diaryl-λ^3-iodanes, have been of interest to synthetic chemists since their discovery well over a century ago[1] and the chemistry of hypervalent iodine has been extensively reviewed.[2] Their popularity is largely due to diverse and intriguing reactivity, and utility in the synthesis of both polymers and small molecules. With respect to the latter, diaryliodonium electrophiles are novel arylation reagents for a wide range of nucleophiles and the use of a transition metal catalyst is not required in many cases. This strategy is attractive because it parallels the simplicity of classic nucleophilic aromatic substitution (S_NAr) but has the potential to achieve the broad scope of transition metal catalyzed reactions without the cost of designer ligands or the requirement to assay and remove trace metal impurities[3] from target compounds. Consequently, unsymmetrical diaryliodonium salts may prove incredibly useful in the synthesis of pharmaceuticals, agrochemicals, or functional materials as aryl groups appear incessantly in these molecules.

The generally accepted mechanism for polar reactions of nucleophiles with diaryliodonium salt electrophiles under metal-free conditions is shown in Figure 1A with a symmetric salt and consists of two steps: ligand exchange and reductive coupling.[2e,4] In the ligand exchange step a labile anion (typically triflate, tetrafluoroborate, tosylate, or halide) is displaced by a

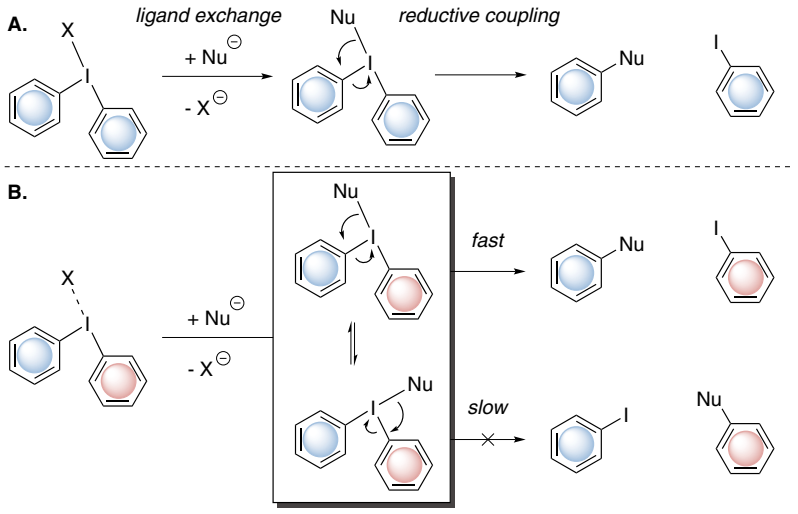

Figure 1. The mechanism of polar reactions of symmetrical or unsymmetrical diaryliodonium salts with nucleophiles

carbon or heteroatom nucleophile. In the reductive coupling step the resulting T-shaped λ³-iodane intermediate undergoes a pseudo-reductive elimination of the nucleophile ligand and one of the aryl ligands to form a new aryl-nucleophile bond and an aryl iodide. The geometry of the T-shaped intermediate is inconsequential when symmetrical diaryliodonium salts are used because reductive elimination of the nucleophile with either aryl group leads to identical products. While this scenario is more straightforward it results in significant aryl waste when diaryliodonium salts that cannot be synthesized from their constituent simple arenes are employed. A potentially less wasteful approach is to use an unsymmetrical diaryliodonium salt (Figure 1B). However, in this approach two geometrically distinct T-shaped intermediates are in equilibrium which may lead to four different products (two different aryl-nucleophile products and two different aryl iodide by-products) upon reductive elimination (Figure 1B). The synthetic utility of this approach is only realized if one of the reductive elimination steps is slower than the other thereby rendering one of the aryl groups an auxiliary or dummy ligand (Figure 1B, red group). Consequently, studies to elucidate the factors that influence and promote (or inhibit) reductive elimination have been an important part of research on diaryliodonium salt chemistry.

Two factors principally control the selectivity of reductive elimination from unsymmetrical T-shaped nucleophile-diaryl-λ³-iodane intermediates: electronic and steric effects of the aryl groups (Figure 2).[5] Electronic effects have been noted since early reaction development with these reagents independently by Beringer,[5a] McEwen[5b] and Wiegand;[5c] steric effects have been noted in specific cases, most notably by Wiegand.[5c] Several decades of reactivity studies have been distilled down to the following general trends. Electronic effects favor reductive elimination of the nucleophile with the more electron deficient aryl group. Steric effects, in the form of *ortho*-substituents, may promote reductive elimination of the nucleophile with the more sterically congested aryl group and this has been termed the "ortho effect".[5c] However, while electronic effects appear to be general across most nucleophiles, steric effects appear to be dependent on the nucleophile and this trend has led to an emergence of the "anti-ortho effect".[5g] Moreover, when electronically disparate aryl groups are present on unsymmetrical diaryliodonium salt electronic effects are generally stronger than steric effects in promoting reductive elimination.[6] Given the greater generality of the electronic effect on reductive elimination, this has been a focal point of studies to develop general auxiliaries for unsymmetrical aryl(auxiliary) iodonium salts.[7]

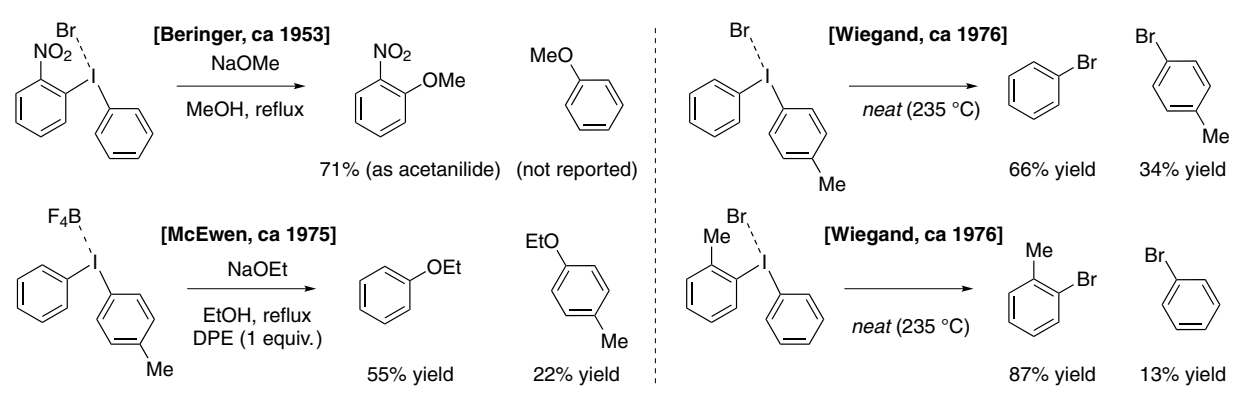

Figure 2. Representative examples of the influence of electronic and steric effects on reductive elimination

2. Synthetic Approaches to Aryl(TMP)iodonium Salts

Aryl(2,4,6-trimethoxyphenyl)iodonium salts have emerged as promising reagents for chemoselective aryl transfer to nucleophiles because the trimethoxyphenyl (TMP) moiety is relatively more electron-rich than many other arenes and thus serves as a "dummy" ligand by exploiting the pronounced electronic effect on reductive elimination. Despite evidence for the utility of these reagents,[5g] their synthesis has remained relatively limited compared to other unsymmetrical diaryliodonium salts. Methods that have previously been employed to prepare aryl(TMP)iodonium salts are presented in Figure 3.[5g,7c,d,8] Notably, the majority of these approaches have used an aryl-λ^3-iodane (four of the six general approaches) which requires independent synthesis.[5g,7d,8a,b,d,e,f] This feature, though reliable, reduces the generality of these methods and as a result between 1988 and 2015 only eight different aryl(TMP)iodonium salts were described in the chemical literature for the synthesis of small molecules.[9] A more general strategy involves the use of aryl iodides as these are widely commercially available. Toward this end, a one-pot process that incorporates an aryl-λ^3-iodane formed *in situ* and reaction with trimethoxybenzene was described in pioneering work by Kita and co-workers in 2012.[8c] In this work phenyl(TMP)iodonium tosylate (85% yield) was the only iodonium salt incorporating a TMP auxiliary. Additionally, aryl iodides that contained strongly electron donating (methoxy) or electron withdrawing (nitro) substituents resulted in low yield under the standard reaction conditions with other auxiliaries; good yield with the nitro substituted aryl iodide could be achieved when HFIP was used as the solvent.

In 2015 we initiated a project to develop a one-pot synthesis of aryl(TMP)iodonium salts from readily available aryl iodides in an effort to substantially broaden the scope of aryl(TMP)iodonium salts and thereby stimulate the development of new reactions with these nascent arylation reagents.[8g] This work builds upon the previous work of Kita,[8b,c] Olofsson,[10] and Pike.[7c,d] A key feature of our experimental set up was the removal of halogenated solvents and we found that acetonitrile was an excellent substituted for both stages (oxidation of iodine and introduction of the auxiliary). The optimization of all continuous reaction variables over two stages (temperature, time stage 1, time stage 2, stoichiometry, and solvent volume) was accomplished by Design of Experiment (DoE).[11] These studies revealed that the reaction is fast and may be complete, from set-up to isolation, within one hour. Moreover, the reaction could be run under relatively concentrated conditions of 1 M and with equal stoichiometry of all reactants. Overall, the reaction conditions provided a broad scope of substrates that could be synthesized in short reaction time and the isolated yields range from 67-96% with an average of 87%. Strongly electron donating and electron withdrawing substituents on the aryl iodides are well tolerated as are potentially reactive functionality including benzyl bromide and free hydroxyl groups. These conditions were also compatible with azine heterocycles and more elaborate aryl moieties that underscore the use of an unsymmetrical diaryliodonium salt in subsequent arylation chemistry. The current scope, to the best of our knowledge, of all aryl(TMP)iodonium salts obtained from our work and all previous methods is presented in Figure 4.

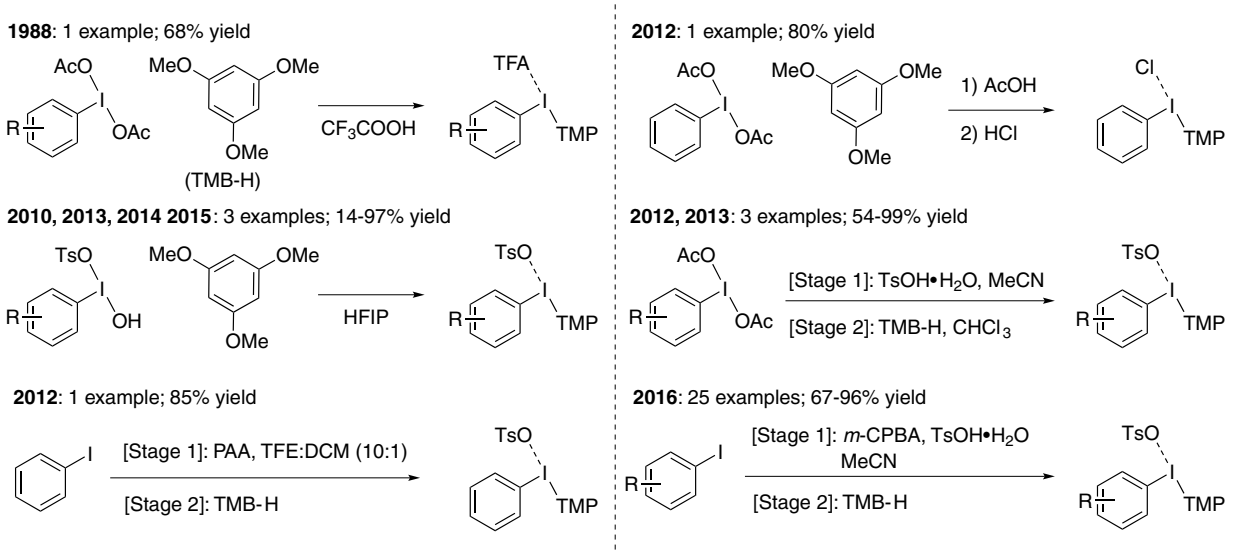

Figure 3. Synthetic approaches to aryl(TMP)iodonium salts

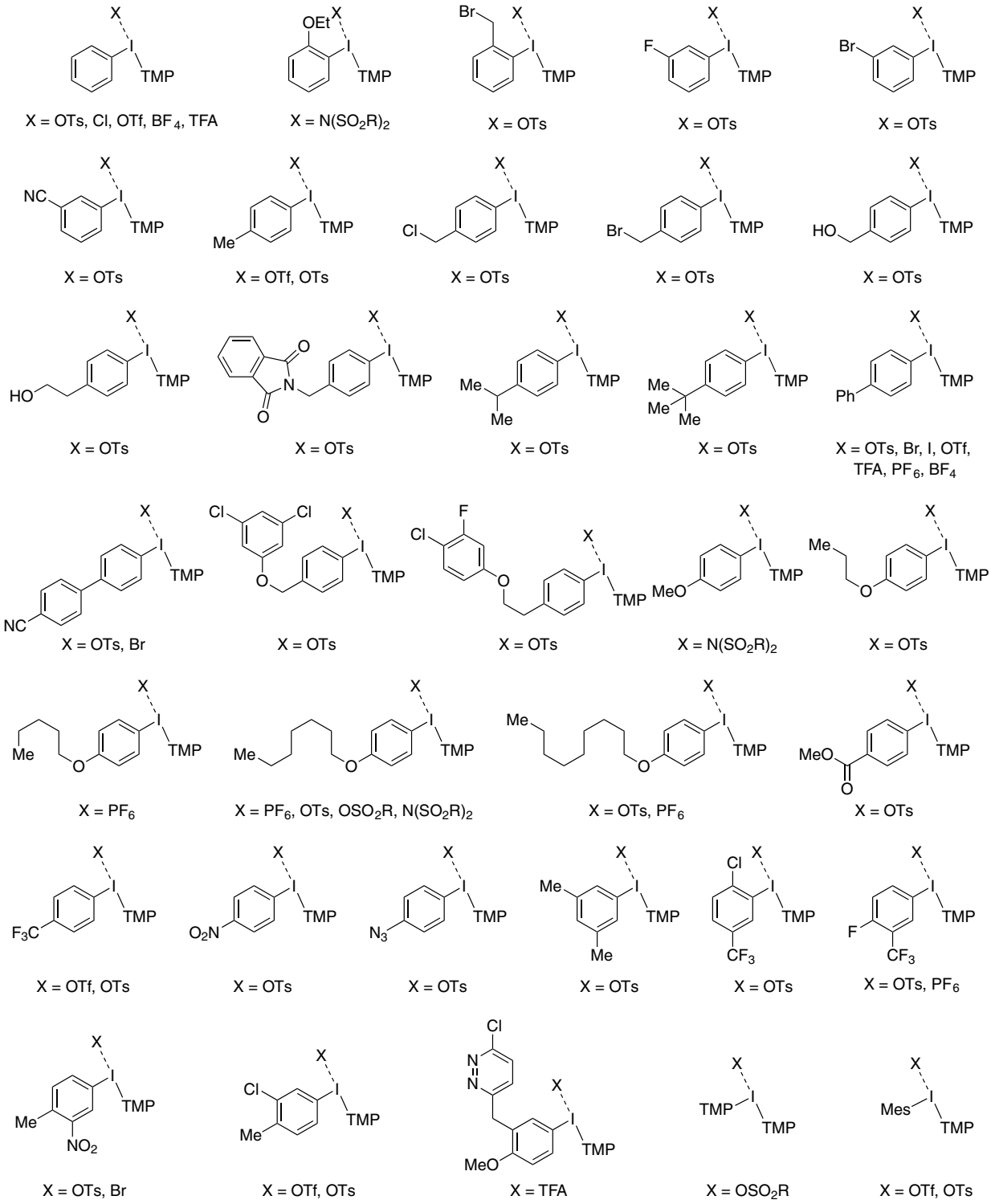

Figure 4. Scope of aryl(TMP)iodonium salts

The counter anion is a useful handle for reactivity of diaryliodonium salts and the ability to access diaryliodonium salts with a range of counter anions is a critical component of reaction development. The vast majority of aryl(TMP) iodonium salts outlined in Figure 4 are the tosylate salts which is a consequence of the method of synthesis (Figure 3). During our development of the one-pot synthesis of aryl(TMP) iodonium salts we found that the tosylate anion could be readily exchanged to other anions under aqueous conditions (Figure 5). Bromide, iodide, trifluoroacetate, triflate, tetrafluoroborate, and hexafluorophosphate were all introduced in good yield; essentially quantitative replacement of the tosylate was observed.

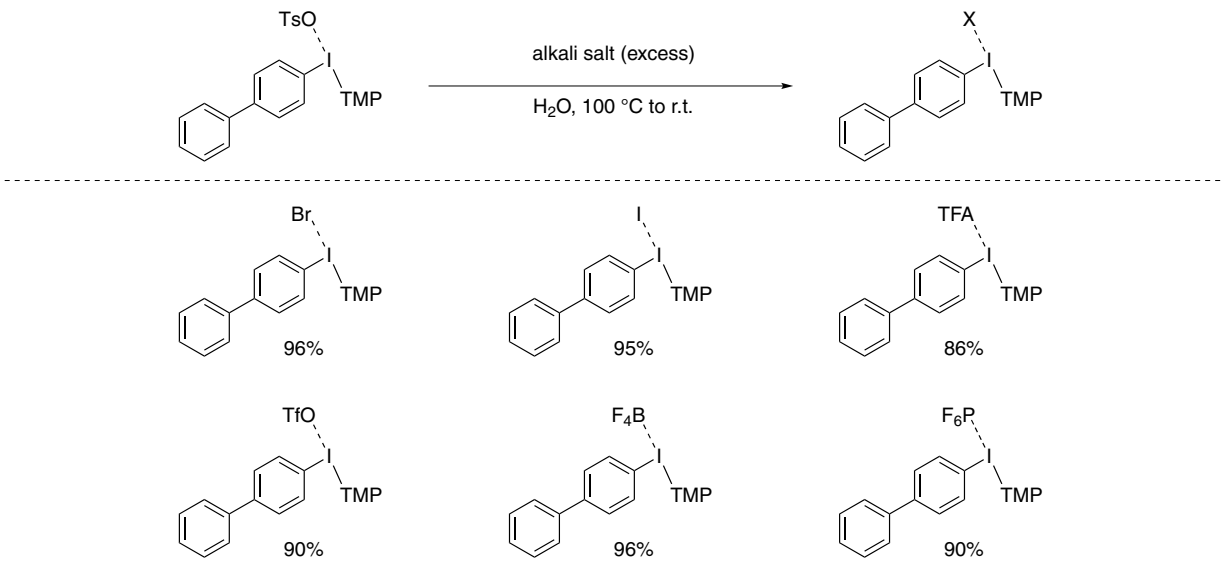

Figure 5. Counter anion exchange from aryl(TMP)iodonium tosylates

3. Metal-free Reactions of Aryl(TMP)iodonium Salts for the Synthesis of Small Molecules

The use of aryl(TMP)iodonium salts as metal-free arylation reagents for small molecule synthesis continues to grow and is outlined in Figure 6.[5g,7d,8g,e,12] The earliest reported case was the arylation of three malonate-type nucleophiles in 1999 (Figure 6, *C*-nucleophiles).[12a] For almost two decades these reagents received little attention and then, beginning in 2013, 14 more examples have emerged to include *F*-, *N*-, *O*-, and *S*-nucleophiles[5g,7d,8e,g,12b] with 7 of the examples reported in 2016.[8g,12b] The examples presented in Figure 6 highlight two exciting features of the aryl(TMP)iodonium reagents relative to other diaryliodonium salts: 1) aryl groups with electron-donating (e.g., *t*-Bu) and withdrawing (e.g., N_3) substituents are chemoselectively transferred to nucleophiles in good yield, 2) elaborate aryl groups (e.g., 4′-cyanobiphenyl) are chemoselectively transferred to nucleophiles. These features specifically indicate the potential utility and generality of these reagents for metal-free synthesis of small molecules.

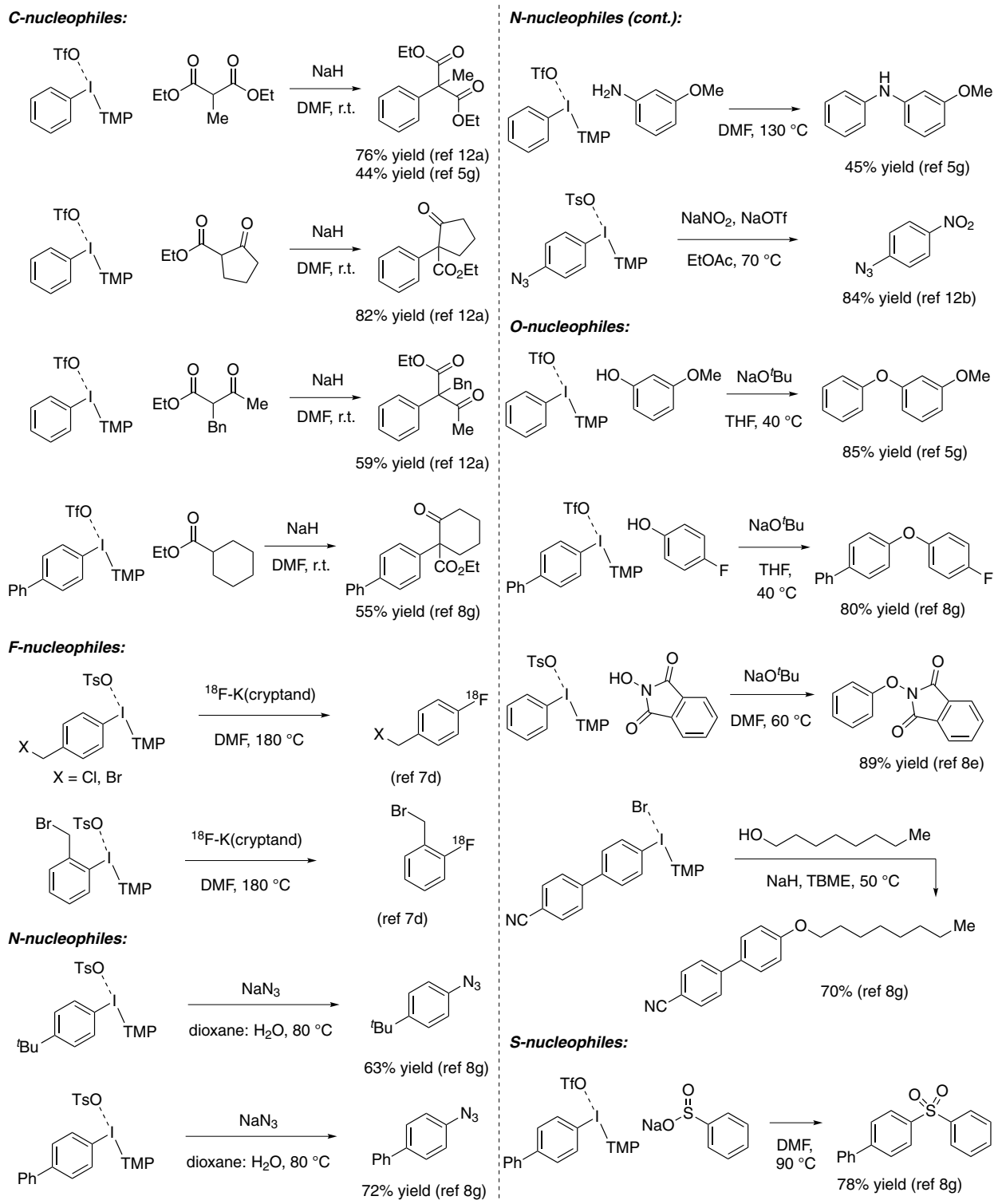

Figure 6. Synthetic applications of aryl(TMP)iodonium salts in metal-free reactions

4. Conclusions and Outlook

Diaryliodonium salts are novel reagents for metal-free arylation of carbon and heteroatom nucleophiles. The aryl(TMP) iodonium derivatives are uniquely promising toward this end as we and others have demonstrated their use with *C*-, *F*-, *N*-, *O*-, and *S*-nucleophiles. As these reagents become more readily available through general synthetic methods and commercial vendors their application in the synthesis of small molecules is anticipated to increase. The surge of use of these reagents in the past year is evidence for that and I am excited to watch with field grow in years to come.

Acknowledgments

I gratefully acknowledge Portland State University and the Donors of the American Chemical Society Petroleum Research Fund (ACS PRF DNI-1 #54405) for financial support of this research. I am especially indebted to my research students who carried out the lab work and made insightful discoveries.

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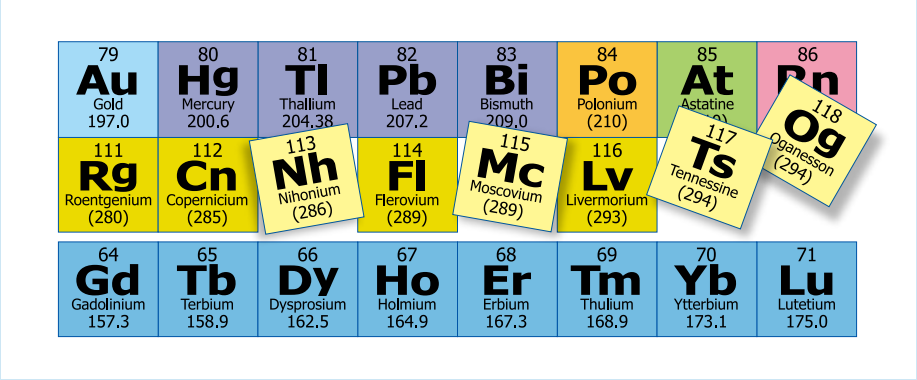
[Specialties] Organic synthesis, hypervalent iodine, reaction discovery and development

Chemistry Chat -Focusing on the Elements-

Naming New Elements

Kentaro Sato



In November 30, 2016, International Union of Pure and Applied Chemistry (IUPAC) announced that it formally approved the names for the elements 113, 115, 117, and 118. The element 113 was named **nihonium** as proposed by the discoverers (with the symbol **Nh**). It is delightful that the name of my country has been added to the periodic table at last (Nihon means Japan in Japanese). The proposed names for the other three elements were approved as well: the element 115 as **moscovium** (symbol **Mc**), the element 117 as **tennessine** (symbol **Ts**), and the element 118 as **oganesson** (symbol **Og**).

Almost a year ago I wrote about how nihonium was proposed for the element 113. This time, let me share the stories of how some of the other recently discovered elements were named.

When a new element is discovered, the discoverer is not allowed to pick a random name. According the IUPAC guidelines, new elements are supposed to be named based on: (1) a mythological concept or character, (2) a mineral or similar substance, (3) a place or geographical region, (4) a property of the element, or (5) a scientist.

There were once many examples where elements were named after minerals from which they were isolated, such as **zirconium** and **molybdenum**. However, since new elements are synthesized by nuclear reactions nowadays, mineral-derived names have become obsolete.

Elements having a name with mythological origins include **helium** (named after Helios, the Greek god of the sun) and **thorium** (named after Thor, the Norse god of thunder). This tradition, however, has become uncommon too and not been followed after the element 94.

The elements such as **astatine** (meaning unstable), **radon** and **radium** (both meaning radioactive), and **actinium** (meaning ray) are named after their property, but these properties actually apply to all of the recently discovered elements. Also, heavy elements with an atomic weight greater than 100 can be synthesized in quantities of only a few to a few hundred atoms, therefore, it is naturally difficult to understand their properties. For these reasons, property has not been adopted either to name elements in recent years.

Accordingly, all of the manmade elements beyond the element 94 have names originating from either a place/ country or a scientist. The naming processes, however, were far from straightforward and sometimes involved controversies.

The heaviest naturally occurring element is **uranium** (the element 92) and heavier elements are synthesized by either bombardment of an atomic nucleus with neutrons or collision of atomic nuclei against each other. Note: Precisely speaking, **neptunium** (the element 93) and **plutonium** (the element 94) were later found to exist in natural uranium ore in minute quantities. From the element 93 to 103, the discoveries were dominated by American scientists. The element 95 was named **americium** and the elements 97 and 98 were named **berkelium** and **californium**, respectively, after University of California, Berkeley, where the discoveries were made.

Instead of just celebrating their nation and university, the American scientists did not forget to credit the great scientists of the past. The element 96 was named **curium** after Marie Curie, the element 99 was named **einsteinium** after Albert Einstein, and the element 100 was named **fermium** after Enrico Fermi.

Lawrencium, the element 103, was named after Ernest Lawrence, who is known as the inventor of cyclotron. Lawrence was the founder and director of the Radiation Laboratory at UC Berkeley, where a number of transuranium elements were discovered. This laboratory was later renamed to the Lawrence Berkeley National Laboratory to honor his name. The Lawrence Livermore National Laboratory, the hub for the recent research on superheavy elements in the US, also recognizes his name.

As I mentioned so far, a majority of the names are taken from the names of nuclear physicists. An exception is the element 102, which is named **nobelium** after Alfred Nobel, who was a chemist. Of course, Nobel did not contribute to the field of nuclear physics directly, but one could say that the well-known prize he established helped advance science in general, including atomic science.

The naming of the element 101 was somewhat controversial, when the scientists at UC Berkeley named it **mendelevium** after Dmitri Mendeleev, the father of the periodic table. The time was 1955 in the midst of the Cold War, so there was uncertainty as to whether it was appropriate for Americans to honor Mendeleev, a Russian scientist. The name was approved nevertheless, and the acceptance perhaps showed openness of the American scientists at that time.

The lead the US had over other nations in the race for discovering new elements suddenly disappeared in 1964. The Russian group led by Georgy Flyorov claimed that they had succeeded in synthesizing the element 104, which they named **kurchatovium** after fellow Russian nuclear physicist Igor Kurchatov.

The report, which had a "Sputnik Crisis-like effect in nuclear physics", stunned the American physicists. They argued back that the Soviets lacked sufficient supporting data and countered by synthesizing the element 104 themselves and named it **rutherfordium**. This name was chosen in honor of physicist Ernest Rutherford.

Over a few decades after this incident, both Americans and Soviets continued to give independent names to the next few elements as they competed to claim the discoveries, creating confusions in scientific world. In particular, the Americans named the element 106 **seaborgium** after Glenn Seaborg, who was still alive at that time. Even though there was no rule that prohibited it, it seemed like a clear political move and the universal respect symbolized once by mendelevium seemed to have vanished.

In 1980's, West Germany joined the race and the three-way competition resulted in continuing confusions and disputes. When IUPAC stepped in and assessed the data to finally determine the names of the elements 104 to 109, it was already 1997, years after the end of Cold War.

Afterwards, the research on superheavy elements in the United States experienced the fabrication incident regarding the element 118 and major budget cuts. Consequently, the American scientists are now forced to work within joint programs with Russia and their national program has slowed down inevitably. Of the four elements for which names have just been approved, the element 117 was named **tennessine** (after Tennessee, where important laboratories such as Oak Ridge National Laboratory and Vanderbilt University are located), while the elements 115 and 118 were named **moscovium** (after Moscow, the Russian capitol) and **oganesson** (after Yuri Oganessian, a leading figure in elements research in Russia), respectively. Oganessian is still alive and was the leader of the Russian research on the aforementioned element 106. The fact that his name was chosen can be viewed as something of a retaliation, as the US took the naming right for the element 106 a few decades ago.

There are many giants in science history whose names have not been used to name new elements, such as Erwin Schrödinger, Werner Heisenberg, and Wolfgang Pauli, to name a few. And I would personally think that for the element 118, which is a group 18 element, a name to honor Sir William Ramsay, the father of noble gases, might have been a good alternative. Amidst intense competitions, it seems that it will take a little longer until scientists regain open-mindedness when naming new elements.

Introduction of the author :

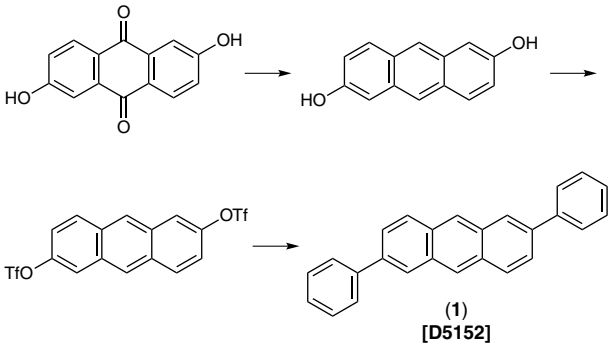
Kentaro Sato

[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 π-system figuration, scientific research on innovative areas.
[Specialty] Organic chemistry
[Website] The Museum of Organic Chemistry <http://www.org-chem.org/yuuki/MOC.html>

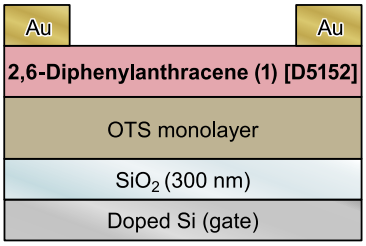
High Mobility Organic Semiconductor: 2,6-Diphenylanthracene

D5152 2,6-Diphenylanthracene (purified by sublimation) (1) **100mg**

Extending the π-conjugation network/system of polyacene derivatives is a good molecular design strategy for the synthesis of high-mobility organic transistor materials. Pentacene and hexacene are well known as high-mobility organic semiconductors; however, their air/chemical instabilities are unsatisfactory. Ding and Hu *et al.* developed a straightforward synthetic pathway (Scheme 1) to 2,6-diphenylanthracene (**1**) and reported its organic transistor characteristics.[1] In a top-contact configuration, the anthracene derivative **1** exhibited a high mobility of more than 10 cm^2/Vs on an OTS-treated Si/SiO_2 substrate (Chart 1). The fabricated device was stable for a long time under an air atmosphere.



Scheme 1. Synthesis of 2,6-diphenylanthracene (**1**)



Mobility: >10 cm^2/Vs
On/off ratio: $>10^7$

Chart 1. Device structure

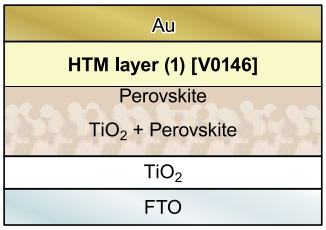
Reference

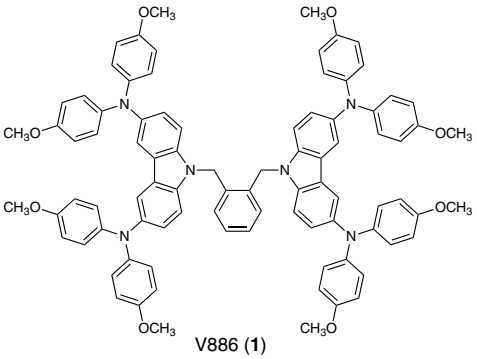
1) Thin film field-effect transistors of 2,6-diphenylanthracene (DPA)
J. Liu, H. Dong, Z. Wang, D. Ji, C. Cheng, H. Geng, H. Zhang, Y. Zhen, L. Jiang, H. Fu, Z. Bo, W. Chen, Z. Shuai, W. Hu, *Chem. Commun.* **2015**, *51*, 11777.

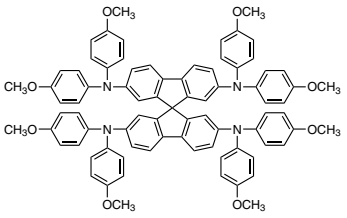
A Novel Hole Transport Material for Perovskite Solar Cells: V886

V0146 V886 (1) **1g 5g**

Recently, perovskite solar cells have received much attention and novel hole transport materials (HTMs) for these solar cell devices have been developed. Nazeeruddin *et al.* have reported a novel HTM containing carbazole structures (V886, **1**).[1] Some advantages of **1** are the simple synthetic pathway at a low cost and higher glass transition temperature compared with those of spiro-OMeTAD. The power conversion efficiency of a perovskite solar cell using **1** was 16.91% as reported in 2015, which was comparable with that of a spiro-OMeTAD device (18.36%).[1]







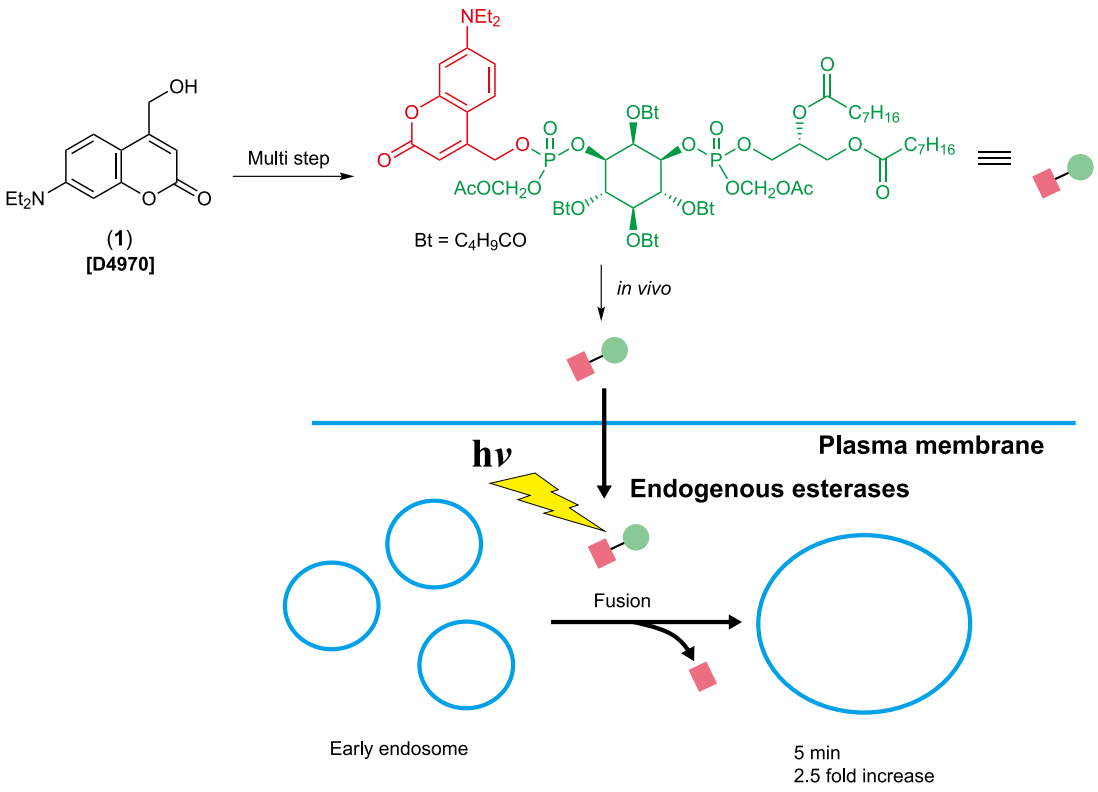
Reference

1) A methoxydiphenylamine-substituted carbazole twin derivative: An efficient hole-transporting material for perovskite solar cells
P. Gratia, A. Magomedov, T. Malinauskas, M. Daskeviciene, A. Abate, S. Ahmad, M. Grätzel, V. Getautis, M. K. Nazeeruddin, *Angew. Chem. Int. Ed.* **2015**, *54*, 11409.

Photoremovable DEACM Protecting Group

D4970 7-(Diethylamino)-4-(hydroxymethyl)coumarin (1) 200mg

7-(Diethylamino)-4-(hydroxymethyl)coumarin (**1**) works as a photolabile protecting group of phosphoric acids and sulfonic acids and can be removed by irradiating at 300–450 nm.[1] **1** is applied to photoinducing endosomal fusion by a caged phosphatidylinositol 3-phosphate in living cells[2] and photo-control of RNA transcription by a caged adenosine triphosphate.[3]



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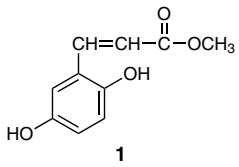
1) (Coumarin-4-yl)methyl esters as highly efficient, ultrafast phototriggers for protons and their application to acidifying membrane surfaces
D. Geißler, Y. N. Antonenko, R. Schmidt, S. Keller, O. O. Krylova, B. Wiesner, J. Bendig, P. Pohl, V. Hagen, *Angew. Chem. Int. Ed.* **2005**, *44*, 1195.

2) Activation of membrane-permeant caged PtdIns(3)P induces endosomal fusion in cells
D. Subramanian, V. Laketa, R. Müller, C. Tischer, S. Zarbakhsh, R. Pepperkok, C. Schultz, *Nat. Chem. Biol.* **2010**, *6*, 324.

3) Light activation of transcription: Photocaging of nucleotides for control over RNA polymerization
A. V. Pinheiro, P. Baptista, J. C. Lima, *Nucl. Acids Res.* **2008**, *36*, e90.

Tyrosine Kinase Inhibitor: Methyl 2,5-Dihydroxycinnamate

M2520 Methyl 2,5-Dihydroxycinnamate (1) 10mg 100mg



1

Table Inhibition activity of methyl 2,5-dihydroxycinnamate[2,3]

Inhibition	IC_{50} (μg/ml)
EGFR-tyrosine kinase (*in vitro*)	0.15
Cell growth (ER12 cells)	
Methyl 2,5-dihydroxycinnamate	0.5
Erbstatin	1.65

Erbstatin, an inhibitor of epidermal growth factor receptor (EGFR)-associated tyrosine kinase, was isolated from Actinomycetes.[1] Methyl 2,5-dihydroxycinnamate (**1**) is an analog of erbstatin and inhibits EGFR-associated tyrosine kinase *in vitro*.[2] **1** has also been shown to inhibit autophosphorylation of EGFR.[2] As shown in the Table, **1** inhibits EGF-induced phenotype change in EGFR-overexpressing NIH3T3 (ER12) cells.[3] **1** is demonstrated to be about 4 times more stable than erbstatin in calf serum.[2]

This product is for research purpose only.

References

1) Studies on a new epidermal growth factor-receptor kinase inhibitor, erbstatin, produced by MH435-hF3
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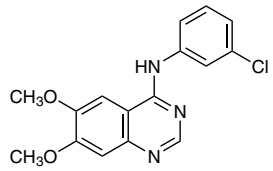
2) Inhibition of epidermal growth factor-induced DNA synthesis by tyrosine kinase inhibitors
K. Umezawa, T. Hori, H. Tajima, M. Imoto, K. Isshiki, T. Takeuchi, *FEBS Lett.* **1990**, *260*, 198.
3) Inhibition of epidermal growth factor receptor functions by tyrosine kinase inhibitors in NIH3T3 cells
K. Umezawa, D. Sugata, K. Yamashita, N. Johtoh, M. Shibuya, *FEBS Lett.* **1992**, *314*, 289.

Tyrosine Kinase Inhibitor: Tyrphostin AG 1478

T2944 Tyrphostin AG 1478 (1) 25mg



1

Table Inhibition of selected protein kinases by AG1478[1]

Protein kinase	IC_{50} (μM)
EGFR	0.003
Her2/neu	> 100
PDGF-R	> 100
$p210^{Bcr\text{-}Abl}$	> 50

Tyrphostin AG1478 (**1**) is an inhibitor of protein tyrosine kinase and is highly selective for epidermal growth factor receptor (EGFR).[1] **1** can inhibit EGFR with IC_{50} of 3 nM, while the IC_{50}s for other kinases are higher as shown in the Table.[1] It was reported that the combination of **1** with cytostatic drugs, Cisplatin or Paclitaxel, induces a synergistic effect of growth inhibition of endometrial cancer cells.[2]

This product is for research purpose only.

References

1) Tyrosine kinase inhibition: An approach to drug development
A. Levitzki, A. Gazit, *Science* **1995**, *267*, 1782.
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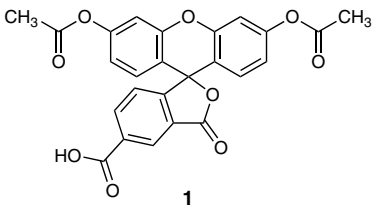
N. Takai, T. Ueda, M. Nishida, K. Nasu, H. Narahara, *Mol. Med. Rep.* **2010**, *3*, 479.

Related Products

D3371	Cisplatin	100mg 1g
P1632	Paclitaxel	100mg

Fluorescent Probe: 5-CFDA

C2859 5-Carboxyfluorescein Diacetate (1) 50mg 200mg



1

Carboxyfluorescein diacetate (CFDA) is used to measure intracellular pH.[1] CFDA easily permeates cells and is converted to carboxyfluorescein. The carboxyfluorescein is retained better in cells compared with fluorescein. Therefore, CFDA is applied in the cell viability assay.[2]

5-Carboxyfluorescein diacetate (5-CFDA, **1**) is used for the FRAP assay by combination with another fluorescent probe. In the study on the heterocyst forming of cyanobacterium by Plominsky *et al.*, **1** and calcein were used for the FRAP assay.[3]

FRAP: fluorescence recovery after photobleaching

This product is for research purpose only.

References

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3) Intercellular transfer along the trichomes of the invasive terminal heterocyst forming cyanobacterium *Cylindrospermopsis raciborskii* CS-505
Á. M. Plominsky, N. Delherbe, D. Mandakovic, B. Riquelme, K. González, B. Bergman, V. Mariscal, M. Vásquez, *FEMS Microbiol. Lett.* **2015**, *362*, fnu009.

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