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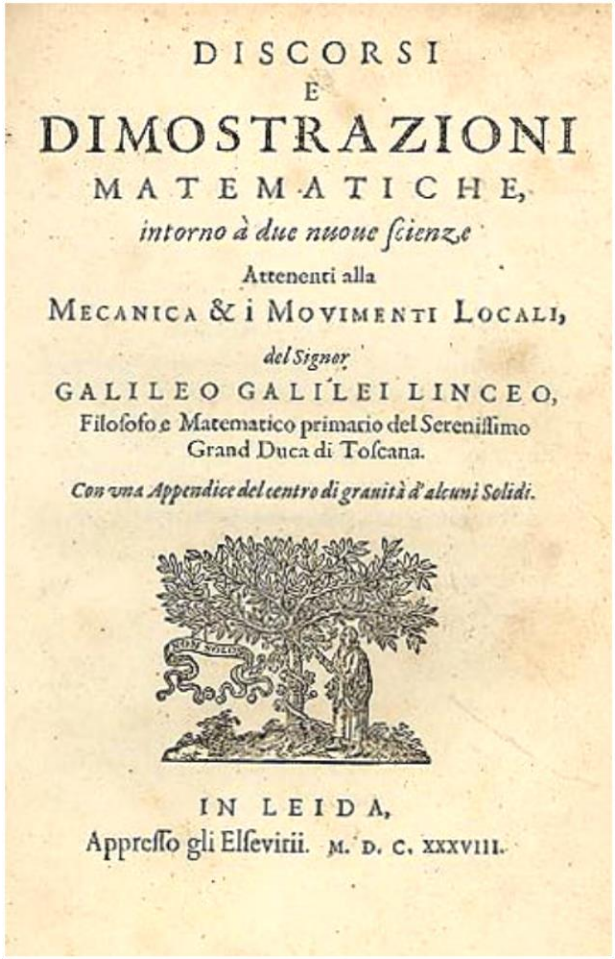

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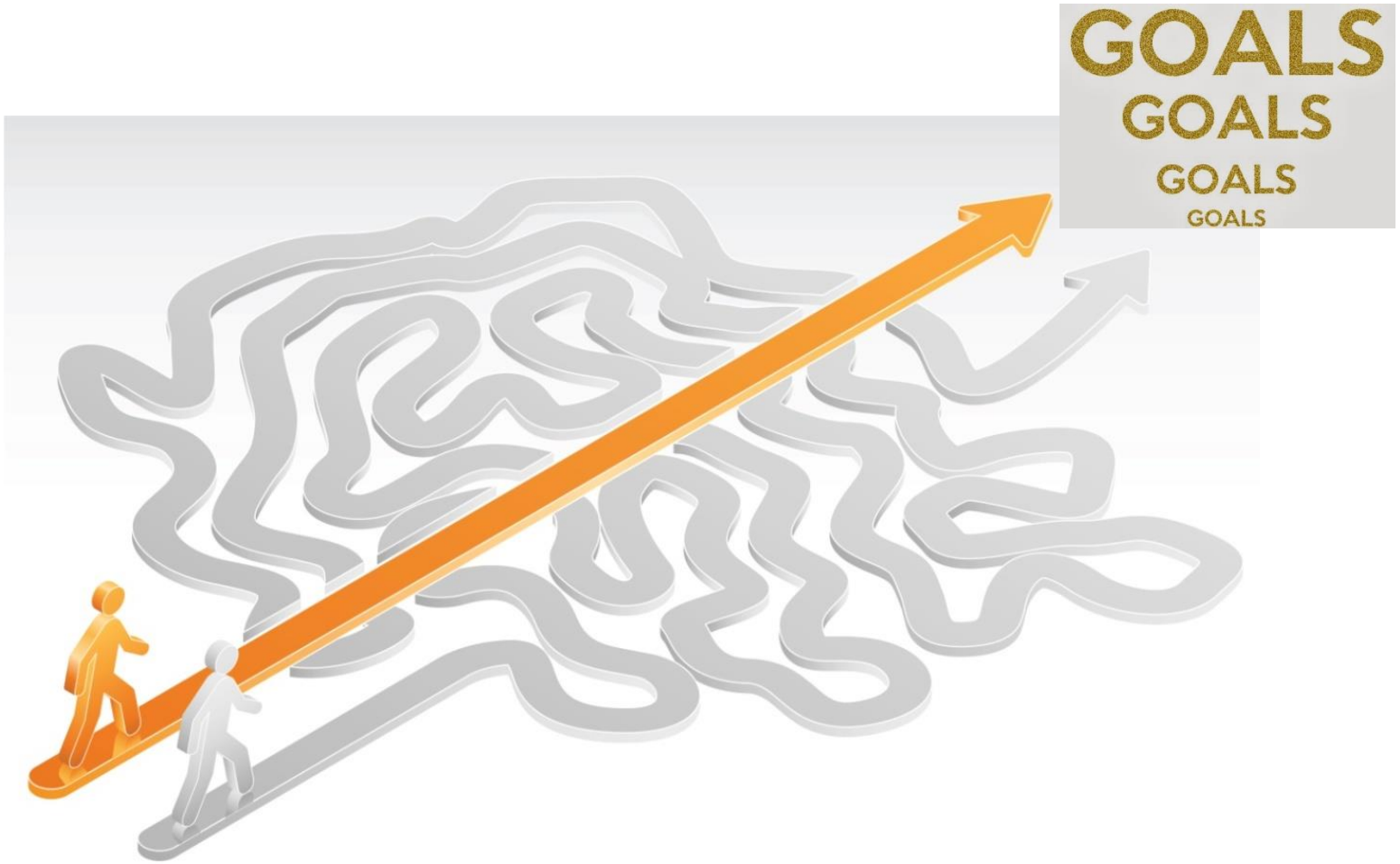

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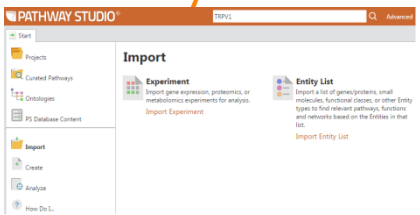

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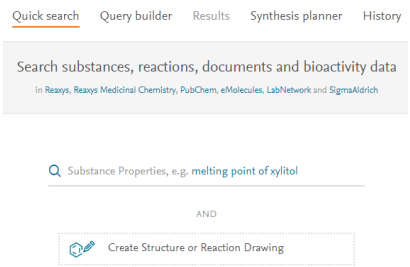

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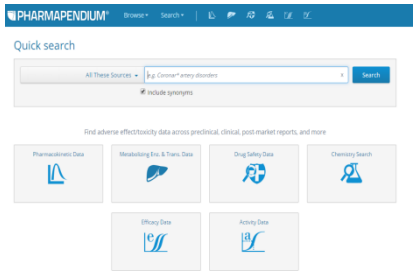

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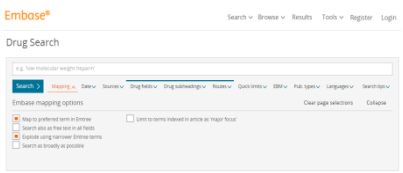

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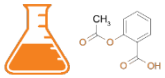

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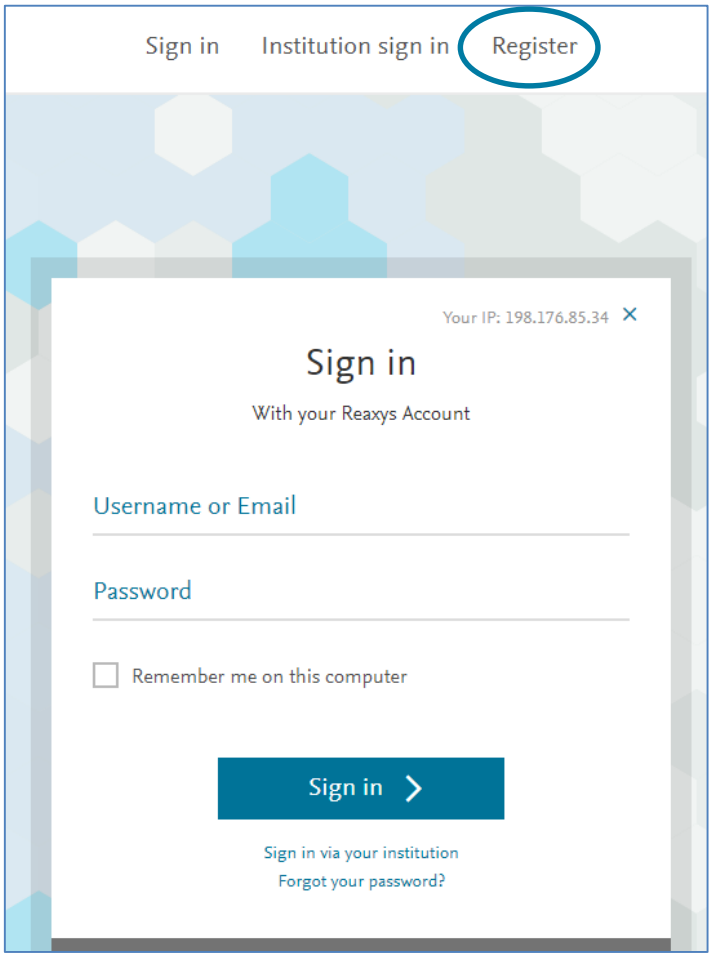

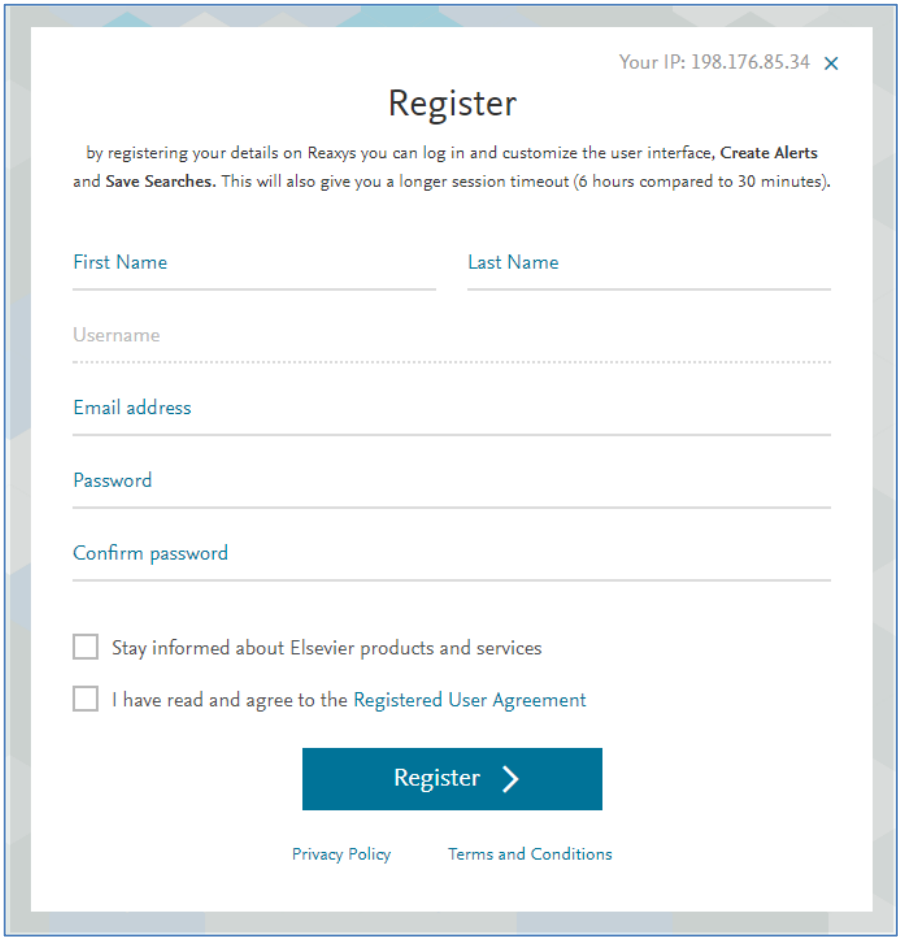

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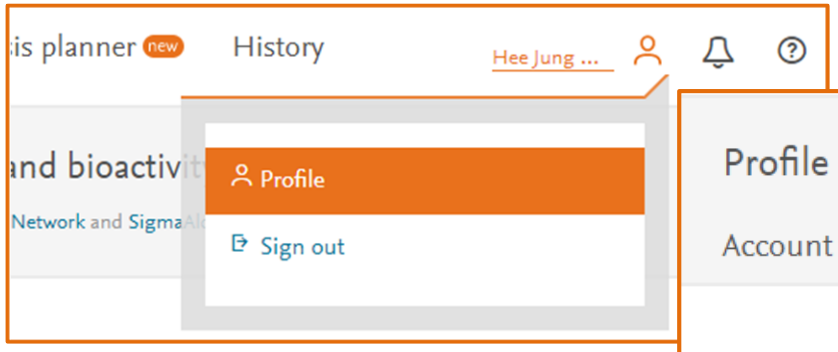

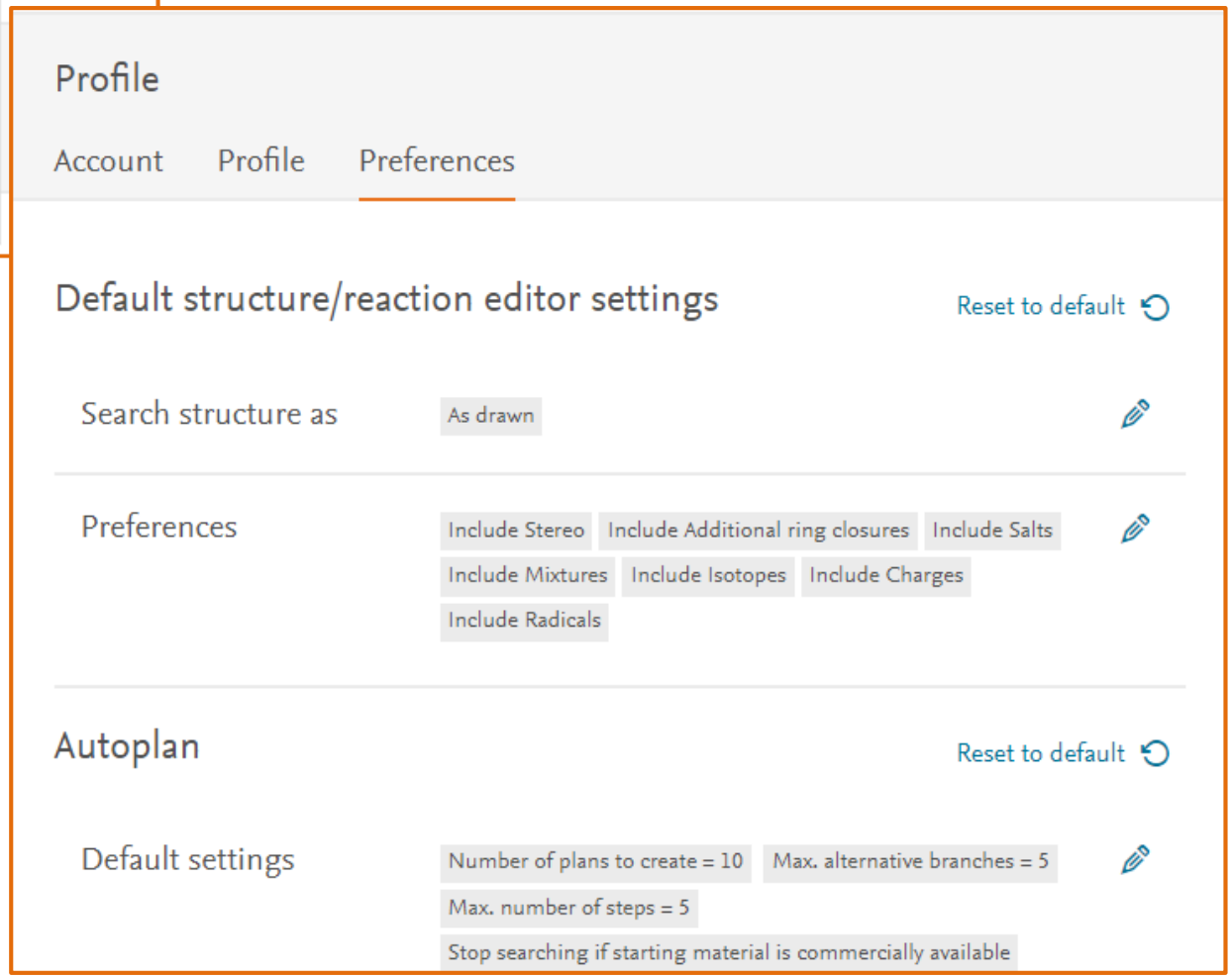

What’s New Reaxys 2.0

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Synthesis, drug release and targeting behaviors of Novel Folated Pluronic F87/poly(lactic acid) block copolymer

Xiang Yuan Xiong *, Xiang Qin, Zi Ling Li, Yan Chun Gong, Yu Ping Li

School of Life Science, Jiangxi Science and Technology Normal University, Nanchang 330013, China

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ABSTRACT

Novel Folated Pluronic F87/poly(lactic acid) block copolymer (FA-F87–PLA) was synthesized by two step reactions. The self-assembling behavior of FA-F87–PLA block copolymer in aqueous solutions was examined by fluorescence measurement, Dynamic Light Scattering (DLS) and Transmission Electron Microscopic (TEM) techniques. The morphology of FA-F87–PLA nanoparticles was found to be spherical micelles. Paclitaxel (PTX) loaded in FA-F87–PLA nanoparticles shows an initial burst release in the first 11 h and followed by a slow release. The in vitro targeting behavior of FA-F87–PLA nanoparticles against OVCAR-3 (folate receptor positive) was investigated by 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) tests. MTT results show that the anticancer effect of PTX in FA-F87–PLA nanoparticle over OVCAR-3 cells was stronger than that of PTX in nontargeted PLA–F87–PLA nanoparticle under the specific targeting interaction between folate groups on the surface of FA-F87–PLA nanoparticles and folate receptor on the surface of OVCAR-3 cells. The targeting behaviors of FA-F87–PLA nanoparticles were further confirmed by fluorescence microscopy (FM) technique. The intracellular distribution of FA-F87–PLA nanoparticles was also studied using a triple-labeling method. It was observed that FA-F87–PLA nanoparticles are mainly localized within the cytoplasm of OVCAR-3 cells.

1. Introduction

Amphiphilic block copolymers have been widely studied in the past few decades for their application in drug delivery systems because they are able to self-assemble into nanoparticles containing a hydrophobic core and a hydrophilic shell [1–5]. Hydrophobic poly(lactic acid) (PLA) are well-known biodegradable and biocompatible polyester [6–9]. Pluronic block copolymers are one of the very few synthetic polymeric materials approved by the U.S. Food and Drug Administration for use as food additives and pharmaceutical ingredients. The biocompatible amphiphilic block copolymers PLA–Pluronic–PLA have been synthesized previously and their application in drug delivery systems have been studied in detail by us [10–14].

There has always been a strong impetus to the development of polymeric nanoparticles with targeting ligands, which are able to increase the selectivity and efficiency of drug delivery to the target cells, leading to a better therapeutic efficacy as

2. Materials and methods

2.1. Materials

Pluronic F87 was kindly supplied by BASF Corporation. L-lactide was purchased from Sigma–Aldrich and recrystallized twice from ethyl acetate (EtAc). The purified L-lactide was stored at 4–5 °C under argon environment. Dichloromethane (CH_2Cl_2) and dimethyl sulfoxide (DMSO) was purified by distillation over CaH_2. Folic acid (FA), stannous octoate [$Sn(Oct)_2$] and sodium phosphotungstate were purchased from Sigma–Aldrich and used as received. Pyrene was purchased from Acros and used as received. N,N′-Dicyclohexylcarbodiimide (DCC), 4-Dimethylaminopyridine (DMAP) was purchased from J&K Chemica and used as received. Paclitaxel (PTX) was kindly supplied by Fujian South Pharmaceutical Co., Ltd. PTX injections was purchased from Sichuan Shenhe Pharmaceutical Co., Ltd. Tetramethylrhodamine-5-carbonyl azide (TMRCA) was purchased from Invitrogen. 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) was purchased from Solarbio and used as received. Dulbecco's Modified Eagle's Medium (DMEM) was purchased from Gibco and used as received. All other chemicals were of reagent grade. Human ovarian cancer cells OVCAR-3 and human lung carcinoma cells A549 were purchased from CICAMS, Beijing.

2.2. Synthesis of FA-F87–OH

Pluronic F87 (20 g, 2.6 mmol) was dissolved in 100 mL of dry CH_2Cl_2. A solution of FA (0.83 g, 1.9 mmol) and DMAP (0.19 g, 1.56 mmol) in anhydrous DMSO was then added to the reaction flask under stirring. After cooling of the above solution to 0 °C, DCC (0.36 g, 1.75 mmol) was added dropwise via a dropping funnel over 30 min and then the reaction was carried out for 48 h at room temperature. The reaction mixture was then extracted with 10% $NaHCO_3$ solution to remove unreacted FA. After this step, the organic phase was frozen overnight and the insoluble substances were removed by filtration. The organic solution was then precipitated twice in cold diethyl ether. The polymers were filtered and dried overnight under vacuum.

2.3. Synthesis of FA-F87–PLA block copolymer

PLA segment was attached to one end of Pluronic F87 by ring-opening polymerization to obtain FA-F87–PLA amphiphilic block copolymer. FA-F87–OH (2.5 g) was distillated by azeotropic distillation under argon. LA (2.5 g) was added at room temperature under argon and was followed by the addition of stannous octoate (about 0.1 wt% of LA). The mixture was stirred at 120 °C for 6 h. After cooling to room temperature, the reaction mixture was dissolved in CH_2Cl_2 and then precipitated into cold ethyl ether. Following this, the product was dissolved in methylene chloride, and precipitated in cold methanol. The white product was then filtered and dried overnight under vacuum.

2.4. Fluorescence measurements

The critical micellization concentration (CMC) of FA-F87–PLA nanoparticles in PBS solutions was determined by fluorescence measurements (HITACHI F2700) using pyrene as a fluorescence probe [27,28]. The pyrene stock solution in acetone (5 μl) was added into a series of test tubes respectively and the acetone was evaporated. Following this, the FA-F87–PLA solutions (5 mL) were added to each test tube and then sonicated for 2 h. The final concentration of pyrene in the solutions was 6×10^{-7} M. For the measurement of pyrene excitation spectra, the slit widths for both excitation and emission sides were maintained at 2.5 nm, and the emission wavelength used was 390 nm.

2.5. Preparation of PTX-loaded FA-F87–PLA and PTX free nanoparticles

FA-F87–PLA block copolymer (25 mg) and hydrophobic drug PTX (15 mg) were dissolved in DMSO (15 mL). The solution with polymer and PTX was added drop-wise to distilled water (90 g) under gentle stirring. The drug loaded polymer aggregates in water were centrifuged and the supernatant was dialyzed against distilled water using a dialysis membrane (molec-

3. Results and discussion

3.1. Synthesis and characterization of FA-F87–PLA block copolymer

FA-F87–PLA block copolymer was synthesized by two steps. Pluronic F87 block copolymer was firstly modified by folic acid to obtain FA-F87–OH. FA-F87–PLA block copolymer was then synthesized by ring opening polymerization of the monomer L-lactide using FA-F87–OH as the initiator and stannous octoate [$Sn(Oct)_2$] as the catalyst (Scheme 1). The possible byproduct FA-F87–FA generated in the first step can be removed by methanol in the second step.

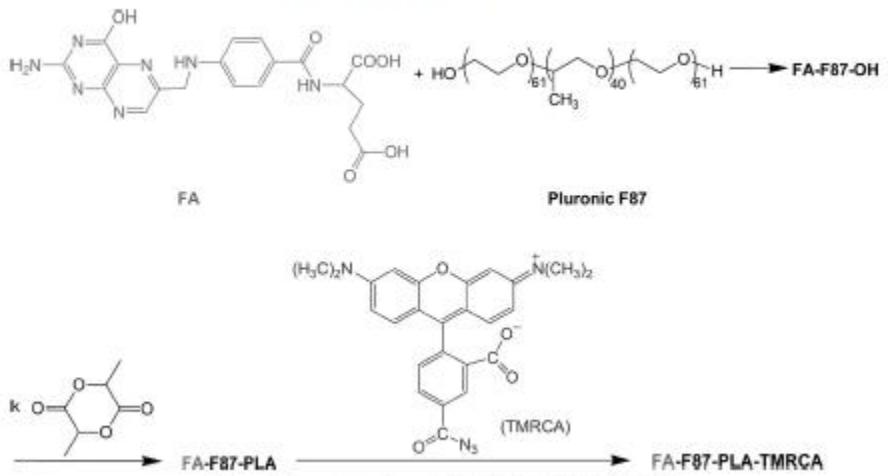
The polymer composition, structure and molecular weight were characterized by NMR and GPC techniques. Fig. 1(A) shows a ^{1}H NMR spectrum of FA-F87–PLA block copolymer in $CDCl_3$. ^{1}H NMR (400 MHz, $CDCl_3$, TMS), δ (ppm): 1.13–1.15 (m, $-OCH_2-CH(\underline{CH_3})-$), 1.41–1.75 (m, $-O-CH(\underline{CH_3})-CO-$ and $HO-CH(\underline{CH_3})-CO-$), 3.40–3.65 (m, $-O\underline{CH_2}-\underline{CH_2}-$ and $-O\underline{CH_2}-\underline{CH}(CH_3)-$), 4.3–4.4 (m, $HO-\underline{CH}(CH_3)-CO-$ and $-CO-O\underline{CH_2}-CH_2-O-$), 5.13–5.18 (m, $-O-\underline{CH}(CH_3)-CO-$). The small peak at δ of 4.35 ppm belongs to methylene protons of PLA–$CO-O\underline{CH_2}-CH_2-O-$PEO– segment, indicating the successful synthesis of FA-F87–PLA block copolymer. The absence of a peak at δ of 4.9–5.0 ppm which could have been contributed by the methine proton of the PLA–$O-\underline{CH}(CH_3)-COOH$ group, suggests that there was negligible or no PLA homopolymer in the FA-F87–PLA block copolymer. The peaks belonging to FA group were hard to see in Fig. 1(A) due to the high molecular weight of FA-F87–PLA block copolymer.

The degree of polymerization (n) of PLA in FA-F87–PLA copolymer was calculated from the peak intensity ratio of methyl protons of PLA ($O-CH(\underline{CH_3})-CO-$: δ = 1.58 ppm) and methyl protons of Pluronic ($-OCH_2-CH(\underline{CH_3})-$: δ = 1.14 ppm). The number-average molecular weight ($\overline{M}_n$) of the FA-F87–PLA_k copolymer was obtained by using the following expression:

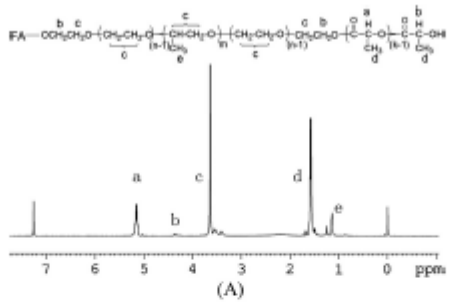
$$\overline{M}_n = \overline{M}_n(\mathrm{F87}) + 72k + 423$$

The molecular weight of FA-F87–PLA copolymer was calculated to be 24,800 and the weight fraction of PLA block was calculated to be 67%.

The amount of –OH groups of FA-F87–PLA copolymer functionalized by FA was determined by UV–vis spectrum. It was shown in Fig. 1(B) that both characteristic peaks belonging to folate groups at 285 and 362 nm are all detected for FA-F87–



Scheme 1. The synthesis scheme of FA-F87–PLA and FA-F87–PLA–TMRCA.



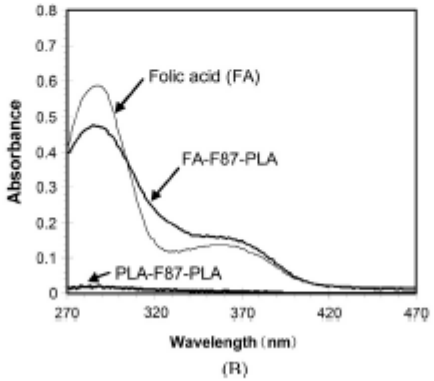


Fig. 1. (A) ^{1}H NMR spectra of FA-F87-PLA block copolymer ($CDCl_3$). (B) UV–vis spectra of FA-F87–PLA copolymer a

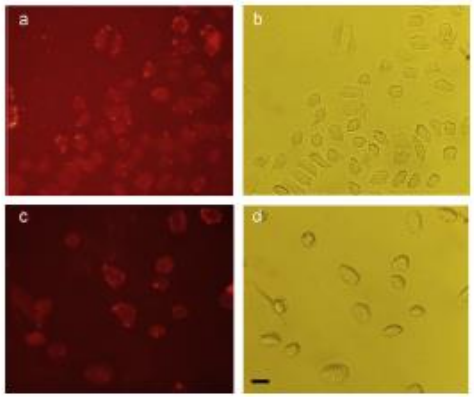
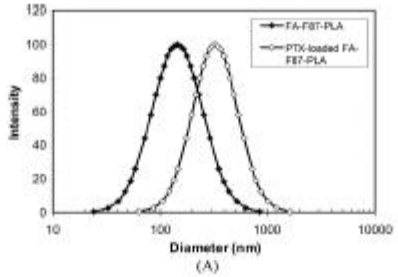
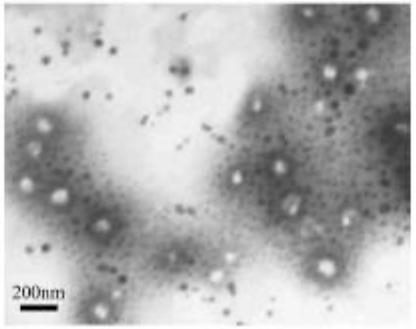


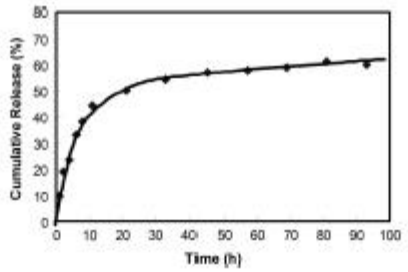
Fig. 6. Internalization of nanoparticles to cancer cells. Fluorescent images for two kinds of cells incubated with FA-F87–PLA–TMRCA nanoparticles. (a) nanoparticles incubated in OVCAR-3 cells for 2 h; (c) nanoparticles incubated in A549 cells for 2 h; (b) and (d) are the corresponding phase-contrast photographs of (a) and (c). Scale bar, 20 μm.

for imaging. The synthesis scheme is shown in Scheme 1. The acyl azide group of TMRCA was first rearranged into isocyanate. Then the hydroxyl end group in the PLA block of FA-F87–PLA reacted the isocyanate group to form a urethane [29,30,36].





A) Size distributions for FA-F87–PLA and PTX-loaded FA–F87–PLA nanoparticles. (B) TEM picture of FA-F87–PLA nanoparticles.



4. Conclusions

In the present study, FA-Pluronic F87–PLA block copolymer was synthesized by two step reactions. The self-assembling behaviors of FA-F87–PLA block copolymer in aqueous solutions were examined. The CMC of FA-F87–PLA block copolymer is pretty low, indicating the good stability of FA-F87–PLA nanoparticles. The morphology of FA-F87–PLA nanoparticles is spherical micelles. The release of PTX loaded in FA-F87–PLA nanoparticles shows an initial burst release in the first 11 h and followed by a pretty slow release. The in vitro targeting properties of FA-F87–PLA nanoparticles over OVCAR-3 and A549 cancer cells were investigated by MTT assays and FM technique. Results from MTT tests show that FA-F87–PLA nanoparticles were delivered more effectively to OVCAR-3 cells (folate receptor positive) than PLA–F87–PLA nanoparticles did, indicating the targeting property of FA-F87–PLA nanoparticles. These results were confirmed by FM through labeling a dye to the PLA end of FA-F87–PLA block copolymers. The intracellular fate of FA-F87–PLA nanoparticles was also studied using a triple-labeling method by FM. It was observed that FA-F87–PLA–TMRCA nanoparticles are mainly localized within the cytoplasm of OVCAR-3 cells.

Acknowledgements

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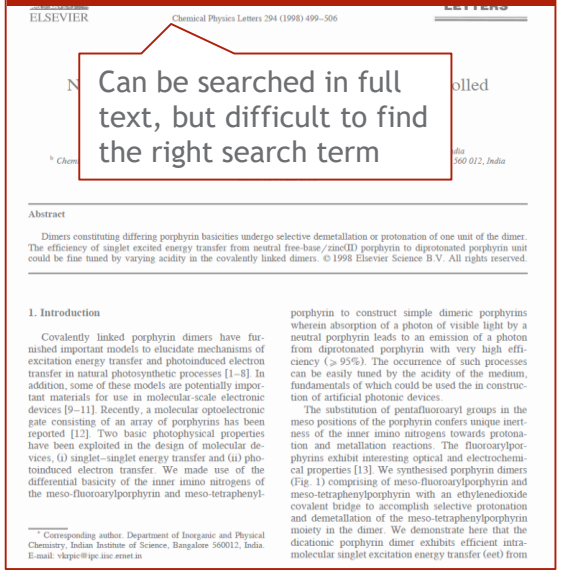
16k 저널/ 7개 특허 원문에서 정보 색인

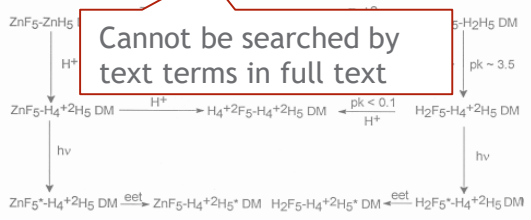
- ✓ 실제 화합물
- ✓ 광범위한 반응정보
- ✓ 정확한 물질 정보와 연구 결과
- ✓ 광범위한 실험 데이터 및 결과

Scientific topic, author



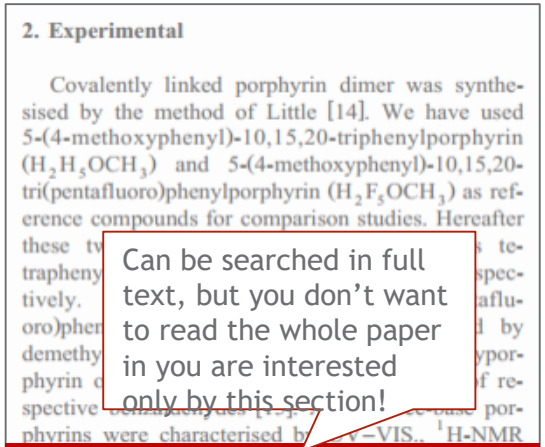
Can be searched in full text, but difficult to find the right search term

Chemical reactions



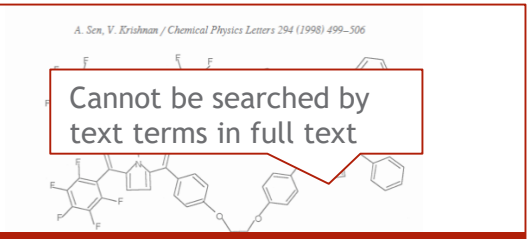
Cannot be searched by text terms in full text

Experimental procedures



Can be searched in full text, but you don't want to read the whole paper in you are interested only by this section!

Chemical structure

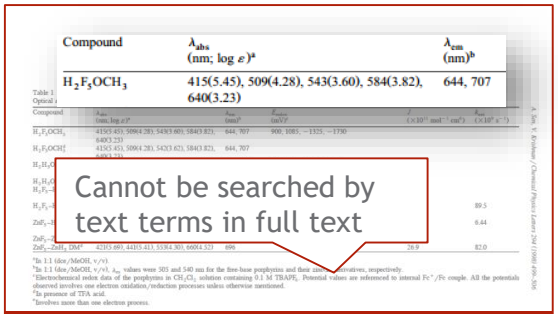


Cannot be searched by text terms in full text

Chemical spectra

Cannot be searched by text terms in full text

Substances and their physicochemical properties



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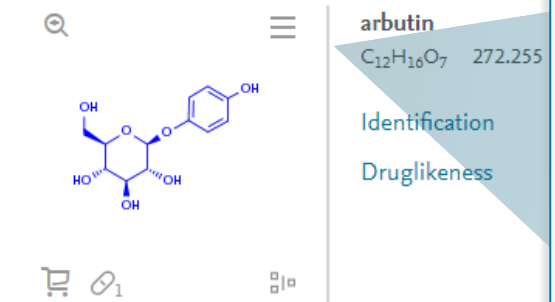
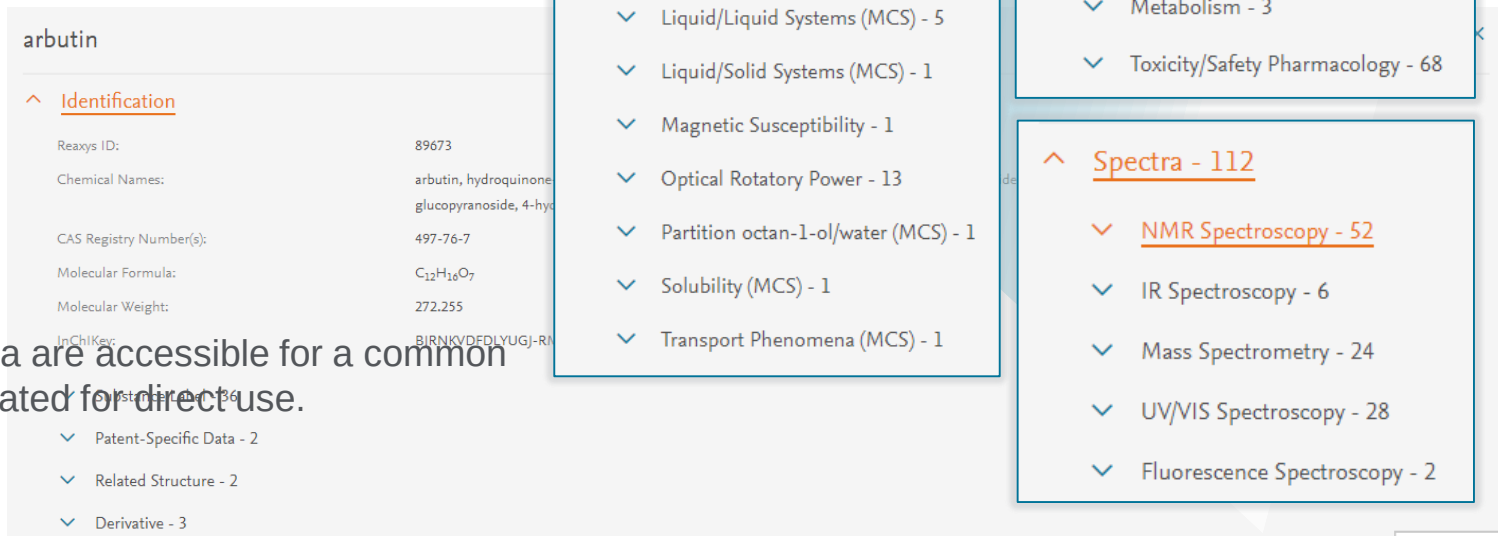
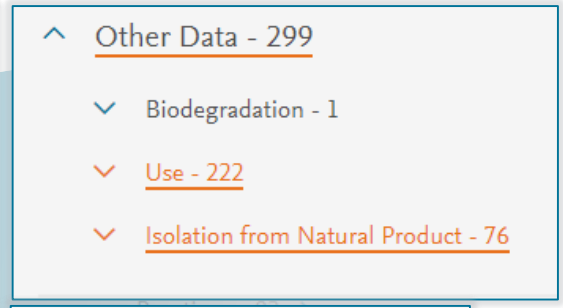
원문에서 발췌한 표준화되고, 잘 정리된 화학 데이타 제공

Arbutin ***에 관련된***
1,588 문헌과 특허







All relevant data are accessible for a common point and tabulated for direct use.

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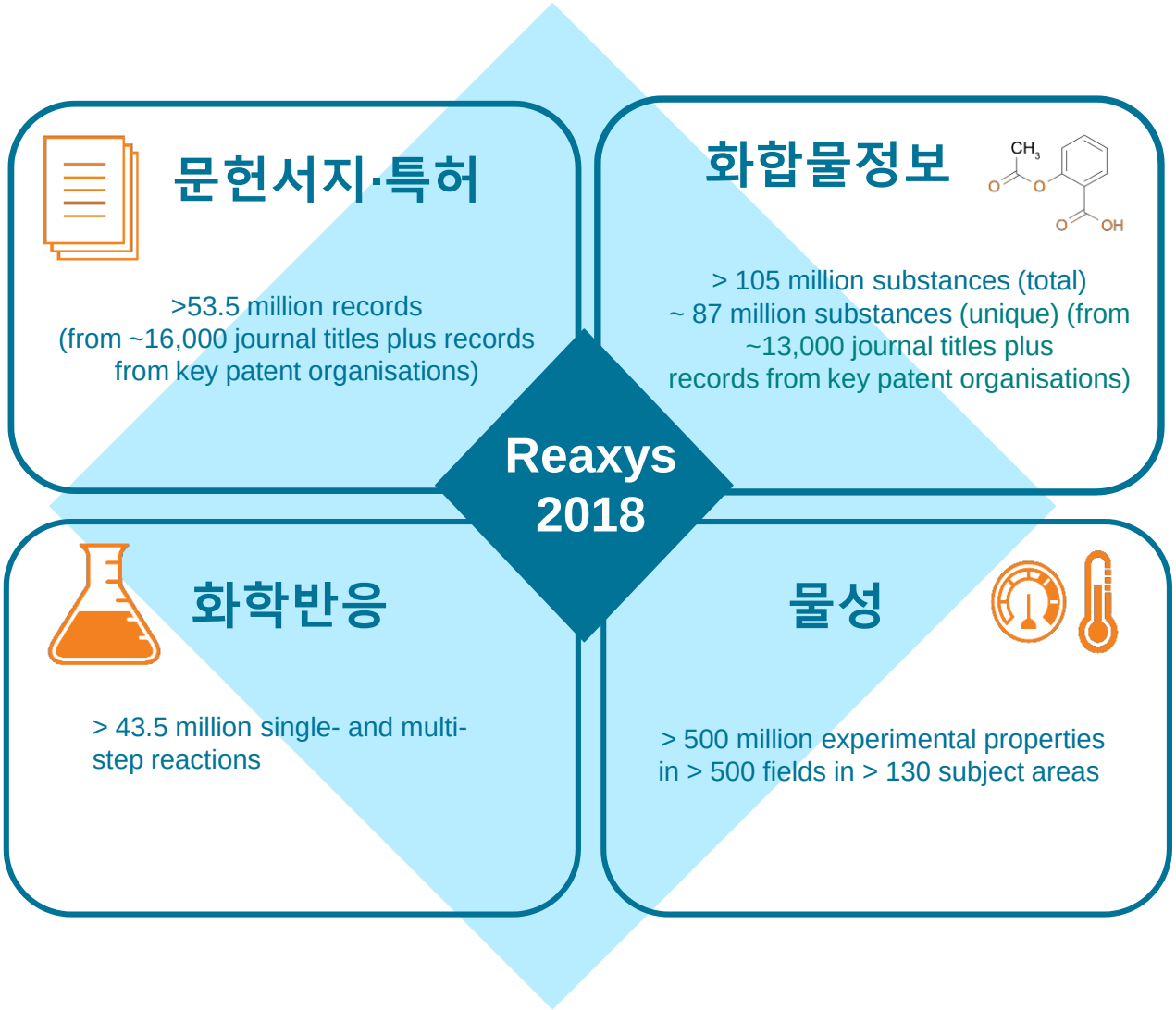
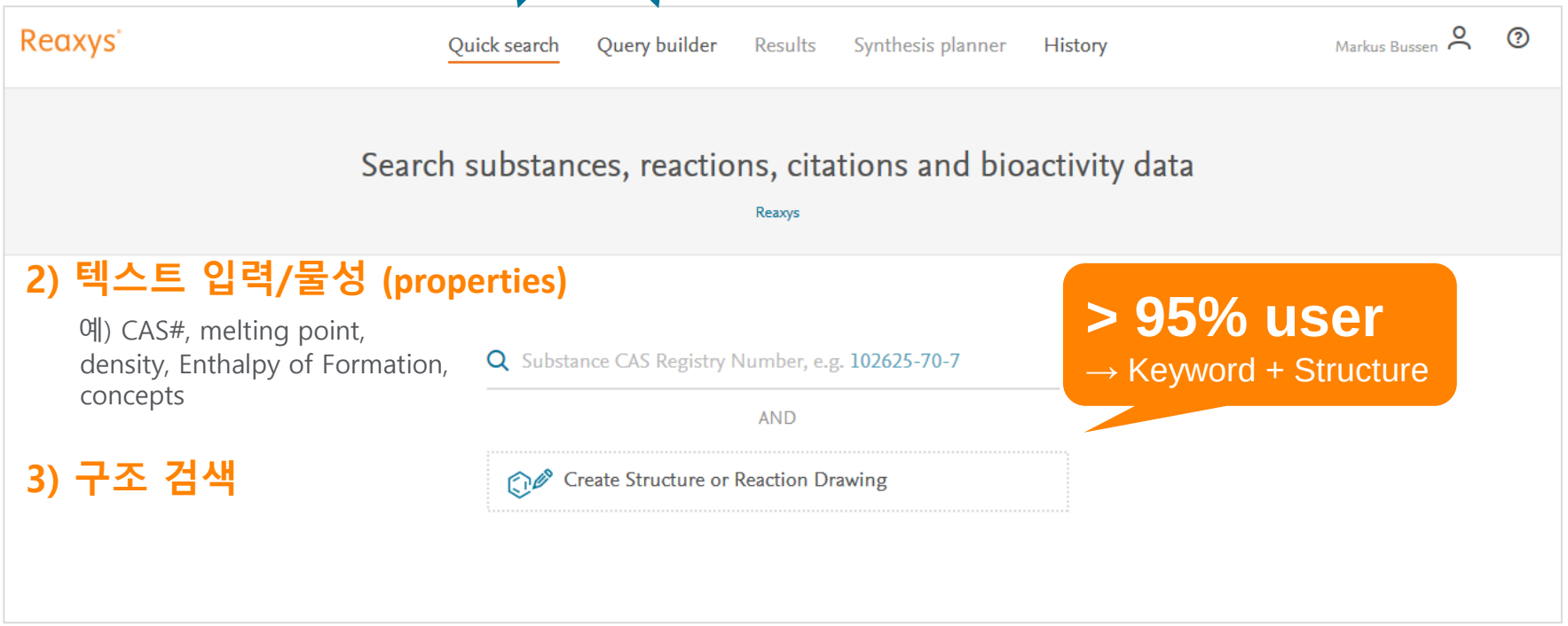


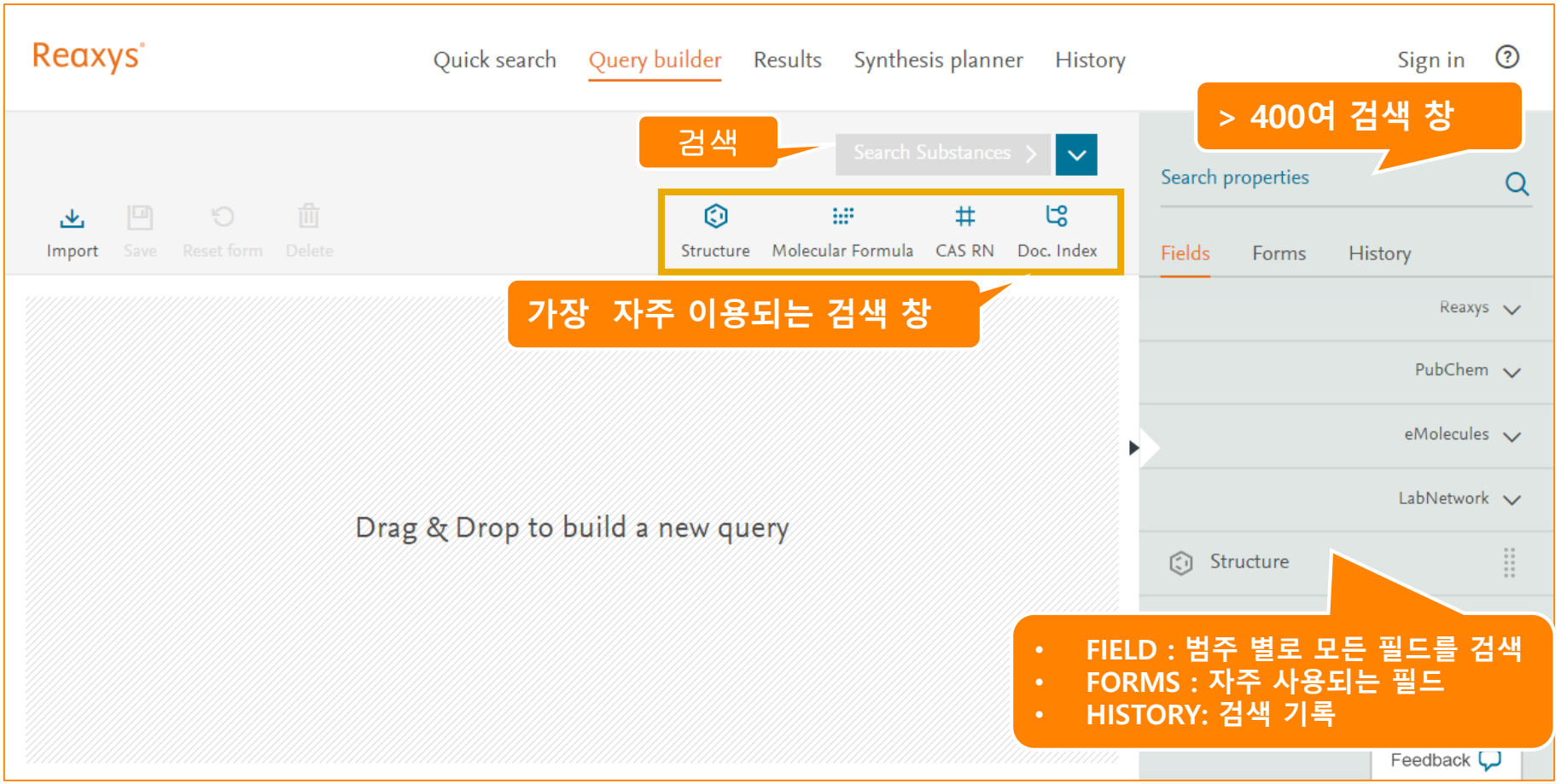
Quick Search (간편검색)

1) 검색 모드
간편/ 고급 검색



Query Builder – 고급 통합검색

Find more specific answer by combined multi fields



ELSEVIER

Part1. 문헌, 특허, 연구동향검색

문헌 내 색인용어 (Index term)

특허 문헌 내 정보 둘러보기 – Abstract 확인, 원문바로보기 링크

문헌/특허 내 물질, 반응 바로 확인하기

문헌을 검색할 때는?

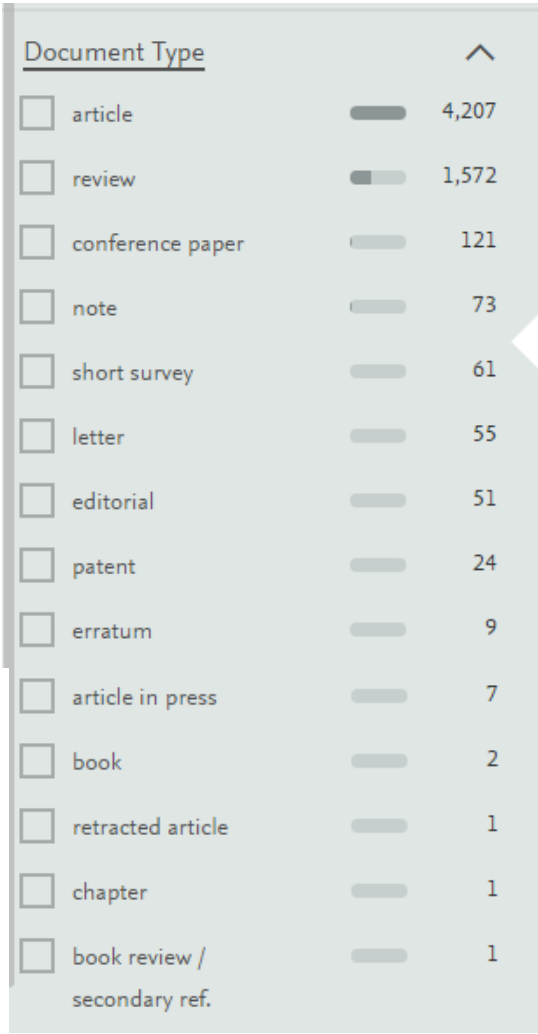
Query Builder – 고급 통합검색 활용 할 것!

-자동 완성 기능
-유사 검색어 추가 용이
-단어 조합 용이

Non-small Cell lung cancer, EGFR inhibitor

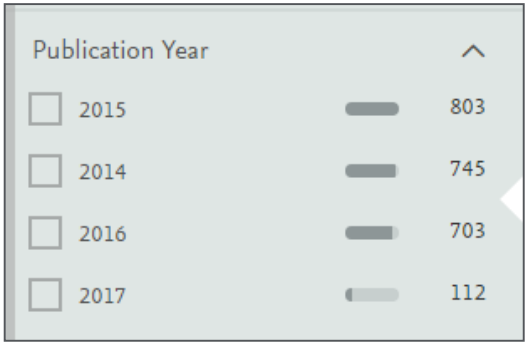
6,615 Documents with 8,351 Substances, 18,025 Reactions, 1,482 Targets

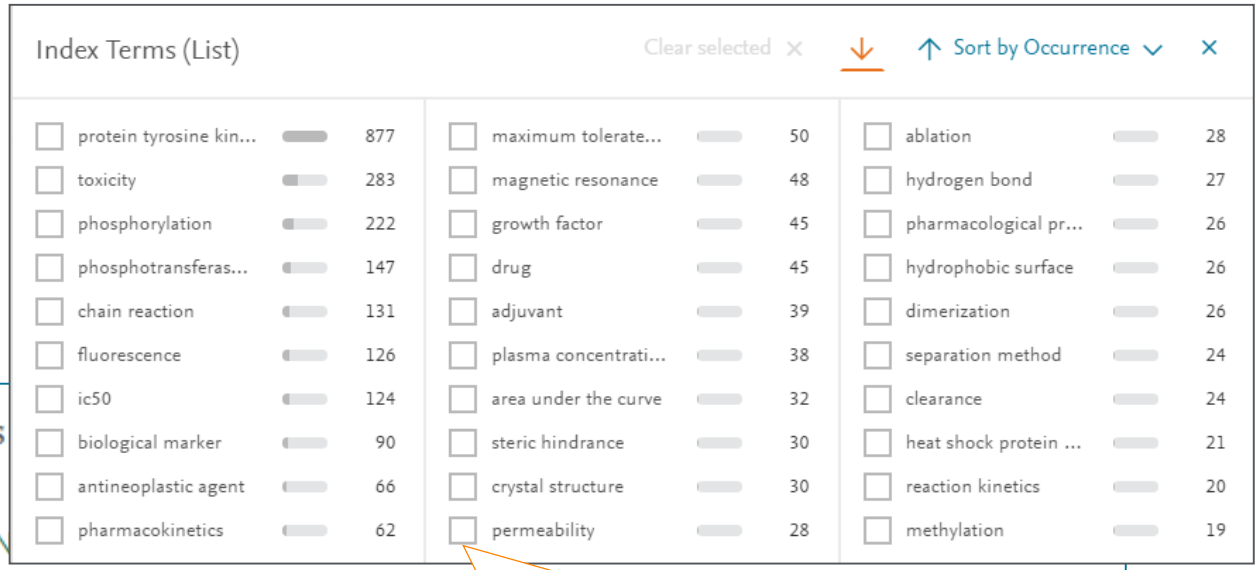
결과에서 저널/ 특허 문헌 by publication type, by journal title



나의 논문을 발표할 상위 저널에 대한 정보를 얻을 수 있어요.

결과에서 연도별, 최신 연구키워드, 추가 연구동향 확인





2 JAK2 inhibition sensitizes kinase inhibitors

Gao, Sizhi P.; Chang, Qing; Mao, N

Abstract Index Terms Substances Full Text

Index terms

EMTREE drug term: 5 chloro n2 [1 (5 fluoro 2 pyrimidinyl) growth factor receptor, erlotinib, gefitinib, Janus kinase 2, pyrimidinyl]oxy]phenyl]acrylamide, STAT3 protein, suppressor of cytokine signaling

EMTREE medical term: animal cell, Article, cell growth, controlled study, drug potentiation, enzyme inhibition, IC50, immunohistochemistry, in vitro study, in vivo study, lung adenocarcinoma, lung cancer cell line, mouse, non small cell lung cancer, nonhuman, priority journal, signal transduction, tumor volume, Western blotting, wild typ

Reaxys Index Terms: heterodimerization, protein tyrosine kinase inhibitor

분야별로 원문에 많이 사용된 용어들을 참고하여 키워드를 추가로 검색을 진행할 수 있고, 최신연구 관련 동향 정보 수집에도 활용할 수 있습니다.

Abstract 확인, 원문보기 링크

5 A decade of EGFR inhibition in EGFR-mutated non small cell lung cancer (NSCLC): Old successes and future perspectives Cited 35 times

Russo, Alessandro; Franchina, Tindara; Ricciardi, Giuseppina Rosaria Rita; +6 others - Oncotarget, 2015, vol. 6, # 29, p. 26814 - 26825

Abstract ^ Index Terms v Substances v Full Text ↗

Abstract

The discovery of Epidermal Growth Factor Receptor (EGFR) mutatio
launched the era of personalized medicine in advanced NSCLC, lead
landscape of this disease. After ten years from the individuation of a
domain of the EGFR in NSCLC patients responding to the EGFR tyr
progresses have been done and first line treatment with EGFR TKIs
mutated NSCLC patients. During the last decade, different EGFR TK
been approved so far in these selected patients. However, despite gr
these molecularly selected patients poses novel therapeutic challeng
brain metastases development or the need to translate these treatm
therapy. The aim of this paper is to provide a comprehensive review
EGFR inhibition in this molecularly-selected subgroup of NSCLC pa
generation EGFR TKIs, Erlotinib and Gefitinib, to the novel irreversib
ultimately the emerging challenges that we, in the next future, are c

Online ISSN: 1949-2553

Oncotarget

Reviews:

A decade of EGFR inhibition in EGFR-mutated non small cell lung cancer (NSCLC): Old successes and future perspectives

PDF | HTML | Order a Reprint

Oncotarget. 2015; 6:26814-26825. doi: 10.18632/oncotarget.4254

Metrics: PDF *1189 views* | HTML *644 views*

Alessandro Russo[1], Tindara Franchina[1], Giuseppina Rosaria Rita Ricciardi[1], Antonio Picone[1], Giuseppa Ferraro[1], Mariangela Zanghi[1], Giuseppe Toscano[1], Antonio Giordano[2], Vincenzo Adamo[1]

[1]Medical Oncology Unit AOOR Papardo-Piemonte & Department of Human Pathology, University of Messina, Messina, Italy
[2]Sbarro Institute for Cancer Research and Molecular Medicine, Center for Biotechnology, Temple University, Philadelphia, Pennsylvania, USA

Correspondence to:
Vincenzo Adamo, e-mail: vadamo@unime.it

Keywords: *EGFR mutations, third generation EGFR TKIs, non small cell lung cancer, tyrosine kinase inhibitors, targeted therapy*

Received: *April 25, 2015* Accepted: *June 01, 2015* Published: *June 12, 2015*

ABSTRACT

The discovery of Epidermal Growth Factor Receptor (EGFR) mutations in Non Small Cell Lung Cancer (NSCLC) launched the era of personalized medicine in advanced NSCLC, leading to a dramatic shift in the therapeutic landscape of this disease. After ten years from the individuation of activating mutations in the tyrosine kinase domain of the EGFR in NSCLC patients responding to the EGFR tyrosine kinase inhibitor (TKI) Gefitinib, several progresses have been done and first line treatment with EGFR TKIs is a firmly established option in advanced EGFR-mutated NSCLC patients. During the last decade, different EGFR TKIs have been developed and three inhibitors have been approved so far in these selected patients. However, despite great breakthroughs have been made, treatment of these molecularly selected patients poses novel therapeutic challenges, such as emerging of acquired resistance, brain metastases development or the need to translate these treatments in earlier clinical settings, such as adjuvant therapy.

The aim of this paper is to provide a comprehensive review of the major progresses reported so far in the EGFR inhibition in this molecularly-selected subgroup of NSCLC patients, from the early successes with first generation EGFR TKIs, Erlotinib and Gefitinib, to the novel irreversible and mutant-selective inhibitors and ultimately the emerging challenges that we, in the next future, are called to deal with

문헌 내의 물질, 반응정보 확인하기

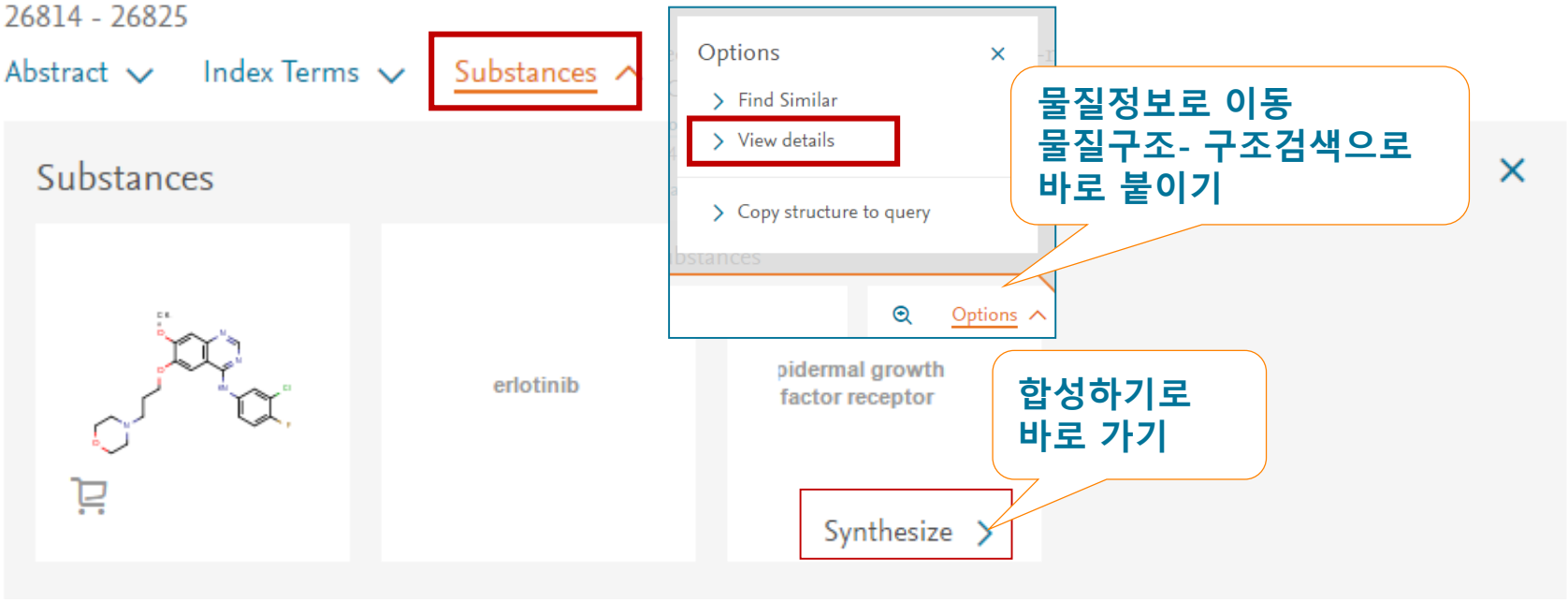
원문 내의 반응이나 물질정보 바로 보기로 원문을 확인하기 전에 화학정보 확인이 용인합니다.

5 A decade of EGFR inhibition in EGFR-mutated non small cell lung cancer (NSCLC): Old successes and future perspectives

Cited 35 times

Russo, Alessandro; Franchina, Tindara; Ricciardi, Giuseppina Rosaria Rita; +6 others - Oncotarget, 2015, vol. 6, # 29, p. 26814 - 26825

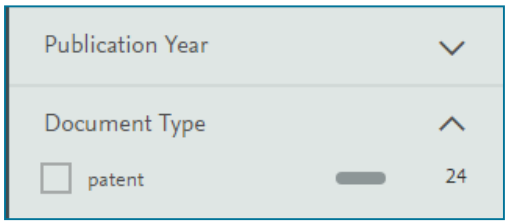
Abstract Index Terms Substances



물질정보로 이동
물질구조- 구조검색으로 바로 붙이기

합성하기로 바로 가기

특허문헌 정보 둘러보기



비 영어권 (한국어, 유럽, 일본, 중국, 대만) 특허에 대해 번역 색인된 특허 현황 확인가능, 원문으로 링크

5 COMBINATION THERAPY FOR NON-SMALL CELL LUNG CANCER POSITIVE FOR EGFR MUTATION

MEDIMMUNE LIMITED; DAR, Mohammed, M; KARAKUNNEL, Joyson, J; +2 others - WO2016/170157, 2016, A1

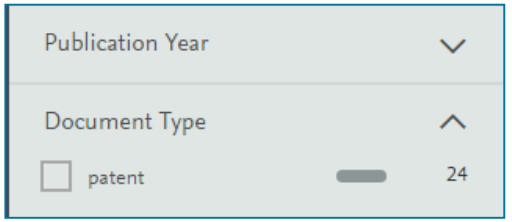
Patent Family Members: WO2016/170157 A1

Abstract ^ Front Page Info v Substances v Full Text ↗

Abstract

The present invention features methods of treating lung cancer (e.g., NSCLC) with an anti-PD-L1 antibody and a tyrosine kinase inhibitor in a subject identified as having an EGFR mutation-positive tumor.

특허문헌 – 특허현황정보(Front page info)



Front page info

Assignees	Inventors (Authors)
ISOFOL MEDICAL AB; GUSTAVSSON, Bengt; CARLSSON, Björn	GUSTAVSSON, Bengt; CARLSSON, Björn

Patent No	Kind Code	Publ. Date	Application No	Filing Date	Indexed Patent
EP2617421	A1	2013/07/24	EP2012-151993	2012/01/20	
WO2013/107883	A1	2013/07/25	WO2013-EP50973	2013/01/18	yes
CA2860889	A1	2013/07/25	CA2860889	2013/01/18	

청구항, 특허 Application, 패밀리특허 확인

Priority No	Priority Date
EP2012-151993	2012/01/20
EP2012-15199	2012/01/20

Patent Classification	
Main IPC	A61K 31/519
Secondary IPC	A61K 39/395; A61K 45/06; A61P 35/00

특허문헌 –특허 내 물질정보확인

Publication Year

Document Type

patent 24

5 COMBINATION THERAPY FOR NON-SMALL CELL LUNG CANCER POSITIVE FOR EGFR MUTATION

MEDIMMUNE LIMITED; DAR, Mohammed, M; KARAKUNNEL, Joyson, J; +2 others - WO2016/170157, 2016, A1

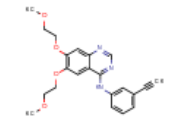
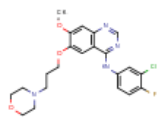
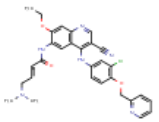
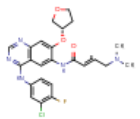
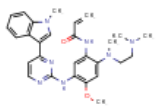
Patent Family Members: WO2016/170157 A1

Abstract Front Page Info Substances Full Text

Abstract

The present invention features n … y and a tyrosine kinase inhibitor in a sub

Substances

anti-PD-L1 antibody BMS-936559

anti-PD-L1 ıtibody MEDI4736

anti-PD-L1 ibody MPDL3280A

특허 원문 내 물질의 원문 페이지 정보 표시

non-small cell lung cancer (NSCLC)	Page/Page column title page; 30-33	**MEDIMMUNE LIMITED; DAR, Mohammed, M; KARAKUNNEL, Joyson, J; +2 others** - WO2016/170157, 2016, A1 Full Text Show details

원문보기

특허 원문보기

5 COMBINATION THERAPY FOR NON-SMALL CELL LUNG CANCER POSITIVE FOR EGFR MUTATION

MEDIMMUNE LIMITED; DAR, Mohammed, M; KARAKUNNEL, Joyson, J; +2 others - WO2016/170157, 2016, A1

Patent Family Members: WO2016/170157 A1

Abstract | Front Page Info | Substances | Full Text

원문보기 클릭

non-small cell lung cancer (NSCLC)

Page/Page column title page; 30-33

MEDIMMUNE LIMITED; DAR, Mohammed, M; KARAKUNNEL, Joyson, J; +2 others - WO2016/170157, 2016, A1

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특허 원문 내 물질의 원문 페이지 정보 표시

원문보기 클릭

Pharmaceuticals

Page/Pa title pag

The following document

Patent Number	WO2016/170157
Patent Kind Code	A1
Publication Date	2016

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WO2016170157 (A1)

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COMBINATION THERAPY FOR NON-SMALL CELL LUNG CANCER POSITIVE FOR EGFR MUTATION

Page 1/38 Abstract Bibliography | Maximise | Download

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
27 October 2016 (27.10.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/170157 A1

(51) International Patent Classification:
A61K 39/395 (2006.01) *A61P 35/00* (2006.01)
A61K 31/517 (2006.01)

(21) International Application Number:
PCT/EP2016/059083

(22) International Filing Date:
22 April 2016 (22.04.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/151,739 23 April 2015 (23.04.2015) US

(74) Agent: WINTER, CHRISTOPHER, SPENCER; MEDIMMUNE LIMITED, Milstein Building, Granta Park, Cambridge Cambridgeshire CB21 6GH (GB).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,

문헌찾기

대두(Soybean) 의 알려진 성분(Phytochemical) 에 관련된 문헌을 찾고 싶습니다.

Query builder로 단어 조합으로 문헌을 찾아보시고 몇 개의 문헌이 나오는지 말해주세요.

Part2. 물질 검색

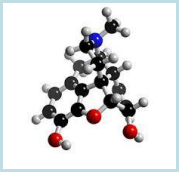
물질의 물성데이터 확인 (실험측정데이터, USE/ Application, 스펙트라 정보 등)
물질의 구매여부 확인
물질의 합성법 바로보기

※ Unknown compound 검색하기 / 특정물성을 가진 물질 찾기

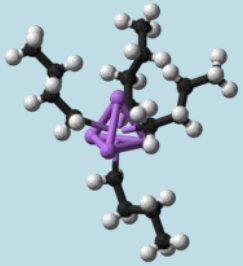
※ Functional group의 종류와 위치의 변화의 따른 물성 변화 검색

화합물 클래스

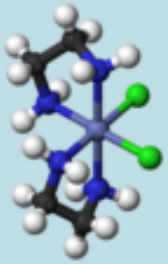
REAXYS SUBSTANCE RECORDS 에서 검색

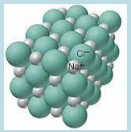


CLASSIC ORGANICS



ORGANOMETALLICS
COORDINATION COMPOUNDS

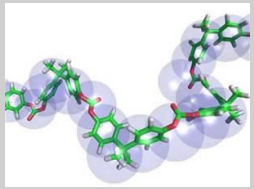


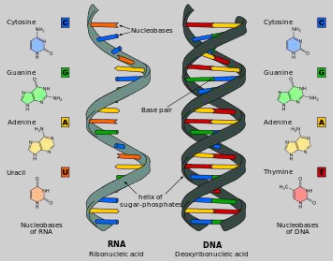


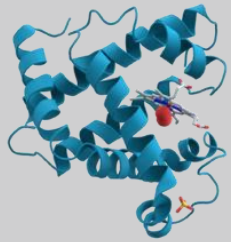
CLASSIC INORGANICS

REAXYS 서지 레코드의 키워드 검색

POLYMERS







NUCLEIC ACIDS & PROTEINS

ALLOYS & METALS

CERAMICS

물질/반응 검색을 통해 검색
(Search Substances)

문헌검색을 통해 검색
Search Literature

Query Builder 활용- Unknown compound/ 특정물성 화합물 찾기

"Identify an unknown antimicrobial compound isolated from a natural product. Experimental results indicate that the substance has 30 carbon atoms and an optical rotation of 75-85°."

① Molecular Formula

eg.C6H5COOH
C30*

Look up

② Optical Rotatory Power — Exist

is	Type (Optical Rotatory Power)	
is	Concentration (Optical Rotatory Power)	
=	Length of Path, cm	
is	Solvent (Optical Rotatory Power)	
=	Optical Rotatory Power, deg	75-85
=	Wavelength (Optical Rotatory Power), nm	
=	Temperature (Optical Rotatory Power), °C	

③ Effect (PharmData)

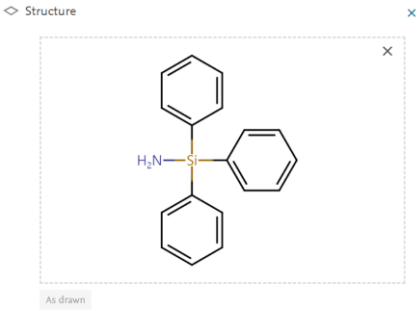
is — Effect (PharmData): antimicrobial;antimicrobial activity

④ Available data 1

Pharmacological Data	4
Mass Spectrometry	4
IR Spectroscopy	4
NMR Spectroscopy	4
Optical Rotatory Power	4
Melting Point	4
Isolation from Natural Product	4

물질 검색을 위한 다양한 검색 창

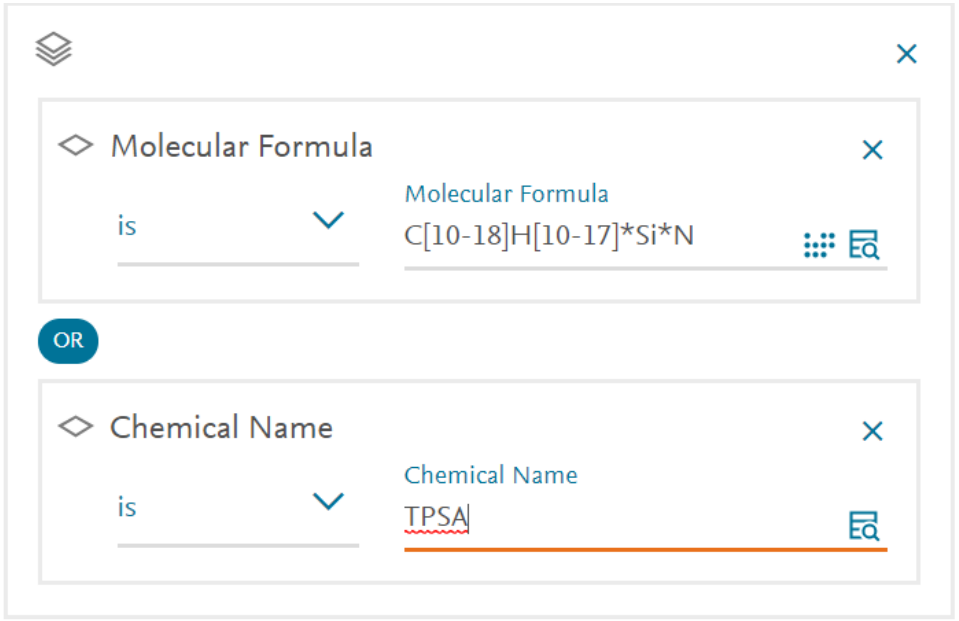
❶ Structure구조검색



❷ Mol. Formula

❸ Chemical Nam

❹ Keyword



Plus Many More!

- NMR Spectroscopy
- IR Spectroscopy
- Mass Spectrometry
- UV/VIS Spectroscopy
- Raman Spectroscopy
- ESR Spectroscopy
- NQR Spectroscopy
- Rotational Spectroscopy
- Luminescence Spectroscopy
- Fluorescence Spectroscopy
- Phosphorescence Spectroscopy
- Other Spectroscopic Methods

Reaxys®

Query builder를 활용한 여러 조건 통합검색- 용매 찾기

Substance Basic Index

is

Substance Basic Index
solvent*

AND

Boiling Point

Exist

=

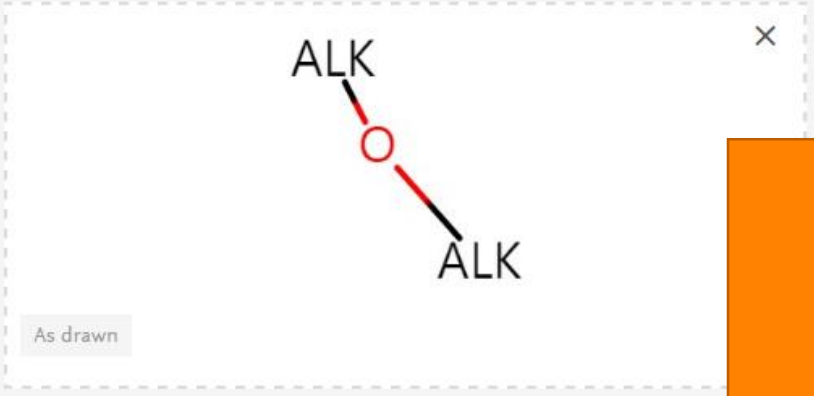
Boiling Point, °C
50-250

=

Pressure (Boiling Point), Torr
740-780

AND

Structure

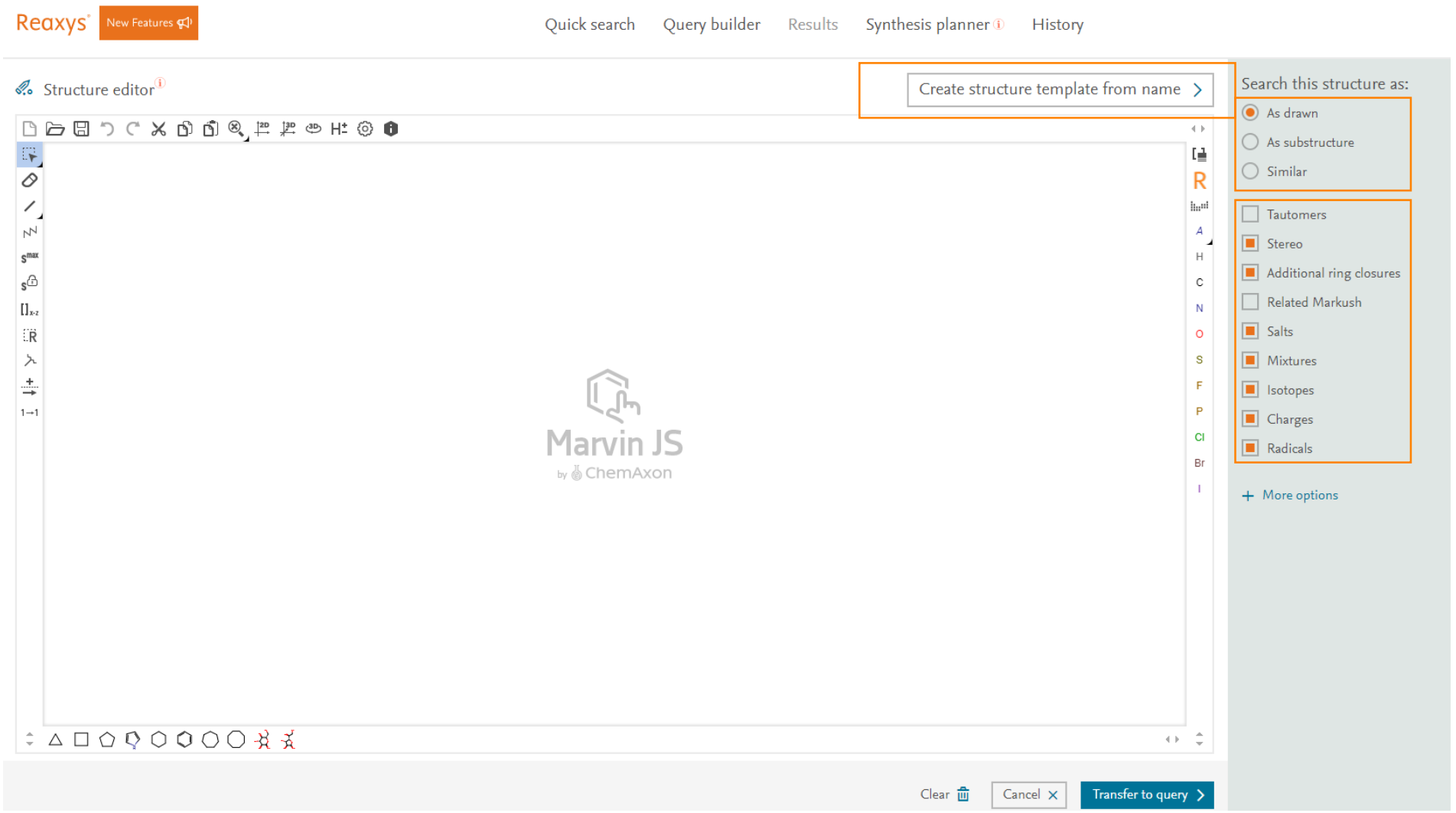


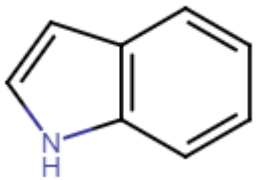
실습

Part 3. 반응 검색

반응검색 입력
반응검색 필터 활용하기 (수득율, 시약, 촉매, 용매, 문헌종류, 1-step/ multi-step 반응 등)
반응실험과정 참고하기
Synthesis planner 에서 반응식 직접 설계하기
※ 생성물/반응물로 검색이 안될 때 – 반응정보 확인하는 법

Marvin JS 를 얼마나 잘 활용하는가?





indole

Search this structure as:

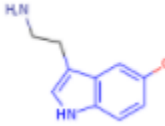
- (•) As drawn
- ( ) As substructure
- ( ) Similar

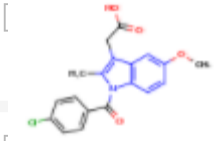
336	Substances	Structure : as drawn; included: only absolute stereo, additional ring closures allowed, salts, mixtures, isotopes, charges, radicals	Preview Results View Results
3,970	Substances	Structure : average similarity; included: only absolute stereo, additional ring closures allowed, salts, mixtures, isotopes, charges, radicals	Preview Results View Results
805	Reactions	Product(s) : as drawn; included: only absolute stereo, additional ring closures allowed, salts, mixtures, isotopes, charges, radicals	Preview Results View Results

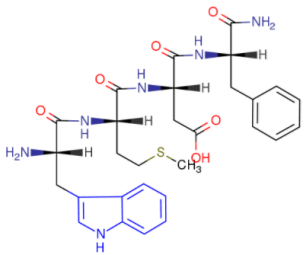
Search this structure as:

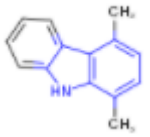
- ( ) As drawn
- (•) As substructure
  - (•) On all atoms
  - ( ) On heteroatoms

1,080,310	Substances	Structure : substructure; included: only additional ring closures allowed, salts, mixture radicals	
14,731	Targets	Structure : substructure; included: only absolute stereo, additional ring cl radicals	Preview Results
1,680,157	Reactions	Product(s) : additional ring cl radicals	Vie





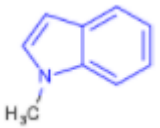


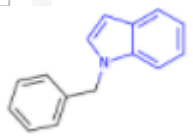


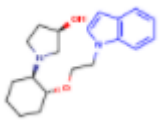
Search this structure as:

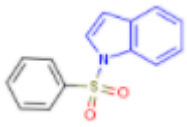
- ( ) As drawn
- (•) As substructure
  - ( ) On all atoms
  - (•) On heteroatoms

7,451	Substances	Structure : substructure on heteroatoms; included: only absolute stereo, additional ring closures allowed, salts, mixtures isotopes, charges, radicals Edit in Query Builder Create Alert	Preview Results View Results
892	Targets	Structure : substructure on heteroatoms; included: only absolute stereo, additional ring closures allowed, salts, mixtures isotopes, charges, radicals	v Result
13,009	Reactions	Product(s) : substructure on heteroatoms; included: on absolute stereo, additional ring closures allowed, salts, mixture isotopes, charges, radicals	Resul



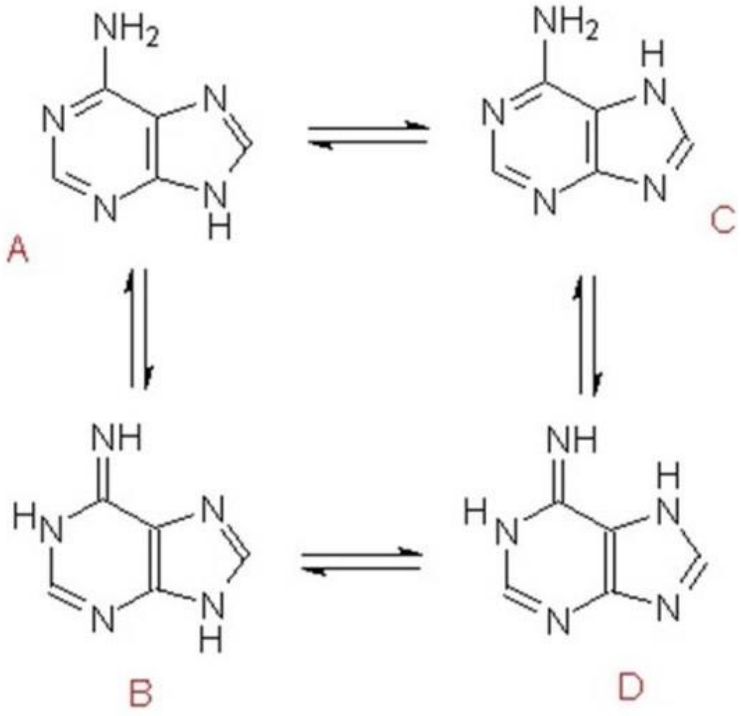


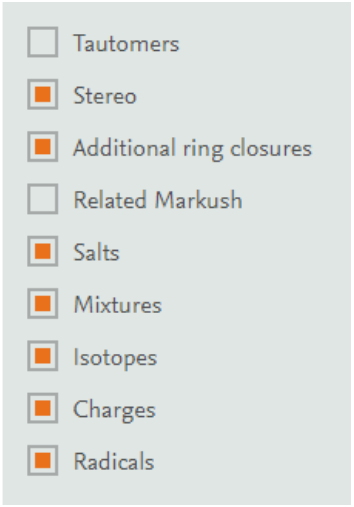




*Tautomers

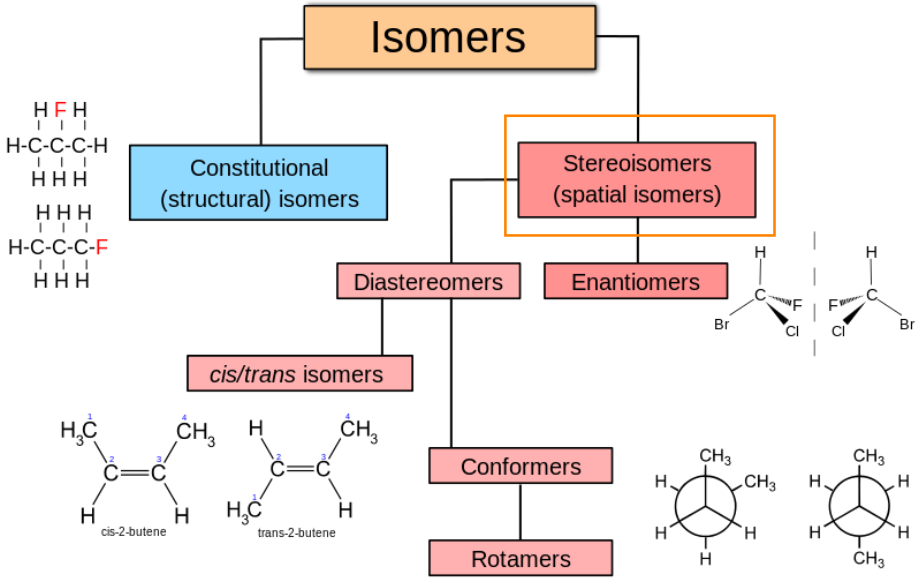
호변이성질체(tautomers)는 유기화합물의
구조이성질체로써 단일결합과 이중결합의 여부에 따라
수소의 위치가 바뀌는 관계가 되는 이성질체입니다. 대표적인
구조는 아데닌(Adenine)이 있습니다.
즉 Reaxys에서 검색시, Tautomers에 표기하게 되면,
호변이성질체까지 결과에 제공합니다.





*Stereo

입체이성질체 - 거울로 사물을 보았을 때 대칭적이나 방향이
다르거나(Enantiomers), 화합물의 molecular는 같지만 위치가
다른 (cis/trans 혹은 conformers) 물질을 제공한다.



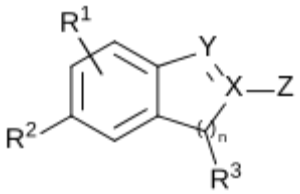
- [ ] Tautomers
- [x] Stereo
- [x] Additional ring closures
- [ ] Related Markush
- [x] Salts
- [x] Mixtures
- [x] Isotopes
- [x] Charges
- [x] Radicals

*Additional ring closures

반응이 일어날수 있는 곳(free sites)에 원자나 그룹이 합쳐서 링을 만든 결과를 제공합니다.

*Related Markush

Markush structure는 어떤화합물에 대한 그룹을 나타내는데 사용됩니다. 주로 특허와 관련이 있고, 어떤 화학구조에 치환기를 R 그룹, R1 그룹 등으로 설정해 두고, 여러가지 화합물을 R이나 R1등에 포함 시킬 수 있습니다.



*Salt

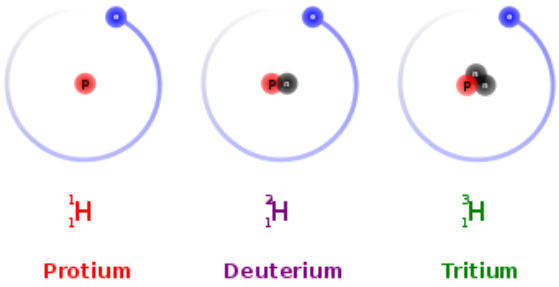
Multi-fragment 화합물, salt나 charge-transfer 같은 물질이 결과에 제공됩니다.

*Mixtures

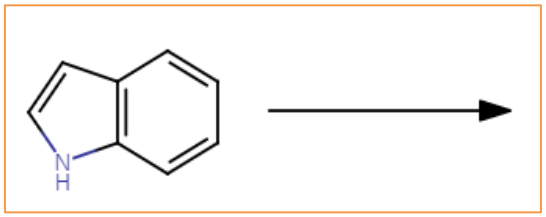
혼합물(고분자도 포함)

*Isotopes

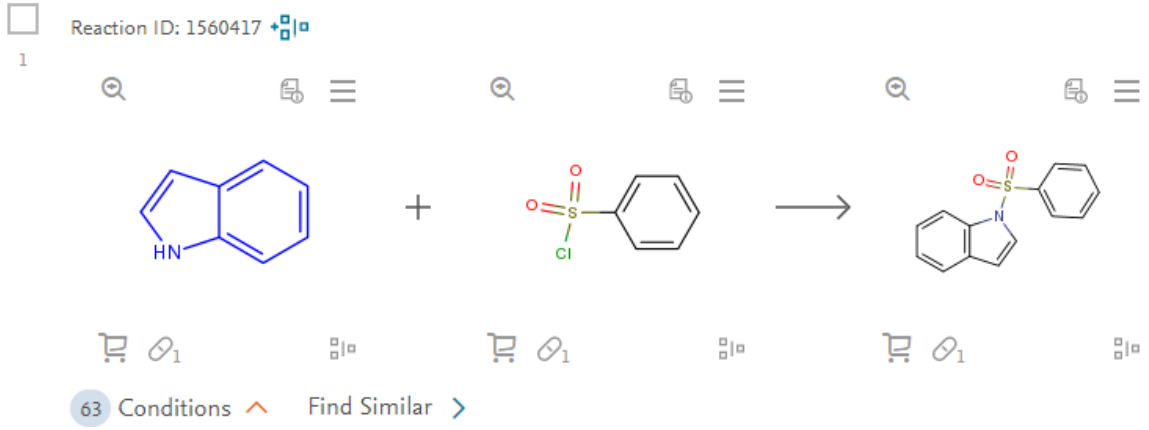
동위원소 -예를 들어 수소의 isotopes는 아래와 같다.

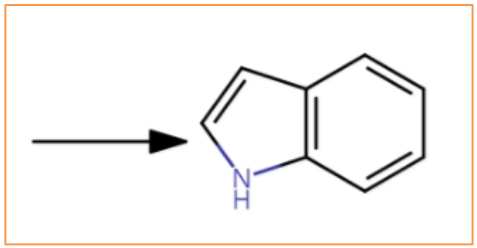


Indole

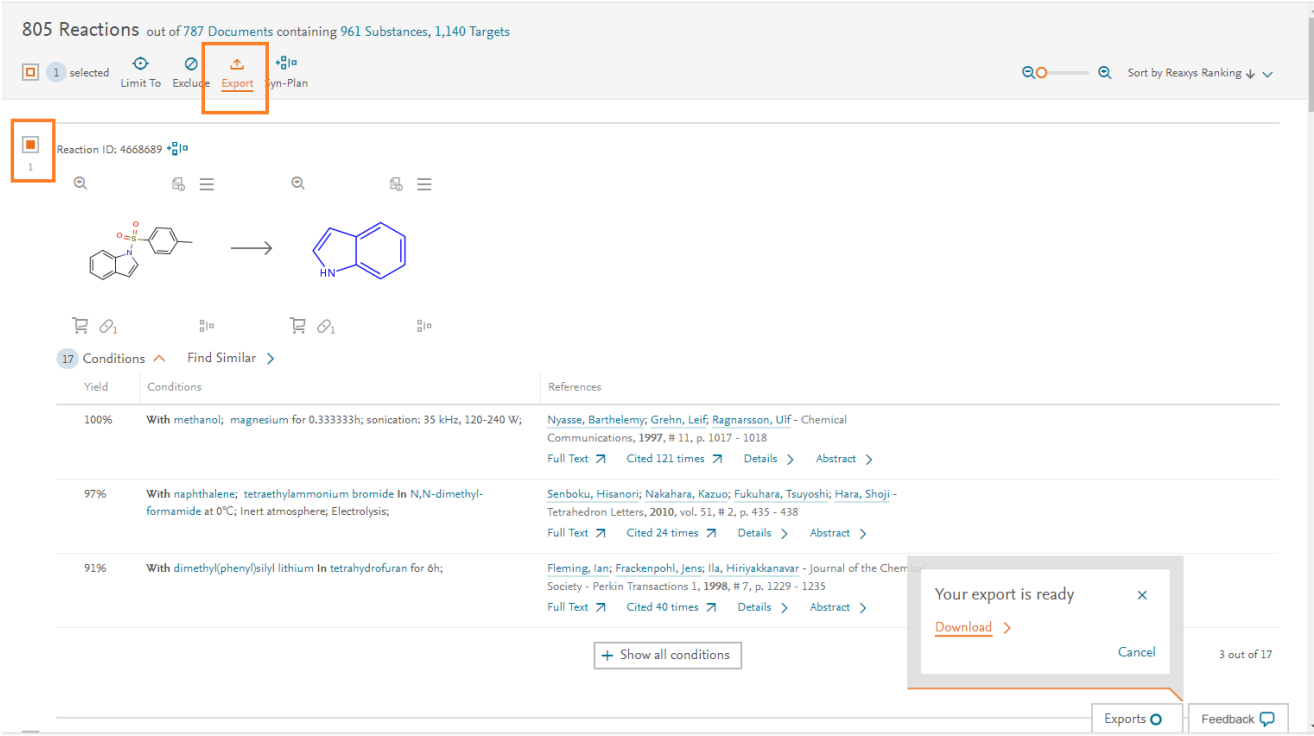


인돌로부터 합성할 수 있는 물질 찾기



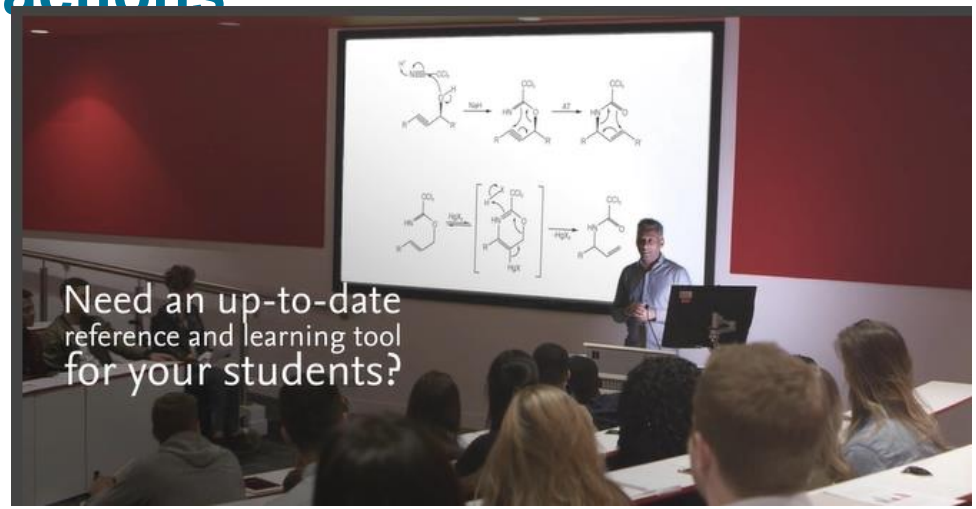


인돌을 만드는 방법 찾기



ReactionFlash Gives Details for 600+ Named Reactions

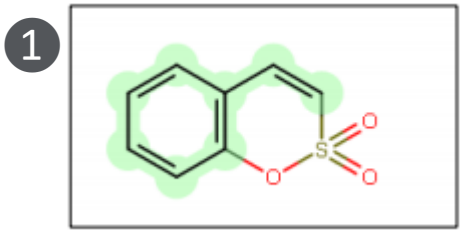
Now available for Android as well as iPhone

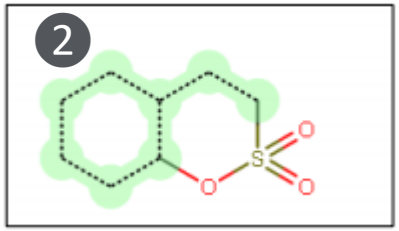


Need to check named reaction during group meeting?

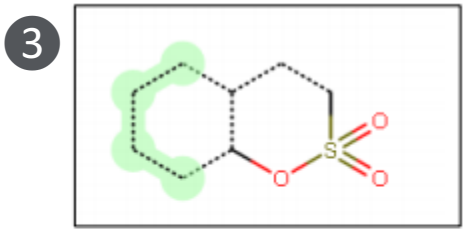
여러 기능기와 물성간의 관계 검색

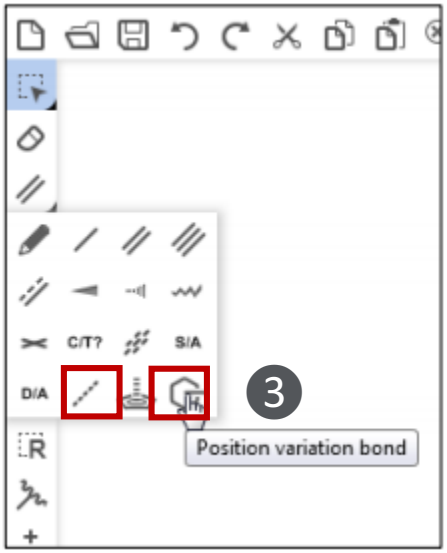
I am interested in sulfocoumarins (1,2-benzoxathiine 2,2-dioxide). I'd like to retrieve *sulfocoumarins with various substituents* and then quickly analyze the results to see *any relationships between functional groups and various properties*.



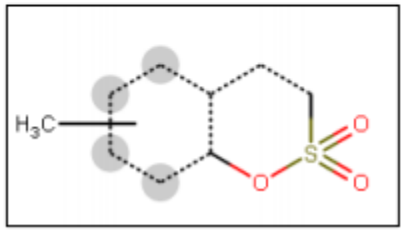


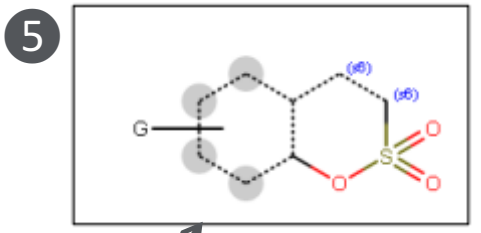
1. 선택 툴을 사용해 구조 선택
2. Any bond 툴 선택
3. Position variation bond 툴로 위치 지정
4. Generic group tool 에서 G 선택
5. Atom property에서 치환 허용개수 설정

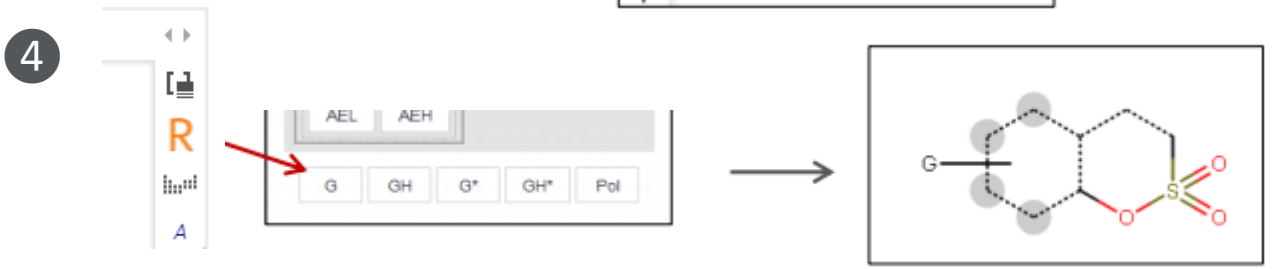




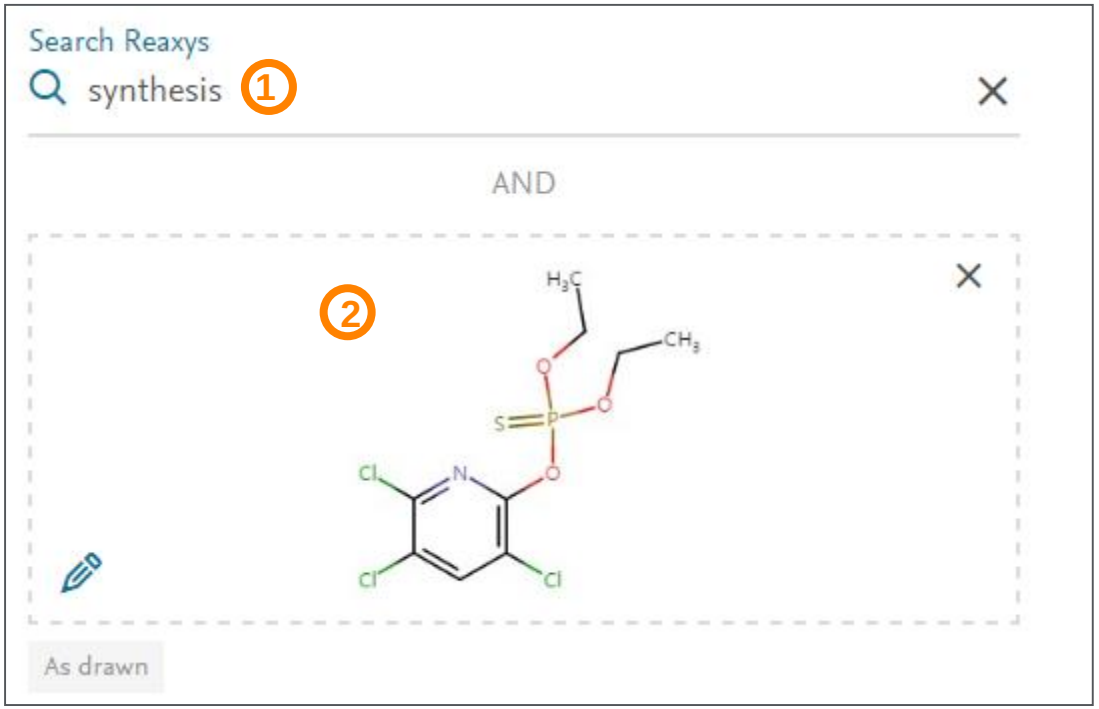
실습2





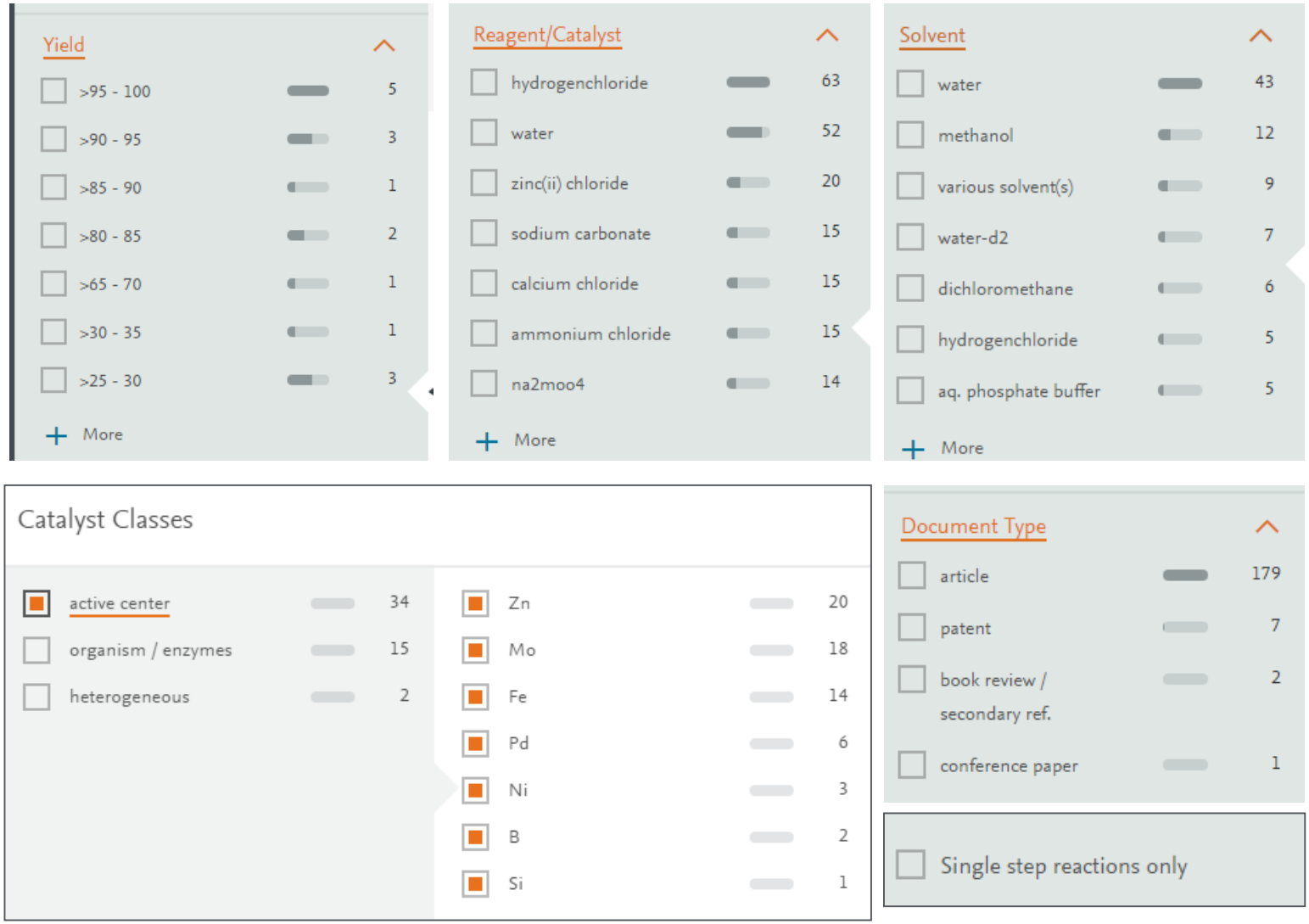


반응검색 – 구조 + synthesis or preparation

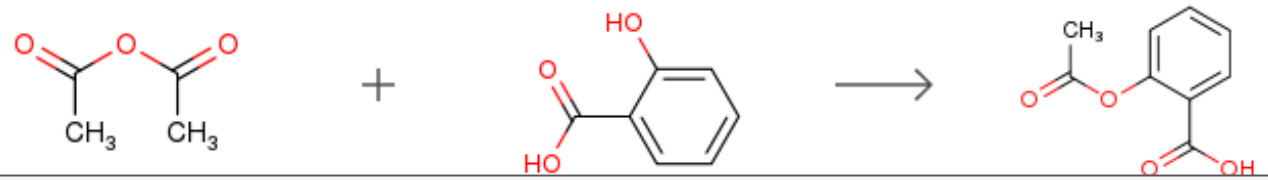


5 Reactions Reaction Query : as drawn; included: only absolute stereo, salts, mixtures, isotopes, charges, radicals Preview Results View Results

반응검색 결과 – 왼쪽 필터 활용하여 검색 결과 내 검색



결과 : 반응정보 / 실험과정 정보 찾기



Yield	Conditions	Reference
100%	**In** neat (no solvent) ;Molecular sieve;Microwave irradiationGreen chemistry Experimental Procedure	**Oliverio, Manuela; Costanzo, Paola; Nardi, Monica; +3 others** - Beilstein Journal of Organic Chemistry, 2016, vol. 12, p. 2222 - 2233 Full Text Show details

Optimized MW-assisted peracetylation

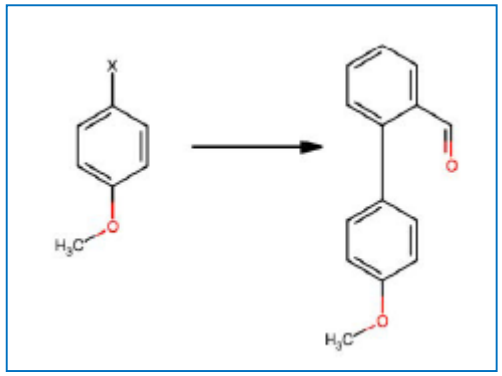
General procedure: The substrate belonging to one of the subset reported in Table 1(NTC, TC, CP, DGNP) (0.1 mmol) was left to react under MWheating (Synthos 3000, Anton Paar) with dry acetic anhydride(1 mL, 10 mmol) in a 3 mL vial (Rotor 64MG5), equipped witha magnetic stirrer in the presence of molecular sieves(10 percent w/w). The microwave, equipped with IR sensor forexternal temperature control (IR limit calculated as follows:Tinternal= 1.214 × TIR), has been set with the power programsprovided for its subset as described in Table 1. At the end of thereaction, the mixture was filtered, diluted with ethanol (2 mL)and left under vigorous stirring for 30 minutes at 50 °C. Themixture was then evaporated under reduced pressure and asmall amount of a saturated solution of sodium bicarbonate(3.8 mL, 10 mmol NaHCO3) was added. After the evolution ofCO2, the precipitation of the peracetylated product was observed. The products were separated by simple decantation. Forcompounds which do not precipitate upon addition of NaHCO3,an extraction with AcOEt was needed. The organic phase, afterdrying with Na2SO4, filtration and evaporation, gave the reaction crude.

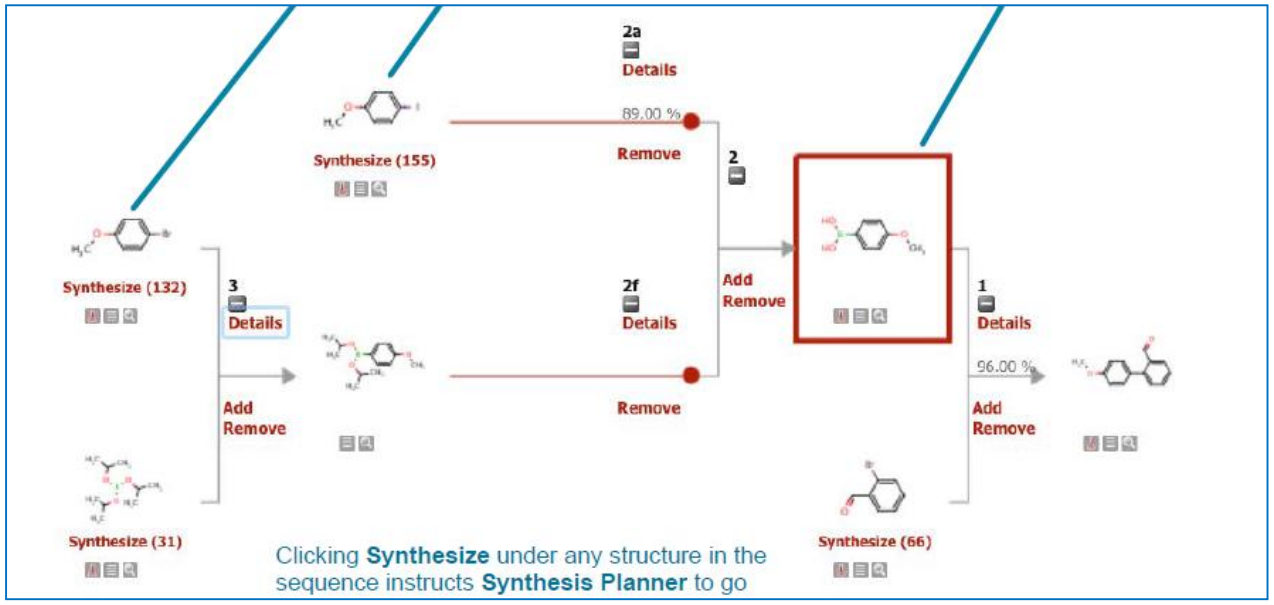
Synthesis Planner 활용- 합성설계하기

반응 검색 구조식으로 검색 시 대부분의 반응레코드는 single-step reaction (A => B)으로 검색 결과를 보여지며, 문헌에 있는 반응과 직접적으로 관련이 있는 sequences (A =>C=> B) 검색 결과에서 빠질 수 있습니다.

Synthesis planner를 활용하면 여러 단계의 합성경로를 캔버스에서 직접 단계 단계 설계가 가능합니다.

예: **Reaction records** for single-step reactions from halo-anisoles to the biphenyl derivative.





Indole의 합성 검색-Query Builder에서 Reaction으로 검색

Reaxys

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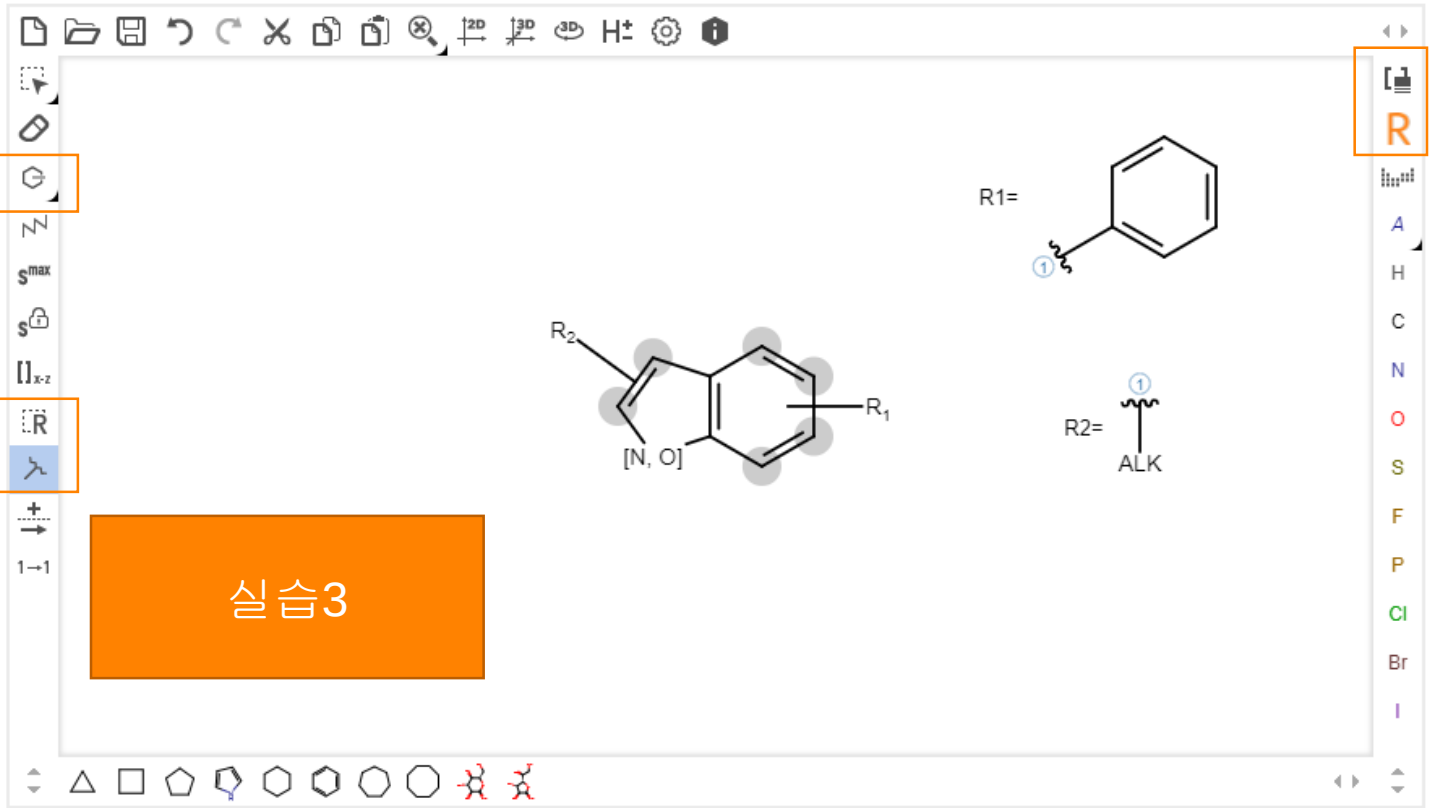
Structure editor

Create structure template from name



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49

Filters and Analysis

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- Yield
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1

Reaction ID: 39495825

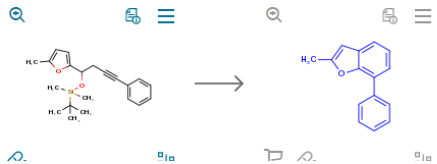
1 Conditions Find Similar

Yield	Conditions	References
90%	**With** palladium on activated charcoal; hydrogen **In** methanol for 4h; Experimental Procedure	Gritzalis, Dimitrios; Park, Jaeok; Chiu, Wei; Cho, Hyungjun; Lin, Yih-Shyan; De Schutter, Joris W.; Lacbay, Cyrus M.; Zielinski, Michal; Berghuis, Albert M.; Tsantrizos, Youla S. - Bioorganic and Medicinal Chemistry Letters, **2015**, vol. 25, # 5, p. 1117 - 1123 Full Text Cited 3 times Details Abstract

1 out of 1

2

Reaction ID: 31180487



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