



**Can a free access structure-centric
community for chemists
benefit drug discovery?**

Antony Williams

ACS Philadelphia 2008



ChemSpider Data

- The database PRESENTLY contains > 21.5 million compounds obtained from
 - Chemical vendors
 - Publishers
 - Commercial Database Vendors
 - US and international patents
 - Structure aggregators
 - Scraped from websites
 - Deposited by users



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- What is the structure of “insert name”?
- What is the name of “insert structure”?
- Where can I find information about “insert name”?
- Where can I buy some “insert name”?
- Where can I find more information about “insert name”?
- What is the “insert property” of “insert name”?



Tell me about Xanax..

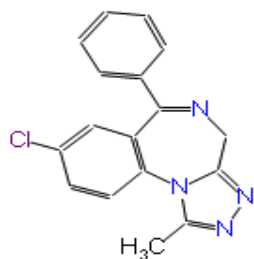
1 hit(s) found in 0.94 seconds
Search term: xanax
Found by synonym

URL Publication Description Link Identifier CIF Spectrum Image Comments

INHERENT PROPERTIES, IDENTIFIERS AND REFERENCES

2D 3D

Quick Links: [Permalink](#) [Similar](#) [Isomers](#)



ChemSpider ID: [2034](#)
Empirical Formula: $C_{17}H_{13}ClN_4$
Molecular Weight: 308.7649
Nominal Mass: 308 Da
Average Mass: 308.7649 Da
Monoisotopic Mass: 308.082874 Da

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Systematic Name: 8-chloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine
SMILES: Clc3cc2\C(=N/Cc1nnc(n1c2cc3)C)c4ccccc4
InChI: [InChI=1/C17H13ClN4/c1-11-20-21-16-10-19-17\(12-5-3-2-4-6-12\)14-9-13\(18\)7-8-15\(14\)22\(11\)16/h2-9H,10H2,1H3](#)
InChIKey: [VREFGVBLTWBCJP-UHFFFAOYAT](#)


WIKIPEDIA ARTICLE(S)

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Alprazolam, also known under the [trade names](#) **Xanax** and **Niravam**, is a short-acting drug of the [benzodiazepine](#) class used to treat moderate to severe [anxiety disorders](#), [panic attacks](#), and as an adjunctive treatment for anxiety associated with [major depression](#). It is also available in an [extended release](#) form, **Xanax XR**. Both forms are now available generically. [Read more...](#) or [Edit at Wikipedia...](#)



Tell me about Xanax

<input checked="" type="checkbox"/> ORIGINAL REFERENCE(S) FILTER EDIT	
Data Source	External ID(s)
FDA	18276
Journal of Heterocyclic Chemistry	19780161_6B , 19800575_1
KEGG	C06817 , D00225 ★
LeadScope	LS-156344
MCISB	18675
MeSH	Alprazolam ★
MLSMR	MLS000559000
Molecule of the Day	Alprazolam ★
Nature Chemical Biology	nchembio747-comp35
NIST	979635492
NIST Chemistry WebBook	979635492
Prous Science Drugs of the Future	91399
PubChem	2118
PubMed	10631626 , 10648728 , 10653202 , 10663429 , 10664927 , 10668858 , 10688619 , 10691246 , 10696114 , 10698361 , 10709776 , 10758169 , 10760357 , 10770452 , 10770483 , 10782977 , 16563516 , 16707239 , 16791582 , 16991019 , 17020957 , 17058100 , 17124639 , 17158196 , 17175036 , 17219217 , 17244765 , 6140317 , 6141159 , 6141930 , 6142907 , 6143507 , 6143633 , 6143649 , 6143766 , 6144090 , 6144110 , 6144136 , 6145358 , 6145360 , 6145365 , 6145726 , 6701100 , 6733175
Sigma-Aldrich 	611026 ALDRICH , A6551 SIGMA , A8800 SIGMA
Thomson Pharma	00000184 , 00038896
Wikipedia	Alprazolam ★



Balloon Call-Out Assistant

<u>Heterocyclic Chemistry</u>	<u>19780181_0B, 19800373_1</u>
KEGG	<u>C06817, D00225</u>
<u>LeadScope</u>	<u>LS-156344</u>
<u>MCISB</u>	18675
<u>MeSH</u>	
<u>MLSM</u>	
<u>Molec Day</u>	
<u>Natur</u>	
<u>Biolog</u>	
<u>NIST</u>	
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<u>Drugs</u>	
<u>Futur</u>	
<u>PubCh</u>	
	<u>10805613, 16563516, 16707239, 16791582, 16991019, 17020957, 170517175036, 17219217, 17244765, 6140317, 6141159, 6141930, 6142907, 6143766, 6144090, 6144110, 6144136, 6145358, 6145360, 6145365, 6150550, 6387913, 6701100, 6733175</u>
<u>PubMed</u>	

Name: KEGG

Description: A grand challenge in the post-genomic era is a complete computer representation of the cell, the organism, and the biosphere, which will enable computational prediction of higher-level complexity of cellular processes and organism behaviors from genomic and molecular information. Towards this end KEGG has been developing a bioinformatics resource named KEGG as part of the research projects of the Kanehisa Laboratories in the Bioinformatics Center of Kyoto University and the Human Genome Center of the University of Tokyo.

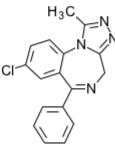
Contributor Classification: Metabolic Pathways

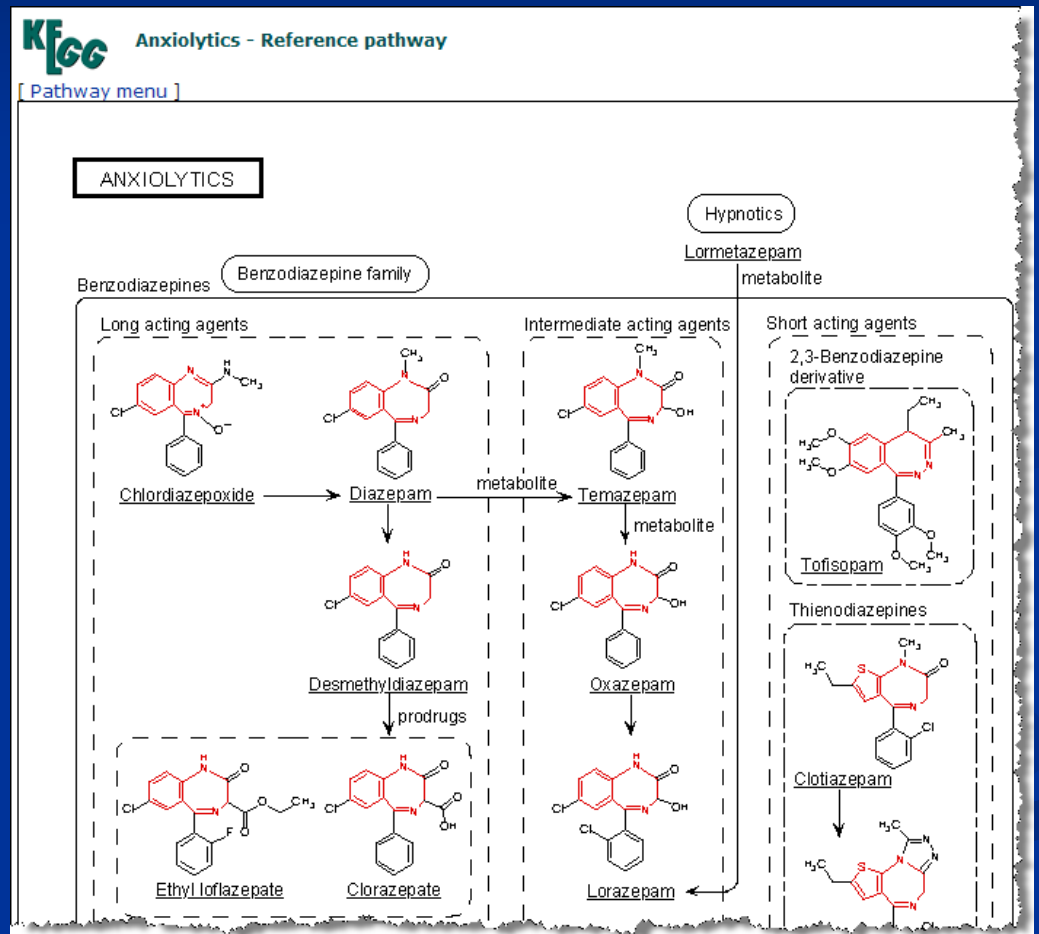
[More Details...](#)



Links to KEGG

KEGG DRUG: D00225 Help

Entry	D00225	Drug
Name	Alprazolam (JP15/USP/INN); Xanax (TN)	
Formula	C17H13ClN4	
Mass	308.0829	
Structure	 <p>D00225</p> <p>Mol file KCF file DB search Jmol KegDraw</p>	
Target	benzodiazepine-receptor agonist	
Activity	Sedative-hypnotic	
Remark	Same as: C06817 Therapeutic category: 1124 ATC code: N05BA12 BRITe hierarchy	
Pathway	PATH: map07030 Anxiolytics	
Other DBs	CAS: 28981-97-7 PubChem: 7847292 ChEBI: 2611 DrugBank: DB00404 DailyMed: alprazolam LigandBox: D00225	
LinkDB	All DBs	
KCF data	Show	





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Suggestions: [Alprazolam](#), [Alprazolam](#), [Loprazolam](#), [Acetazolam](#), [Durazolam](#), [Adinazolam](#), [Triazolam](#), [Alprafenone](#), [Midazolam](#), [Mexazolam](#), [More...](#)

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- Select PubMed under the Links menu to retrieve all records for the MeSH Term.
- Select [NLM MeSH Browser](#) under the Links menu for additional information.

1: Alprazolam Links

A triazolobenzodiazepine compound with antianxiety and sedative-hypnotic actions, that is efficacious in the treatment of PANIC DISORDERS, with or without AGORAPHOBIA, and in generalized ANXIETY DISORDERS. (From AMA Drug Evaluations Annual, 1994, p238)
Year introduced: 1987

Subheadings: This list includes those paired at least once with this heading in MEDLINE and may not reflect current rules for allowable combinations.

- administration and dosage
- adverse effects
- agonists
- analogs and derivatives
- analysis
- antagonists and inhibitors
- blood
- chemistry
- contraindications
- diagnostic use
- isolation and purification
- metabolism
- pharmacokinetics
- pharmacology
- poisoning
- radiation effects
- therapeutic use
- toxicity
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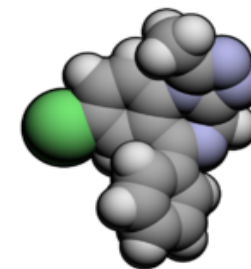
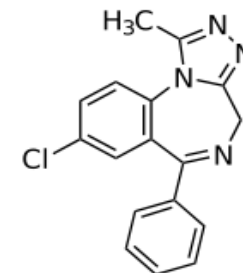
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Alprazolam

From Wikipedia, the free encyclopedia

[Categories: Anxiolytics](#) | [Benzodiazepines](#) | [Hypnotics](#) | [Triazoles](#)

Alprazolam, also known under the [trade names](#) **Xanax** and **Niravam**, is a short-acting drug of the [benzodiazepine](#) class used to treat moderate to severe [anxiety disorders](#), [panic attacks](#), and as an adjunctive treatment for anxiety associated with [major depression](#). It is also available in an [extended release](#) form, **Xanax XR**. Both forms are now available generically.



Alprazolam

Systematic (IUPAC) name

8-chloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine

Contents [\[hide\]](#)

- [1 History](#)
- [2 Pharmacology](#)
- [3 Pharmacokinetics](#)
- [4 Indications](#)
- [5 Availability](#)
- [6 Packaging](#)
- [7 Side effects](#)
- [8 Physical dependence and withdrawal](#)
- [9 Contraindications](#)
 - [9.1 Overdose](#)
 - [9.2 Pregnancy](#)
 - [9.2.1 Teratogenicity classification](#)
 - [9.2.2 Effects on the fetus](#)
 - [9.2.3 Labor and delivery](#)
 - [9.2.4 Nursing mothers \(neonates\)](#)



Multiple Journal Articles

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Data Source	External ID(s)
FDA	18276
Journal of Heterocyclic Chemistry	19780161_6B , 19800575_1 ★
KEGG	C06817 , D00225
LeadScope	LS-156344
MCISB	18675
MeSH	Alprazolam
MLSMR	MLS000559000
Molecule of the Day	Alprazolam
Nature Chemical Biology	nchembio747-comp35 ★
NIST	979635492
NIST Chemistry WebBook	979635492
Prous Science Drugs of the Future	91399
PubChem	2118
PubMed	10631626 , 10648728 , 10653202 , 10663429 , 10664927 , 10668858 , 10688619 , 10691246 , 10696114 , 10698361 , 10709776 , 10758169 , 10760357 , 10770452 , 10770483 , 10782977 , 16563516 , 16707239 , 16791582 , 16991019 , 17020957 , 17058100 , 17124639 , 17158196 , 17175036 , 17219217 , 17244765 , 6140317 , 6141159 , 6141930 , 6142907 , 6143507 , 6143633 , 6143649 , 6143766 , 6144090 , 6144110 , 6144136 , 6145358 , 6145360 , 6145365 , 6145726 , 6701100 , 6733175 ★
Sigma-Aldrich	611026 ALDRICH , A6551 SIGMA , A8800 SIGMA
Thomson Pharma	00000184 , 00038896
Wikipedia	Alprazolam



What's it called???

Names and Synonyms

Validated by Experts, Validated by Users, Non-Validated, Removed by Users, Redirected by Users, **Redirect Approved by Experts**

249-349-2 [EINECS/ELINCS]

28981-97-7 [RN]

4H-(1,2,4)Triazolo(4,3-a)(1,4)benzodiazepine, 8-chloro-1-methyl-6-phenyl-

4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine, 8-chloro-1-methyl-6-phenyl-

8-Chlor-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepin

8-chloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine

8-chloro-1-méthyl-6-phényl-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazépine

Alprazolam [Wiki]

Alprazolam (JP15/USP)

Alprazolam [USAN:BAN:INN:JAN]

Anxyl

Panistat

Staccato-alprazolam

Xanax (TN)

4H-s-Triazolo(4,3-a)(1,4)benzodiazepine, 8-chloro-1-methyl-6-phenyl-

8-Chloro-1-methyl-6-(phenyl-d5)-4H-(1,2,4)triazolo[4,3-a][1,4]benzodiazepine

8-Chloro-1-methyl-6-phenyl-4H-s-triazolo(4,3-a)(1,4)benzodiazepine

8-Chloro-1-methyl-6-phenyl-4H-s-triazolo[4,3-a][1,4]benzodiazepine

Alcelam

Algad

Alpaz

Alpax

Alpram

Alprax

alprazolam extended-release

Alprazolamum [INN-Latin]

Alpronax

Alprox

Algam



LogP? LogD? PSA?

⊗ PREDICTED PROPERTIES

LogP:	ACD/LogP: 2.50 XLogP: 4.90	# of Rule of 5 Violations:	0
ACD/LogD (pH 5.5):	2.5	ACD/LogD (pH 7.4):	2.5
ACD/BCF (pH 5.5):	46.67	ACD/BCF (pH 7.4):	46.71
ACD/KOC (pH 5.5):	544.74	ACD/KOC (pH 7.4):	545.23
#H bond acceptors:	4	#H bond donors:	0
#Freely Rotating Bonds:	1	Polar Surface Area:	43.07 Å ²
Index of Refraction:	1.71	Molar Refractivity:	88.22 cm ³
Molar Volume:	225.5 cm ³	Polarizability:	34.97 10 ⁻²⁴ cm ³
Surface Tension:	52.1 dyne/cm	Density:	1.36 g/cm ³
Flash Point:	261.6 °C	Enthalpy of Vaporization:	77.94 kJ/mol
Boiling Point:	509 °C at 760 mmHg	Vapour Pressure:	1.77E-10 mmHg at 25°C



EPI Suite Predictions & Experimental Data

⌵ EPI SUMMARY

Log Octanol-Water Partition Coef (SRC):

Log Kow (KOWWIN v1.67 estimate) = 3.87

Log Kow (Exper. database match) = 2.12

Exper. Ref: BioByte (1995)

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPWIN v1.42):

Boiling Pt (deg C): 441.81 (Adapted Stein & Brown method)

Melting Pt (deg C): 185.42 (Mean or Weighted MP)

VP(mm Hg,25 deg C): 1.65E-008 (Modified Grain method)

Subcooled liquid VP: 7.84E-007 mm Hg (25 deg C, Mod-Grain method)

Water Solubility Estimate from Log Kow (WSKOW v1.41):

Water Solubility at 25 deg C (mg/L): 13.1

log Kow used: 2.12 (expkow database)

no-melting pt equation used

Water Sol Estimate from Fragments:

Wat Sol (v1.01 est) = 0.15855 mg/L

ECOSAR Class Program (ECOSAR v0.99h):

Class(es) found:

Aliphatic Amines



Are you kidding?

Log Octanol-Water Partition Coef (SRC): Log Kow (KOWWIN v1.67 estimate) = 3.87 Log Kow (Exper. database match) = 2.12 Exper. Ref: BioByte (1995) Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPWIN v1.42): Boiling Pt (deg C): 441.81 (Adapted Stein & Brown method) Melting Pt (deg C): 185.42 (Mean or Weighted MP) VP(mm Hg,25 deg C): 1.65E-008 (Modified Grain method) Subcooled liquid VP: 7.84E-007 mm Hg (25 deg C, Mod-Grain method) Water Solubility Estimate from Log Kow (WSKOW v1.41): Water Solubility at 25 deg C (mg/L): 13.1 log Kow used: 2.12 (expkow database) no-melting pt equation used Water Sol Estimate from Fragments: Wat Sol (v1.01 est) = 0.15855 mg/L ECOSAR Class Program (ECOSAR v0.99h): Class(es) found: Aliphatic Amines Henrys Law Constant (25 deg C) [HENRYWIN v3.10]: Bond Method : 9.77E-012 atm-m³/mole Group Method: Incomplete Henrys LC [VP/WSol estimate using EPI values]: 5.117E-010 atm-m³/mole Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]: Log Kow used: 2.12 (exp database) Log Kaw used: -9.399 (HenryWin est) Log Koa (KOAWIN v1.10 estimate): 11.519 Log Koa (experimental database): None Probability of Rapid Biodegradation (BIOWIN v4.10): Biowin1 (Linear Model) : 0.6009 Biowin2 (Non-Linear Model) : 0.2660 Expert Survey Biodegradation Results: Biowin3 (Ultimate Survey Model): 2.2574 (weeks-months) Biowin4 (Primary Survey Model) : 3.1733 (weeks) MITI Biodegradation Probability: Biowin5 (MITI Linear Model) : -0.1488 Biowin6 (MITI Non-Linear Model): 0.0042 Anaerobic Biodegradation Probability: Biowin7 (Anaerobic Linear Model): -0.4906 Ready Biodegradability Prediction: NO Hydrocarbon Biodegradation (BioHCwin v1.01): Structure incompatible with current estimation method! Sorption to aerosols (25 Dec C)[AEROWIN v1.00]: Vapor pressure (liquid/subcooled): 0.000105 Pa (7.84E-007 mm Hg) Log Koa (Koawin est) : 11.519 K_p (particle/gas partition coef. (m³/ug)): Mackay model : 0.0287 Octanol/air (Koa) model: 0.0811 Fraction sorbed to airborne particulates (phi): Junge-Pankow model : 0.509 Mackay model : 0.697 Octanol/air (Koa) model: 0.866 Atmospheric Oxidation (25 deg C) [AopWin v1.92]: Hydroxyl Radicals Reaction: OVERALL OH Rate Constant = 7.6246 E-12 cm³/molecule-sec Half-Life = 1.403 Days (12-hr day; 1.5E6 OH/cm³) Half-Life = 16.834 Hrs Ozone Reaction: No Ozone Reaction Estimation Fraction sorbed to airborne particulates (phi): 0.603 (Junge,Mackay) Note: the sorbed fraction may be resistant to atmospheric oxidation Soil Adsorption Coefficient (PCKOCWIN v1.66): K_{oc} : 2.151E+006 Log K_{oc}: 6.333 Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v1.67]: Volatilization from Water: Henry LC: 9.77E-012 atm-m³/mole (estimated by Bond SAR Method) Half-Life from Model River: 1.053E+008 hours (4.388E+006 days) Half-Life from Model Lake : 1.149E+009 hours (4.786E+007 days) Removal In Wastewater Treatment: Total removal: 2.37 percent Total biodegradation: 0.10 percent Total sludge adsorption: 2.27 percent Total to Air: 0.00 percent (using 10000 hr Bio P,A,S) Level III Fugacity Model: Mass Amount Half-Life Emissions (percent) (hr) (kg/hr) Air 0.000217 33.7 1000 Water 21 900 1000 Soil 78.9 1.8e+003 1000 Sediment 0.094 8.1e+003 0 Persistence Time: 1.48e+003 hr



Toxicity/Safety Information

• Miscellaneous

Appearance: white crystalline powder or tablets [?](#) [↗](#)

Appearance: Odorless, colorless to white, crystal-line powder. [aspirin] [Note: Develops the vinegar-like odor of acetic acid on contact with moisture.] [?](#) [↗](#)

Stability: Stable. Keep dry. Incompatible with strong oxidizing agents, strongbases, strong acids, various other compounds such as iodides, iron salts,quinine salts, etc. [?](#) [↗](#)

Toxicity: ORL-RAT LD50 200 mg kg-1 , SKN-RBT LD50 > 7940 mg kg-1 , ORL-MAM LD50 1750 mg kg-1 , ORL-MAN LD50 (estimated) 400 mg kg-1 [?](#) [↗](#)

Safety: WARNING: Irritates skin and eyes, harmful if swallowed [?](#) [↗](#)

Safety: Safety glasses. [?](#) [↗](#)

First Aid: Eye: Irrigate immediately Skin: Soap wash Breathing: Respiratory support Swallow: Medical attention immediately [?](#) [↗](#)

Exposure Routes: inhalation, ingestion, skin and/or eye contact [?](#) [↗](#)

Symptoms: Irritation eyes, skin, upper respiratory system; increased blood clotting time; nausea, vomiting; liver, kidney injury [?](#) [↗](#)

Target Organs: Eyes, skin, respiratory system, blood, liver, kidneys [?](#) [↗](#)

Incompatibilities And Reactivities: Solutions of alkali hydroxides or carbonates, strong oxidizers, moisture [Note: Slowly hydrolyzes in moist air to salicydic & acetic acids.] [?](#) [↗](#)

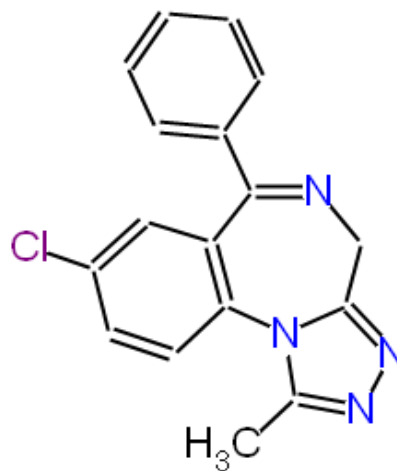
Personal Protection And Sanitation: Skin: Prevent skin contact Eyes: Prevent eye contact Wash skin: When contaminated Remove: No recommendation Change: Daily Provide: Eyewash, Quick drench [?](#) [↗](#)



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Identifiers

SMILES:	<chem>Clc2cc3/C(=N\Cc1nnc(C)n1c3cc2)c4ccccc4</chem>
InChI:	InChI=1/C17H13ClN4 /c1-11-20-21-16-10-19-17(12-5-3-2-4-6-12)14-9-13(18)7-8-15(14)22(11)16 /h2-9H,10H2,1H3
InChIKey:	VREFGVBLTWBCJP-UHFFFAOYAT

Inherent Properties

Empirical Formula:	C ₁₇ H ₁₃ ClN ₄
Molecular Weight:	308.7649
Nominal Mass:	308 Da
Average Mass:	308.7649 Da
Monoisotopic Mass:	308.082874 Da

Calculated Properties

ACD/LogP:	2.499+/-1.076
# of Rule of 5 Violations:	0
Number of Hydrogen Bond Acceptors:	4
Number of Hydrogen Bond Donors:	0
Number of Freely Rotatable Bonds:	1
Polar Surface Area:	43.07 Å ²
Boiling Point:	509.0+/-60.0 Celsius at 760 mmHg
Flash Point:	261.6+/-32.9 Celsius
Enthalpy of Vaporization:	77.94+/-3.0 kJ/mol
Molar Volume:	225.5+/-7.0 cm ³
Index of Refraction:	1.710+/-0.05
Molar Refractivity:	88.22+/-0.5 cm ³
Polarizability:	34.97+/-0.5 10 ⁻²⁴ cm ³
Surface Tension:	52.1+/-7.0 dyne/cm
Density:	1.36+/-0.1 g/cm ³
Dielectric Constant:	Cannot calculate
Parachor:	606.2+/-8.0 cm ³

Predicted By



Advanced
Chemistry
Development

ACD/Labs



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| <input checked="" type="checkbox"/> Royal Society of Chemistry | |

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Open Access Literature Searching

1-(2-Pyridyl)-8H-pyrrolo[2,1-c]-s-triazolo[4,3-a][1,4]benzodiazepinium chloride (Acta Cryst E 2001 Volume 57 Part 2 Page o122-o124) - International Union of Crystallography

M. Kubicki, P.W. Coddling

... are used clinically as anxiolytics and hypnotics (for example, alprazolam, marketed as **Xanax**, and triazolam, marketed as Halcion). The protonation takes place at ...

Structure of an analogue of the triazolobenzodiazepine alprazolam (Acta Cryst C 1988 Volume 44 Part 10 Page 1823-1825) - International Union of Crystallography

H.J. Kemmish, T.A. Hamor

... ,3-a][1,4]- benzodiazepine. Marketed as **Xanax** (Upjohn). ~: 8-Chloro-6-(2 ...

Structure of 5-chloro-2-{3-[(diethylamino)methyl]-5-methyl-4H-1,2,4-triazol-4-yl}benzophenone (I) and of its methylamino analogue (II) (Acta Cryst C 1990 Volume 46 Part 3 Page 459-462) - International Union of Crystallography

H.J. Kemmish, T.A. Hamor

... 3-a][1,4]benzo- diazepine. Marketed as **Xanax** (Upjohn). 0108-2701/90/030459-04503. ...

Structural Basis for the Function of Stringent Starvation Protein A as a Transcription Factor (J. Biol. Chem. 2005 Volume 280 Issue 17 Page 17380) - American Society for Biochemistry and Molecular Biology

Anne-Marie Hansen, Yijun Gu, Mi Li, Michelle Andrykovitch, David S. Waugh, Ding Jun Jin, Xinhua Ji

... Vibfi, Vibrio fischeri; Vibpa, Vibrio parahemolyticus; Vibvu, Vibrio vulnificus; **Xanax**, Xanthomonas axonopodis; Xanca, Xanthomonas campestris; Xylfa, Xylella fastidiosa; ...

GH97 is a new family of glycoside hydrolases, which is related to the Î±-galactosidase superfamily (BMC Genomics 2005 Volume 6 Page 112) - PubMed Central Open Archives Service

Daniil G Naumoff

... GH97, 97a Azotobacter vinelandii AvOP EAM07225 ORF: alpha-glucosidase 673 97A1_ **XANAX** GH97, 97a Xanthomonas axonopodis pv. citri 306 AAM37448 ORF: alpha- ...

Competitive Inhibition of Beef Heart Cyclic AMP Phosphodiesterase by Cytokinins and Related Compounds (PNAS 1974 Volume 71 Issue 12 Page 4670) - National Academy of Sciences of the USA

Sidney M. Hecht, Robert D. Faulkner, S. D. Hawrelak

... ,R =H, R' = -- (4100) and 222 (5800); **XAnax** (sh) and 228 (5500), Xmin 252 (3200) and 224 (5400 ...

An internet survey of 2,596 people with fibromyalgia (BMC Musculoskeletal Disorders 2007 Volume 8 Page 27) - PubMed Central Open Archives Service

Robert M Bennett, Jessie Jones, Dennis C Turk, I Jon Russell, Lynne Matallana

...] 33 12 36 51 Gabapentin [Neurontin] 33 12 36 46 Aprazolam [**Xanax**] 33 10 30 70 Oxycodone+ APAP [Percocet, Roxice] 32 ...



What is ChemSpider now?

- A chemistry search engine
- Allows text-searching of ca. 500,000 open access chemistry articles from over a dozen publishers
- Online Physchem Prediction
- Web-services for searching and integration
- A platform for depositing and curating data



Presently Integrating...

- ChemSpider will be the small-molecule hub for entering into protein and pathway-based online resources
- WikiProteins
- WikiPathways
- Protein Data Bank



ChemSpider as a “Property Database”

Pharmaceutical Research, Vol. 24, No. 12, December 2007 (© 2007)

DOI: 10.1007/s11095-007-9435-9

Research Paper

Computational Models to Assign Biopharmaceutics Drug Disposition Classification from Molecular Structure

Akash Khandelwal,¹ Praveen M. Bahadduri,¹ Cheng Chang,^{1,3} James E. Polli,¹ Peter W. Swan,^{1,4} and Sean Ekins^{1,2}

diverse arrays of data. In this study, we have captured a range of applicable descriptors for physicochemical properties, including easily interpretable descriptors determined by widely available chemical drawing software (e.g. ChemDraw) or web-based tools (e.g. PubChem or **ChemSpider**), as well as complex descriptor sets from commercial vendors such as MolconnZ



ChemSpider as a “Property Database”

Current Drug Metabolism, 2008, 9, 000-000

Molecular Characterization of CYP2B6 Substrates

Sean Ekins^{1,2,3,#,*}, Manisha Iyer⁴, Matthew D. Krasowski⁴ and Evan D. Kharasch⁵

The current QSAR and statistical analysis using simple, interpretable molecular properties that are freely available from **ChemSpider**, PubChem (or other reliable sources of chemistry data on the internet), suggests that 64 molecules (Tables 1, 2 and 3) demonstrating CYP2B6 affinity are to varying degrees hydrophobic, with one or more HBAs, and in good agreement with the properties obtained in previous pharmacophore and QSAR models for CYP2B6.

ChemSpider as a “Ligand Database”

0026-895X/08/7403-662-672\$20.00

MOLECULAR PHARMACOLOGY

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Mol Pharmacol 74:662–672, 2008

Vol. 74, No. 3

49487/3379712

Printed in U.S.A.

Computational Discovery of Novel Low Micromolar Human Pregnane X Receptor Antagonists[§]

Sean Ekins, Vladyslav Kholodovych, Ni Ai, Michael Sinz, Joseph Gal, Lajos Gera, William J. Welsh, Kenneth Bachmann, and Sridhar Mani

Collaborations in Chemistry, Jenkintown, Pennsylvania (S.E.); Department of Pharmaceutical Sciences, University of Maryland, Baltimore, Maryland (S.E.); Department of Pharmacology, University of Medicine and Dentistry of New Jersey

Substructure Searching. The molecule SPB 03255 was used as a query for substructure searching using two data bases that contain information on commercially available molecules namely, ChemSpider (<http://www.chemspider.com/>) and eMolecules (<http://emolecules.com/databases>). The two-dimensional molecular structures of re-



ChemSpider – Research in Progress

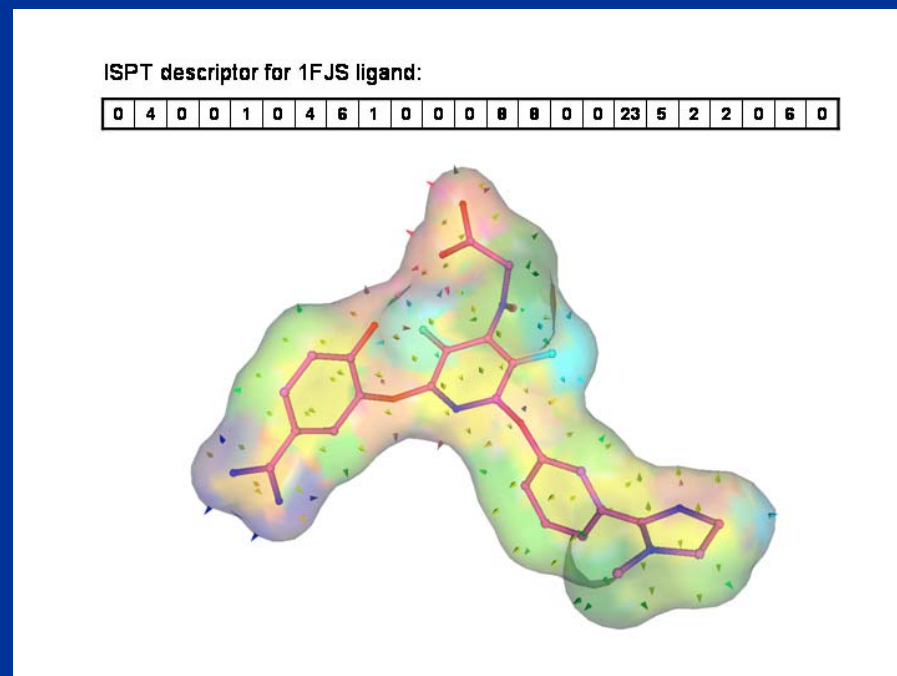
- ChemSpider for the purpose of online virtual screening
- Applying descriptors of various types to filter a database of 20 million compounds
- In progress:
 - Utilizing SimBioSys' LASSO Descriptor
 - Collaboration based on ECCR's ChemModLab

Ligand Activity by Surface Similarity Order



- LASSO uses 23 kinds of Interactive Surface Point Descriptors and
 - is conformation independent
 - screens at 1 million structures/min
 - is proven to enrich screened databases
 - provides scaffold hopping

- Hbond Donors (5 kinds)
- Acceptors (5 kinds)
- Ambivalent H donor/acceptor
- Aromatic Pi-stacking (5 kinds)
- Hydrophobic (3 kinds)
- Metal ions
- Misc (Sulfur, Halogens)



<http://dx.doi.org/10.1007/s10822-007-9164-5>



LASSO Descriptors on ChemSpider

- 40 target receptors chosen
 - From the Database of Useful Decoys dataset
 - <http://dud.docking.org/>
 - Brian Shoichet, UCSF
- Wide range of receptor classes
- Each target family had 10s-100s of known actives
- Actives used as query files for LASSO
- LASSO similarity descriptors generated across all 40 targets and deposited on ChemSpider



LASSO Descriptors on ChemSpider



⚙ SIMBIOSys LASSO

Descriptors: 0, 0, 0, 0, 0, 0, 0, 0, 3, 0, 0, 0, 0, 3, 8, 2, 0, 17, 0, 1, 1, 0, 3, 0, 0

Category	Target	PDB Code	LASSO Score
Other Enzymes	PARP, poly(ADP-ribose) polymerase	1efy	0.74
Kinases	PDGFRb, platelet derived growth factor receptor kinase	N/A	0.70
Other Enzymes	COX-2, cyclooxygenase-2	1cx2	0.21
Kinases	EGFR, epidermal growth factor receptor	1m17	0.09
Nuclear Hormone Receptors	PPARg, peroxisome proliferator activated receptor	1fm9	0.08
Other Enzymes	HIVRT, HIV reverse transcriptase	1rt1	0.02
Nuclear Hormone Receptors	RXRa, retinoic X receptor R	1mvc	0.02
Kinases	P38 MAP, P38 mitogen activated protein	1kv2	0.02
Kinases	VEGFR2, vascular endothelial growth factor receptor	1vr2	0.02
Serine Proteases	FXa, factor Xa	1f0r	0.02
Metalloenzymes	PDE5, phosphodiesterase 5	1xp0	0.02

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Languages: Deutsch

Poly ADP ribose polymerase

(Redirected from **PARP**)

Poly (ADP-ribose) polymerase (PARP) is a **protein** involved in a number of c

Contents [hide]

- Members of PARP family
- Functions
 - Role in forming polymer of ADP-ribose (PAR)
 - Role in repairing DNA nicks
 - Role of tankyrases
- External links

1efy

DOI: 10.2210/pdb/1efy/pdb

Crystal Structure of the Catalytic Fragment of Poly (ADP-Ribose) Polymerase Complexed with a Benzimidazole Inhibitor

Authors: White, A.W., Almassy, K., Calvert, A.H., Curtin, N.J., Griffin, B.J., Hostencky, Z., Mungley, K., Newell, D.R., Sridharan, K., Gidding, S.T.

Primary Citation: White, A.W., Almassy, K., Calvert, A.H., Curtin, N.J., Griffin, B.J., Hostencky, Z., Mungley, K., Newell, D.R., Sridharan, K., Gidding, S.T. (2006) Resistance-modifying agents: 3. Chemical and biological properties of benzimidazole inhibitors of the DNA repair enzyme poly(ADP-ribose) polymerase. *J Med Chem* 49: 4054-4067 [Abstract]

History: Deposition: 2000-02-10 Release: 2001-01-17

Experimental Method: X-RAY DIFFRACTION Data File

Parameters	Resolution	R-value	R-free	Space Group
	2.20	0.202 (004)	0.274	P 2 ₁ 2 ₁ 2 ₁

Unit Cell

Length (Å)	a	b	c	Volume
Å	58.36	90.00	94.20	5036
Angle (°)	alpha	beta	gamma	
	90.00	90.00	90.00	

Molecular Description: Polymer 1: MONOMER POLY (ADP-RIBOSE) POLYMERASE Fragment CATALYTIC FRAGMENT Chain: A EC no. 2.4.2.30

Display Options: KIQ, 3D, 2D, Wasmol, MBT SimpleViewer, MBT Protein Workbench, QuickFit, All Images



LASSO Searching Method 1 LASSO Searching Method 1

ACE, angiotensin-converting enzyme \geq 0.80
AND ALR2, aldose reductase \geq 0.65 [Add Remove](#)

OPTIONS

About

244 hits found in 4.47 seconds

**LASSO_SIMILAR(ACE, angiotensin-converting enzyme desc 0.8) AND LASSO_SIMILAR(ALR2, aldose reductase desc 0.65)
AND SingleComponent AND NonIsotopic**

- Example question: “What are the top 1000 molecules with LASSO descriptors similar to the actives for the Estrogen Receptor”



LASSO Searching Method 2

Find structure with LASSO Score \geq for and \leq for

Nuclear Hormone Receptors

- AR, androgen receptor
- ER, estrogen receptor; agonist
- ER, estrogen receptor; antagonist
- GR, glucocorticoid receptor
- MR, mineralocorticoid receptor
- PPARg, peroxisome proliferator activated receptor
- PR, progesterone receptor
- RXRa, retinoic X receptor R

Serine Proteases

- FXa, factor Xa
- Thrombin
- Trypsin

Folate Enzymes

- DHFR, dihydrofolate reductase

Kinases

- CDK2, cyclindependent kinase 2
- EGFr, epidermal growth factor receptor
- FGFr1, fibroblast growth factor receptor kinase
- HSP90, human heat shock protein 90
- P38 MAP, P38 mitogen activated protein
- PDGFrB, platelet derived growth factor receptor kinase
- SRC, tyrosine kinase SRC
- TK, thymidine kinase
- VEGFr2, vascular endothelial growth factor receptor

Metalloenzymes

- ACE, angiotensin-converting enzyme
- ADA, adenosine deaminase
- COMT, catechol O-methyltransferase
- PDE5, phosphodiesterase 5

Other Enzymes

- AChE, acetylcholinesterase

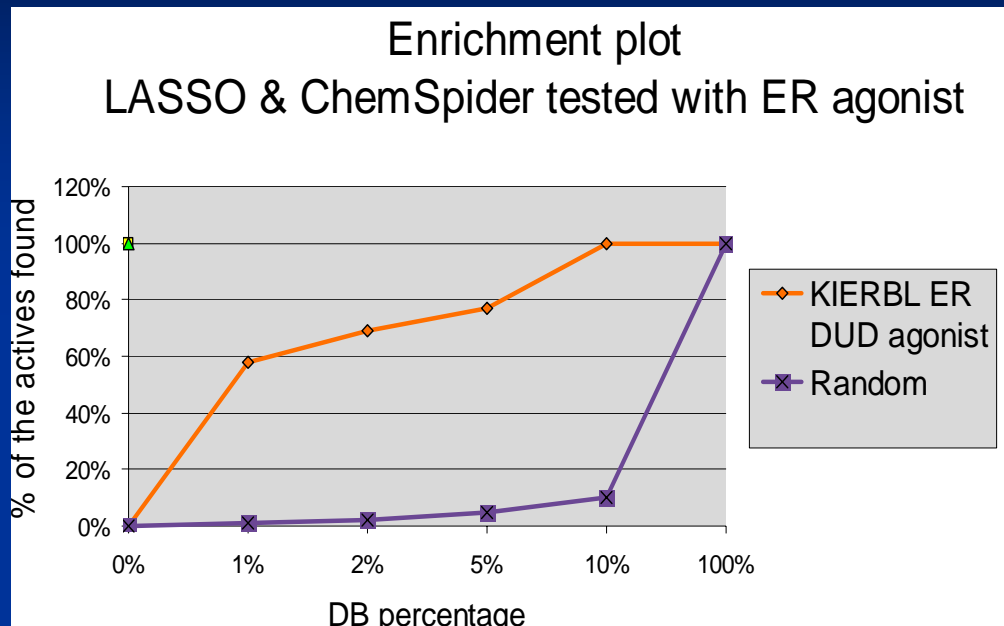


Example for ER enrichment

- KIERBL Dataset (EPA's DSSTox)
 - Estrogen Receptor Binding K_i values for 50 compounds of environmental relevance: Laws *et. al.* Toxicol Sci. 2006 Nov; 94(1):46-56. Epub 2006 Aug 29
- 15 “binders”: 3-5x weaker the natural ligand 17-beta-estradiol
- 14 million structure subset of LASSO descriptors
- Are known actives recovered?



Enrichment Plot



- 60% of actives were recovered in the top 1% of the database
- “Environmental binders” are weak binders!
- Top ranked compounds might be active ER binders
- Candidates for experimental investigation?



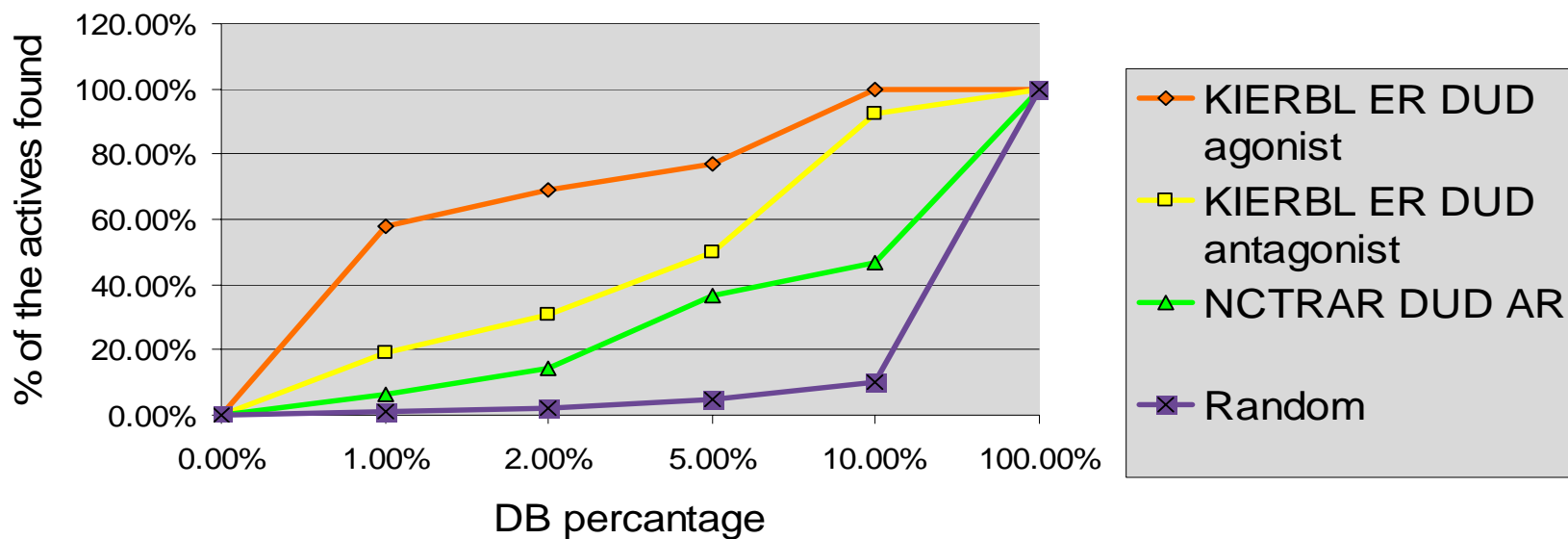
Work to be Done Yet To Validate Further

- Run LASSO descriptors on remaining members of database
- Use PhysChem filters at time of Searching (already pre-calculated and in properties)
- Use Structure filters at time of searching
- Use Patent filters at time of searching
- Validate on **real examples** from drug discovery



General Trends?

Enrichment plots: LASSO & ChemSpider tested with AR + ER





“The ChemSpider Appliance”

- Queries from ChemSpider users expose their IP
- We have been told that companies have told their users to NOT use ChemSpider – NOT because it’s not useful!

And so..the ChemSpider Appliance...



What's Coming?

- Watch this space.....
- <http://www.collaborativedrug.com/>

CDD COLLABORATIVE
DRUG
DISCOVERY

[Home](#) | [Product Overview](#) | [Why Use CDD?](#) | [Who Uses CDD?](#) | [Privacy & Security](#) | [Commur](#)

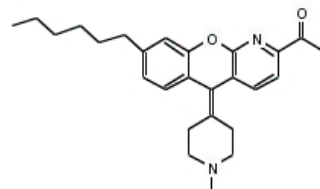
Collaborative Drug Discovery's web-based software organizes preclinical research data to help scientists advance new drug candidates more effectively.



Route Designer

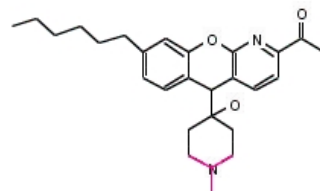


What if....



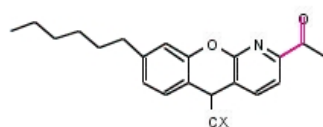
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[Resubmit Molecule]

Rule #1
25 Examples with [28] of 35
Avg. yield 82.04%



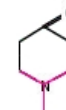
[New path][Molfile] [!]
[Resubmit Molecule]

Rule #2
25 Examples with [1] of 3
Avg. yield 76.72%



[New path][Molfile] [!]
[Resubmit Molecule]

+



[New path][Molfile][Details]
Database: Lancaster
catalog.number:6204



A Question...

- Is there enough novel chemistry on ChemSpider to be indexed?
 - Novel fully characterized compounds are deposited on ChemSpider on a weekly basis.
- Can ChemSpider host Open Notebook Science efforts?
 - System presently hosts ONS efforts but needs to switch workflow from structure-centric to sample-centric
 - Nevertheless...



UsefulChem Open Notebook Science

1 hit(s) found in 0.03 seconds

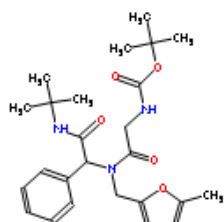
Search term: UsefulChem UC 0008
Found by synonym

Please [login](#) to be able to add spectra, identifiers, links and publications.

Add: [Comments](#)

INHERENT PROPERTIES, IDENTIFIERS AND REFERENCES

Quick Links: [Permalink](#) [Similar](#) [Isomers](#)



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ChemSpider ID: [10481766](#)
Empirical Formula: [C₂₅H₃₅N₃O₅](#)
Molecular Weight: 457.5625
Nominal Mass: 457 Da
Average Mass: 457.5625 Da
Monoisotopic Mass: 457.257671 Da

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Systematic Name:

SMILES:

O=C(CNC(=O)OC(C)(C)C)N(Cc1ccc(C)o1)C(c2ccccc2)C(=O)NC(C)(C)C

InChI:

InChI=1/C25H35N3O5/c1-17-13-14-19(32-17)16-28(20(29)15-26-23(31)3-25(5,6)7)21(18-11-9-8-10-12-18)22(30)27-24(2,3)4/h8-14,21H,15-16H2,1-7H3,(H,26,31)(H,27,30)

InChIKey:

[WDAGUORBKBNETC-UHFFFAOYAD](#)

ORIGINAL REFERENCE(s)

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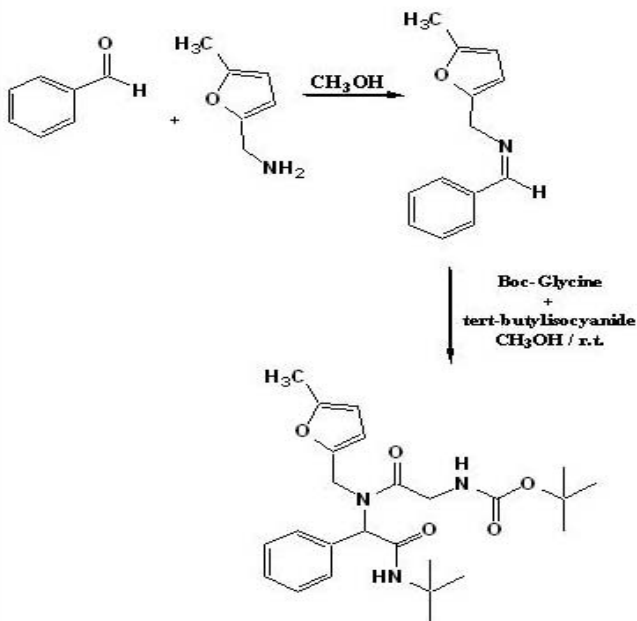
External ID(s)

[UsefulChem](#)

[UC0235](#)

UsefulChem Open Notebook Science

DESCRIPTION



Objective

To synthesize the Ugi product from benzaldehyde, 5-methylfurfurylamine, tert-butyl isocyanide and Boc-Gly-OH in methanol via a 4CR ugi reaction

Procedure

A solution of benzaldehyde (212 μL , 2 mmol) and 5-methylfurfurylamine(5-MFA) (244 μL , 2.2 mmol, 10% excess) was made in methanol in a 4mL volumetric flask. The reaction mixture was allowed to sit for about 6 hours without stirring to form the imine. A solution of Boc-Gly-OH(350 mg, 2 mmol), and tert-butyl isocyanide (226 μL , 2 mmol) was made up in 4 ml volumetric flask in methanol. This solution was added to the preformed imine solution. The reaction mixture was allowed to sit undisturbed overnight, when a crystalline Ugi product was obtained which was filtered and washed with cold methanol. The crystalline product was saved in a vial.
Write the procedure following standard format, including the full characterization of the product. See any experimental section from BJOOC



UsefulChem Open Notebook Science

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Write the procedure following standard format, including the full characterization of the product. See any experimental section from BJOC

Results

Benzaldehyde

H NMR

C NMR

DEPT

5-methylfurfurylamine

H NMR

C NMR

tert-butyl isocyanide

H NMR

C NMR

Boc-Gly-OH

H NMR

C NMR

86A

H NMR (t = 5 h 44 min) [no deuterated solvent, unlocked]

86B (C₂₅H₃₅N₃O₅, Mol. Wt.: 457.56)

H NMR -500 MHz

H NMR -300 MHz

C NMR

DEPT

All protonated carbons

Overlay of C NMR and All protonated carbons

FAB



UsefulChem Open Notebook Science

SPECTRA

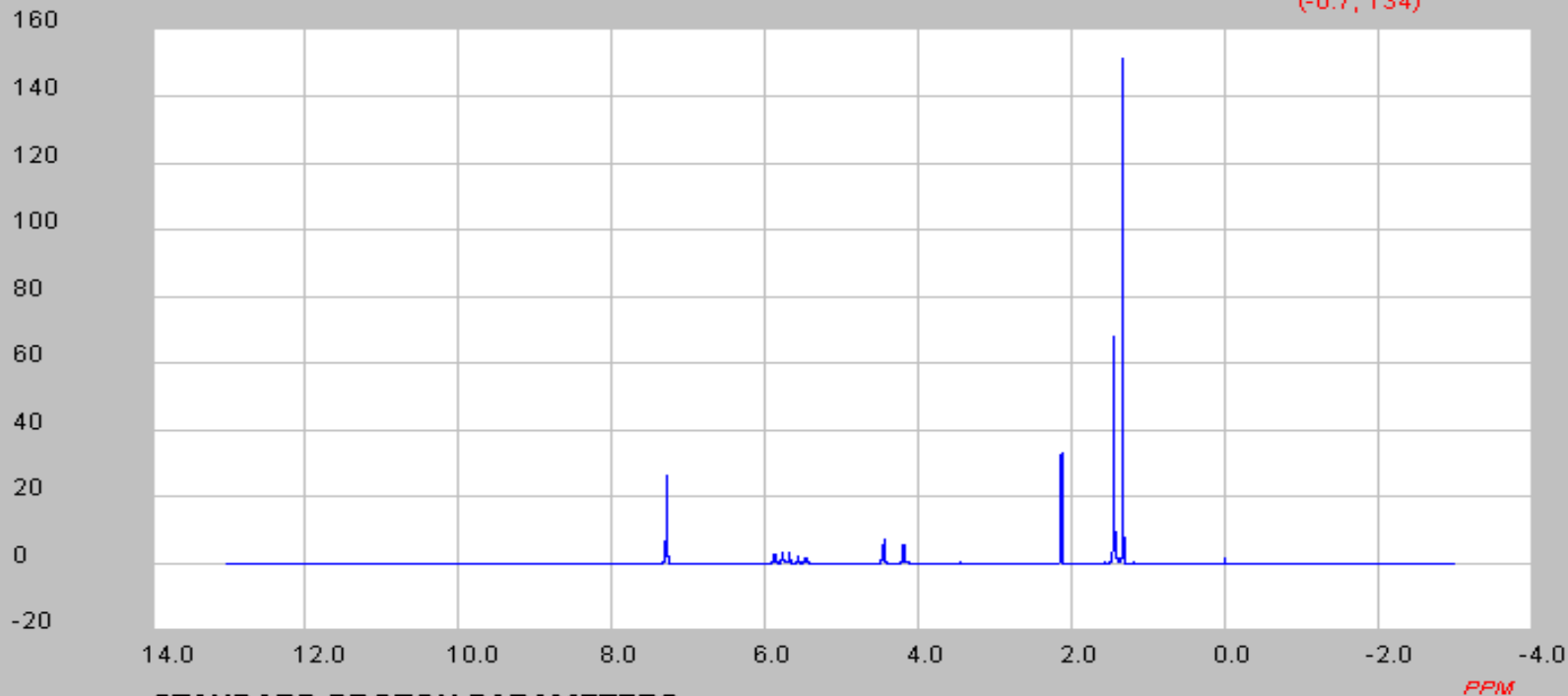
TYPE: HNMR

Associated Hyperlink: <http://usefulchem.wikispaces.com/Exp086>

Comments: taken by Khalid Mirza of Bradley Research Group at Drexel University

ARBITRARY UNITS

(-0.7, 134)



Conclusions

- Can a free access structure-centric community for chemists benefit drug discovery?
 - Already being used as such – publications are growing
 - ONS activities supported on ChemSpider – public drug discovery
 - “Ligand Screening” proof of concept done



Acknowledgements: Friends of ChemSpider

- Aniko Simon and Zsolt Zsoldos, SimBioSys
- Bob Boethling and Ann Richard, EPA
- Rocky Goldsmith, ChemSpider Advisory Group
- Rudy Potenzzone, Microsoft
- Jean-Claude Bradley, Drexel University
- Sean Ekins, Collaborations in Chemistry
- Barry Bunin, Collaborative Drug Discovery
- Stan Young, National Institute of Statistical Sciences
- Alex Tropsha, UNC – Chapel Hill