

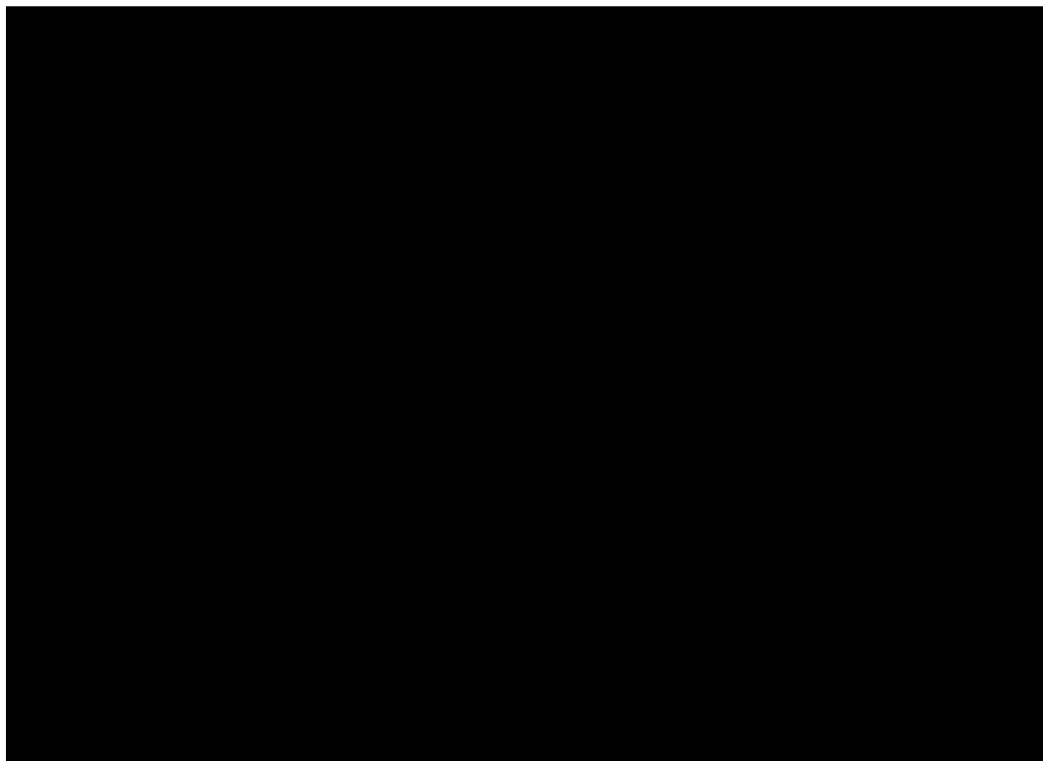
“What’s in Your Water?”



SciFinder®

Kristen Arienti
Applications Specialist
Fall 2011 ACS National Meeting

The 1960s – dawning of the age of artificial sweeteners?



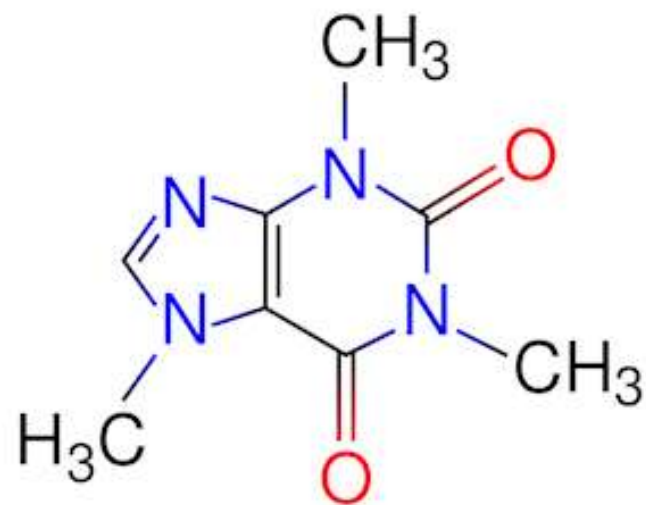
Packets of Assugrin, a brand of cyclamate



Americans crave that sweet taste, minus the calories



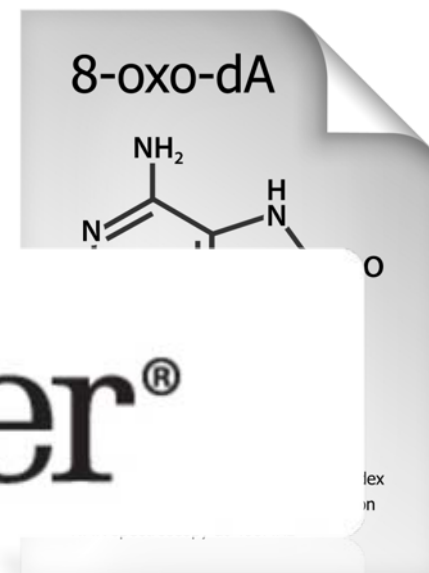
Many artificially sweetened drinks get an extra kick from caffeine



How can we investigate the chemistry behind artificial sweeteners? SciFinder® is the world's best chemistry research tool



SciFinder®



IRMS spectroscopy at 400MHz
of its purity was accomplished by proton
identification of the product and an index
accuracy and purified by HPLC
analysis of base-catalyzed
(8-oxo-dA) was also confirmed.

Let's start our search in CAS REGISTRYSM, the gold standard for chemical substance information ...

The screenshot displays the SciFinder web interface. At the top, there are navigation tabs for 'Explore References', 'Explore Substances', and 'Explore Reactions'. The main search area shows 'Research Topic "sucralose" with limiters > references (670) > get substances (9690)'. Below this, there are options to 'Get References', 'Get Reactions', and 'Tools'. A sidebar on the left lists 'Substances' with '9690 Substances' and '0 Selected'. The main content area shows three search results, each with a chemical structure and detailed information.

1. Substance Detail
1313233-99-6
No Structure Diagram Available
Unspecified
Polacrilix
~1 References
Reactions
Commercial Sources
Regulatory Information
Link

2. Substance Detail
1312996-49-8
(Component: 79350-37-1)

Absolute stereochemistry. Double bond geometry as shown.
C₁₆ H₁₅ N₅ O₇ S₂ · 2 H₂ O
5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[[(2Z)-2-(2-amino-4-thiazolyl)-2-[(carboxymethoxy)imino]acetyl]amino]-3-ethenyl-8-oxo-, hydrate (1:2), (6R,7R)-
~1 References
Reactions
Commercial Sources

3. Substance Detail
1312996-48-7
(Component: 79350-37-1)

Absolute stereochemistry. Double bond geometry as shown.
C₁₆ H₁₅ N₅ O₇ S₂ · H₂ O
5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[[(2Z)-2-(2-amino-4-thiazolyl)-2-[(carboxymethoxy)imino]acetyl]amino]-3-ethenyl-8-oxo-, hydrate (1:1), (6R,7R)-
~1 References
Reactions
Commercial Sources

Analysis | Refine
Analyze by: Substance Role
Click bar to view only those substances within the current answer set

Uses	9671
Biological Study	9669
Properties	9382
Preparation	8874
Process	7281
Reactant or Reagent	6786
Analytical Study	6755
Occurrence	3681
Formation, Nonpreparative	3070
Miscellaneous	2352

Show More

... and the source of more than 4 billion predicted and experimental properties, spectra and data tags

Molecular Weight	397.63		(7)	
pKa	12.52±0.70	Most Acidic Temp: 25 °C	(7)	
Vapor Pressure	8.79E-21 Torr	Temp: 25 °C	(7)	
Density Properties				
	Value	Condition	Note	Top
Density	1.69±0.1 g/cm3	Temp: 20 °C Press: 760 Torr	(7)	
Molar Volume	234.7±5.0 cm3/mol	Temp: 20 °C Press: 760 Torr	(7)	
Lipinski and Related Properties				
	Value	Condition	Note	Top
Freely Rotatable Bonds	10		(7)	
H Acceptors	8		(7)	
H Donors	5		(7)	
H Donor/Acceptor Sum	13		(7)	
logP	0.229±0.706	Temp: 25 °C	(7)	
Molecular Weight	397.63		(7)	
Spectra Properties				
	Value	Condition	Note	Top
Carbon-13 NMR Spectrum	See spectrum		(8)	
Proton NMR Spectrum	See spectrum		(8)	
Structure-related Properties				
	Value	Condition	Note	Top
Polar Surface Area	129 A2		(7)	
Thermal Properties				
	Value	Condition	Note	Top
Boiling Point	669.4±55.0 °C	Press: 760 Torr	(7)	
Enthalpy of Vaporization	112.59±6.0 kJ/mol	Press: 760 Torr	(7)	
Flash Point	358.7±31.5 °C		(7)	
(7) Calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02 (© 1994-2011 ACD/Labs)				
(8) Predicted NMR data calculated using Advanced Chemistry Development, Inc. (ACD/Labs) Software V11.01 (© 1994-2011 ACD/Labs)				
Experimental Properties: Chemical Spectra Thermal				
Chemical Properties				
	Value	Condition	Note	Top
Solubility	See full text		(6) CAS	
Spectra Properties				
	Value	Condition	Note	Top
Carbon-13 NMR Spectrum	See full text		(1) CAS	
Carbon-13 NMR Spectrum	See full text		(2) CAS	
Mass Spectrum	See full text		(3) CAS	
Mass Spectrum	See full text		(4) CAS	
Proton NMR Spectrum	See full text		(1) CAS	
Thermal Properties				
	Value	Condition	Note	Top
Melting Point	130 °C		(5) SRC	

From REGISTRY, you can search in many directions, such as for regulatory information

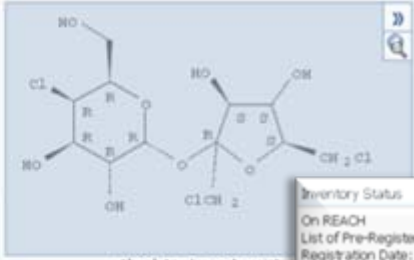
Substance Detail

Get References Get Reactions Get Commercial Sources **Get Regulatory Info** Send to SciPlanner

Link Save Print Export

Return

CAS Registry Number: 56038-13-2
 C₁₂ H₁₈ Cl₂ O₈
 α-D-Galactopyranoside, 1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl 4-chloro-4-deoxy-
 1',4,6'-Trichloro-galacto-sucrose; 4,1',6'-Trichloro-4,1',6'-trideoxygalactosucrose; Acucar Light; Aspartiv; San Sweet SA 8020; Sansweet SJ 100; Splenda; Sucralose; Sucrazit; TGS



Absolute stereochemistry

~2,442 References

Document Types: Conference, Journal, Patent

CAS Role	Patents	Nonpatents	Nonspecific Derivatives from Patents
Analytical Study	✓	✓	✓
Biological Study	✓	✓	✓
Formation, Nonpreparative	✓		
Miscellaneous		✓	
Occurrence		✓	
Preparation	✓	✓	✓
Process	✓	✓	✓
Properties	✓	✓	
Prophetic in Patents	✓		
Reactant or Reagent	✓	✓	✓
Uses	✓	✓	✓

Predicted Properties: Biological Chemical Density Lipinski and Related Spectra Structure Thermal

Biological Properties	Value	Condition
Bioconcentration Factor	1.0	pH 1 Temp: 25 °C
Bioconcentration Factor	1.0	pH 2 Temp: 25 °C
Bioconcentration Factor	1.0	pH 3 Temp: 25 °C

Inventory Status

On REACH
 List of Pre-Registered Substances, March 2009
 Registration Date: 30-NOV-2010.

On ENECS
 Annex to Official Journal of the European Communities, 15 June 1990

On AICS
 Commonwealth of Australia Gazette, No. C1 (03 Jan 2006)

On ASIA-PAC
 2006

On NZIoC
 New Zealand Inventory of Chemicals, 2006

Regulatory Inventories

==== U.S. FDA Regulations ====

==== European Community Regulations ====

==== U.S. FDA Regulations ====

FDA Priority-Based Assessment of Food Additives

Priority-Based Assessment of Food Additives (PAFA) File, FDA Center for Food Safety and Applied Nutrition (CFSAN) (1998)
 Listed Name(s): Sucralose

FDA Regulations

CFR Title 21 - Food and Drugs - URL: <http://www.fda.gov> (2004).
 CFR Title: 21 CFR Part Section: 172.831
 CFR Subpart: Multipurpose Additives
 Listed Name(s): Sucralose
 Use: May be safely used in foods as defined by 21CFR172.831.

==== European Community Regulations ====

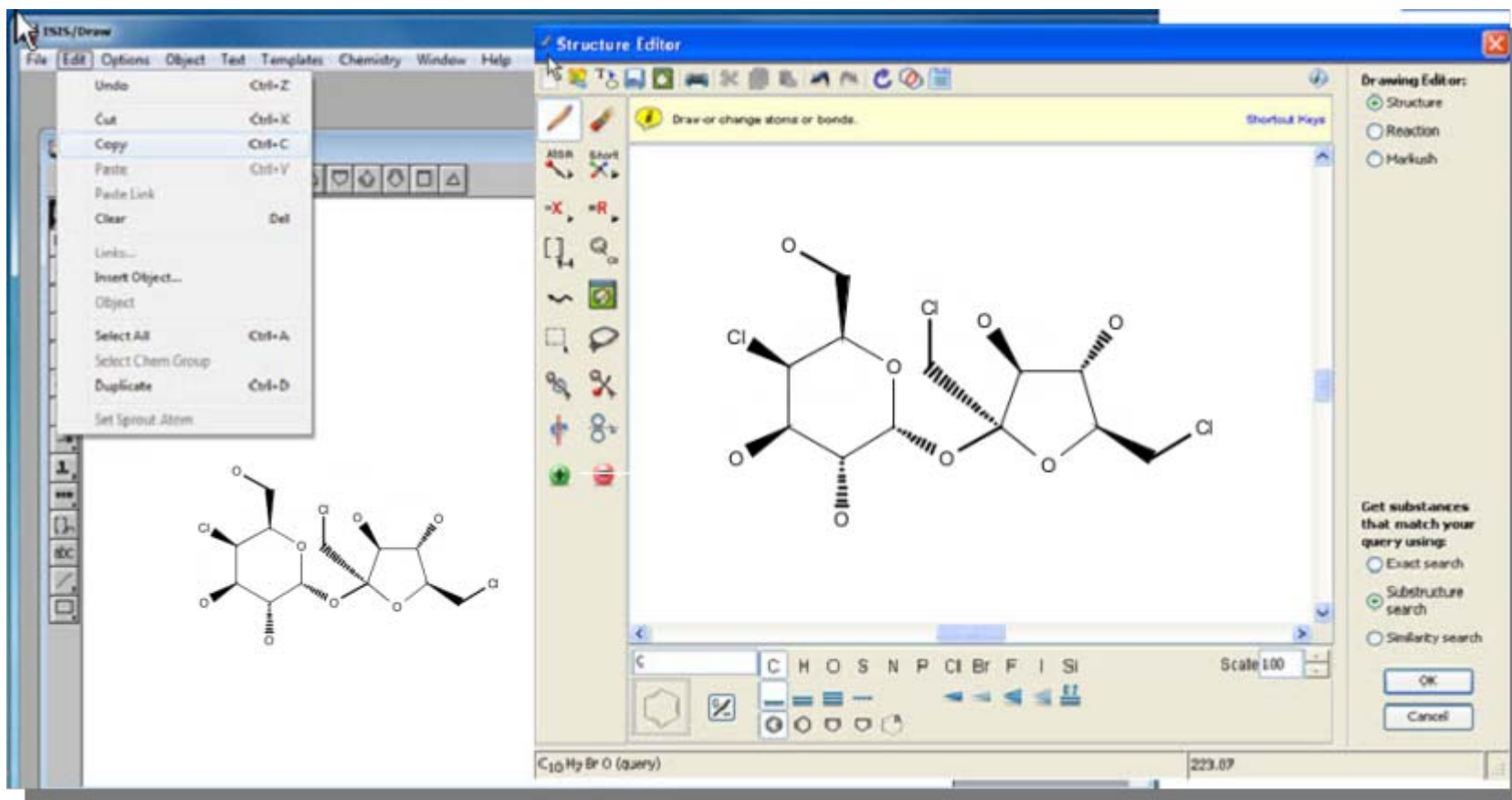
European Community Legislation

Official Journal of the European Union L114 #47:15.
 Commission Directive 2004/46/EC of 16 April 2004 amending Directive 95/31/EC as regards E955 sucralose and E962 salt of aspartame-acesulfame. Member States shall bring into force the laws, regulations and administrative provisions necessary to comply with this Directive by 1 April 2005.

What else can we learn about artificial sweeteners from SciFinder?



Conveniently search by pasting from ISIS/Draw



Precisely locate substance preparation information

Experimental Procedure

Step 1

(b) Preparation of 2,3,4,3',4'-Penta-O-acetylsucrose (4-PAS) A solution of TRISPA in Toluene obtained in example-1 was cooled to 0°C under N₂ atmosphere. Dry HCl(g) was bubbled slowly through reaction at the same temperature for 3 to 4 hr. The progress of the reaction was monitored on TLC. Sodium carbonate (32kg) in Water (67L) was added to the reaction mixture at 10°C to 25°C during 30min and stirred for 20 min. Both layers were separated. Aq. layer was washed with toluene (10L). The pH of aq. layer was adjusted to 7 to 7.5 with sodium bicarbonate (6.5kg) at 15°C and stirred for 20min. Dichloromethane (20L) was added and extracted. Organic layer was separated. Sodium chloride (18kg) was added to the aqueous layer, stirred for 10 min and then extracted with Dichloromethane (8L). Organic layer was separated. Both organic layers were combined and filtered through cartridge. The clear organic layer was evaporated to dryness. A mixture of ethylacetate: hexane (7:3) (2L) was added to the residue and again distilled out to give 4-PAS and it was taken further for migration step.

Step 2

(c) Preparation of 2,3,6,3',4'-Penta-O-acetylsucrose (6-PAS) A mixture of ethyl acetate: hexane (7:3) (30L) was added to 4-PAS obtained in the example-2. The reaction mixture was heated to 66°C to 67°C and dehydrated. The reaction mixture was cooled to 50°C and t-Butyl amine (0.5L) was added. The reaction mixture was stirred for 5hr at 50°C to 55°C. After completion of conversion to 6-PAS, the reaction mixture was cooled to 30°C and stirred at the same temperature for 2hr. The solid was filtered, washed with mixture of ethylacetate: Hexane. The product was dried at 55°C to 65°C till constant weight obtained (8.0 kg).

Step 3

(d) Preparation of 4,1',6'-trichloro-4,1',6'-trideoxygalactosucrose pentaacetate (TOSPA) To slurry of 6-PAS (7.0 kg) and triphenyl phosphine oxide (TPPO) in toluene (21.0L) was added thionyl chloride (32.8 ml) and the mixture was heated at 110°C within 2.5 hr and maintained for 2.5 hr. The reaction was monitored on TLC. After completion of reaction, the mixture was cooled to 70°C. Aq. Sodium acetate solution was added to the reaction mixture at 10-15°C within 20-30min and stirred for 20-30min. Sodium bicarbonate (3.5kg) was added to it within 20min and stirred for 30min. The product was filtered and washed with cold water (2.0L). The filtrate is settled and both aqueous and organic layers were separated. The organic layer (i.e. toluene layer) is taken for TPPO recovery. The wet cake is charged to toluene (21.0L) and water (21.0L) and heated to 70-75°C and stirred for 10-15min. The toluene layer is separated and washed with hot water. The toluene layer is dehydrated to remove traces of water and filtered through line filter at 70-75°C. It is cooled to 10°C. The compound is filtered and washed with chilled toluene, suck dried and dried in oven (5.5 kg).

Step 4

(e) Preparation of Sucralose TOSPA (100 g) is stirred at 20°C with sodium methoxide (30%) (3ml) in methanol (250 ml) for 2 hours at 20°C±2°C. TOSPA dissolves within 10 mins. The completion of reaction is monitored on TLC. The solution is neutralized by stirring with (H⁺) resin (10g). The resin is removed by filtration and washed with methanol (25 ml), the filtrate and wash then being stirred with decolorizing charcoal (4 g) for 30 mins at 20°C. The solution is filtered through hyflow bed followed by membrane filter to remove any carbon particles. Total filtrate was distilled to remove methanol. Trace amount of methanol was removed by vacuum distillation. To the oily product, methyl acetate was added and distilled out methylacetate and methanol azeotropically. The reaction mixture was cooled to 10°C over one hour. The precipitate was filtered, washed with methyl acetate and suck dried. The solid was dried in vacuo at 40°C for 12 hours to give solid (50 g).

Link directly to patents and references of interest

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Oxazolidindione substituted indole derivatives

Page 1/12 Abstract Bibliography Maximise Download

US005334606A
United States Patent [19] [11] **Patent Number: 5,334,606**
MacLeod [45] **Date of Patent: Aug. 2, 1994**

[54] **OXAZOLIDINDIONE SUBSTITUTED INDOLE DERIVATIVES**
 [75] Inventor: **Angus M. MacLeod**, Bishops Stortford, England
 [73] Assignee: **Merck Sharpe & Dohme Ltd.**, Hoddesdon, England
 [21] Appl. No.: **982,794**
 [22] Filed: **Nov. 30, 1992**
 [30] **Foreign Application Priority Data**

by M. Rour, entitled Thiohydantoins and Their Derivatives and Use of Some of Them in the Estimation of Silver, Mercury and Copper. *Angem. Chem.*, vol. 95, 11, pp. 892-893 (1983).
J. Med. Chem. vol. 33, pp. 1418-1423, by A. Zask, et al., entitled Synthesis & Antihyperglycemic Activity of Novel 5-Naphthalenylsulfonyl-2,4-thiazolidinediones (1990).
J. Gootjes, et al., Arzneimittel Forschung Drug Research, vol. 9, pp. 1145-1149 (1967).

Quickly identify historically influential articles and authors

Research Topic "artificial sweeteners in waste..." > references (23)

References

23 References 4 Selected Save Print Export

Select All Deselect All Sort by: Citing References (New) Answers per Page [20] 1 2

Display:

1. Ubiquitous Occurrence of the Artificial Sweetener Acesulfame in the Aquatic Environment: An Ideal Chemical Marker of Domestic Wastewater in Groundwater
 By Buerge, Ignaz J.; Buser, Hans-Rudolf; Kahle, Marek; Müller, Markus D.; Poiger, Thomas
 From Environmental Science & Technology (2009), 43(12), 4301-4305. Language: English, Database: CAPLUS
 Artificial low-calorie sweeteners are consumed in considerable quantities with food and beverages. After ingestion, some sweeteners pass through the human metab. largely unaffected, are quant. excreted via urine and feces, and thus reach the environment assoc. with domestic wastewater. We document the widespread occurrence of 4 sweeteners in the aquatic environment and show that one of these compds., acesulfame, meets all of the criteria of an ideal marker for the detection of domestic wastewater in natural waters, particularly groundwater. Acesulfame was consistently detected in untreated and treated wastewater (12-46 µg/L), in most surface waters, in 65% of the studied groundwater samples, and even in several tap water samples (≤2.6 µg/L) from Switzerland. The sweetener was not eliminated in wastewater treatment plants (WWTPs) and was quite persistent in surface waters, where concns. increased with population in the catchment area and decreased with water throughflow. The highest concns. in groundwater, ≤4.7 µg/L, were obsd. in areas with significant infiltration of river water, where the infiltrating water received considerable discharges from WWTPs. Given the currently achieved detection limit of ~0.01 µg/L, it is possible to trace the presence of ≥0.05% wastewater in groundwater.
 ~19 Citings

2. Analysis and occurrence of seven artificial sweeteners in German waste water and surface water and in soil aquifer treatment (SAT)
 By Scheurer, Marco; Brauch, Heinz-J.; Lange, Frank T.
 From Analytical and Bioanalytical Chemistry (2009), 394(6), 1585-1594. Language: English, Database: CAPLUS
 A method for the simultaneous detn. of 7 commonly used artificial sweeteners in water is presented. The analytes were extd. by solid phase extr. using Bakerbond SDB 1 cartridges at pH 3 and analyzed by liq. chromatog. electrospray ionization tandem mass spectrometry in neg. ionization mode. Ionization was enhanced by post-column addn. of the alk. modifier Tris(hydroxymethyl)amino methane. Except for aspartame and neohesperidin dihydrochalcone, recoveries were >75% in potable water with comparable results for surface water. Matrix effects due to reduced extr. yields in undiluted waste water were negligible for aspartame and neotame but considerable for the other compds. The widespread distribution of acesulfame, saccharin, cyclamate, and sucralose in the aquatic environment could be proven. Concns. in 2 influents of German sewage treatment plants (STPs) were ≤190 µg/L for cyclamate, ~40 µg/L for acesulfame and saccharin, and <1 µg/L for sucralose. Removal in the STPs was limited for acesulfame and sucralose and >94% for saccharin and cyclamate. The persistence of some artificial sweeteners during soil aquifer treatment was demonstrated and confirmed their environmental relevance. The use of sucralose and acesulfame as tracers for anthropogenic contamination is conceivable. In German surface waters, acesulfame was the predominant artificial sweetener with concns. exceeding 2 µg/L. Other sweeteners were detected up to several hundred ng/L in the order saccharin > cyclamate > sucralose.
 ~15 Citings

3. Occurrence of the artificial sweetener sucralose in coastal and marine waters of the United States
 By Mead, Ralph N.; Morgan, Jeremy B.; Avery, G. Brooks; Kieber, Robert J.; Kirk, Alessandra M.; Skrabal, Stephan A.; Wiley, Joan D.
 From Marine Chemistry (2009), 116(1-4), 13-17. Language: English, Database: CAPLUS
 The first concn. data for the artificial sweetener sucralose (Splenda) is presented for North American coastal and open ocean waters. Large vol. water samples were collected and pre-concd. using solid phase extr. followed by GC/MS anal. The concn. of sucralose varied over several orders of magnitude in these environmental samples with the greatest abundance in a waste water treatment plant effluent (300 nM). The concn. decreased in receiving waters of the Cape Fear River Estuary, NC (CFRE) where surface water concns. at the mouth of the estuary were 0.94 nM. Sucralose was also detected in the oligotrophic waters of the Gulf Stream (33 28.6 N -76 48.2 W) where it ranged in concn. from below detection limit to 0.17 nM. In the Northern and Middle Florida Keys values were similar to the CFRE with concns. of 0.37 nM and 0.99 nM, resp. The data presented here suggest the persistence and widespread distribution of sucralose in natural aquatic matrices with subsequent incorporation into a major oceanog. current, the Gulf Stream, where global distribution may take place.
 ~10 Citings

4. Biodegradation of sucralose, a chlorinated carbohydrate, in samples of natural environments

Analysis

Analyze by:

Database

Click bar to view only those references within the current answer set

CAPLUS	16
MEDLINE	7

Categorize

More detailed analysis based on CAS indexing

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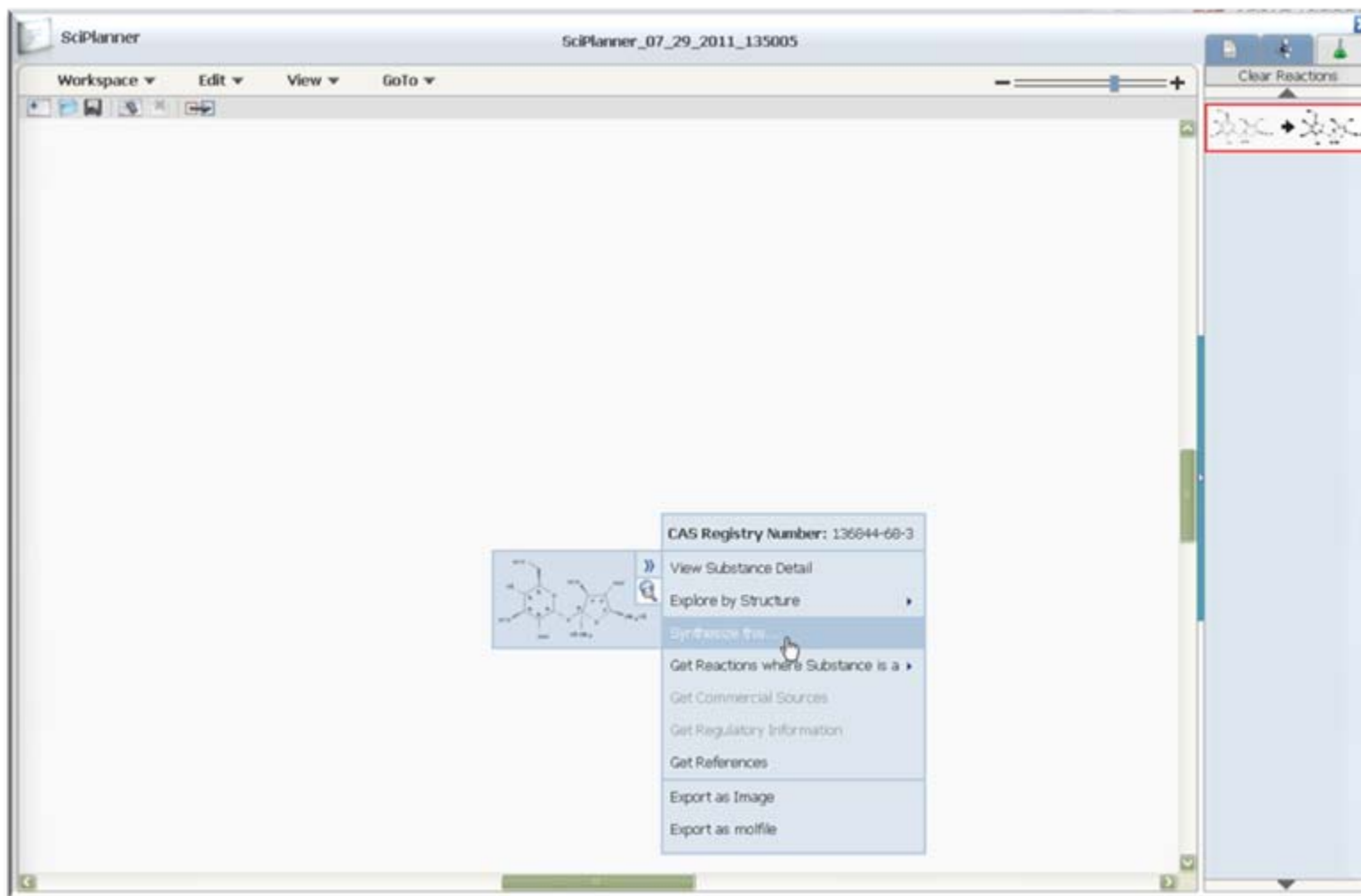
The screenshot displays the SciPlanner software interface. The main workspace contains a reaction scheme with three steps, labeled 1, 2, and 3, showing the conversion of a complex starting material into a final product. The starting material is a complex molecule with multiple hydroxyl groups and a glycosidic linkage. Step 1 involves a reaction with a reagent (H₂O) and a catalyst (H⁺). Step 2 involves a reaction with a reagent (H₂O) and a catalyst (H⁺). Step 3 involves a reaction with a reagent (H₂O) and a catalyst (H⁺).

Four literature references are listed in the workspace:

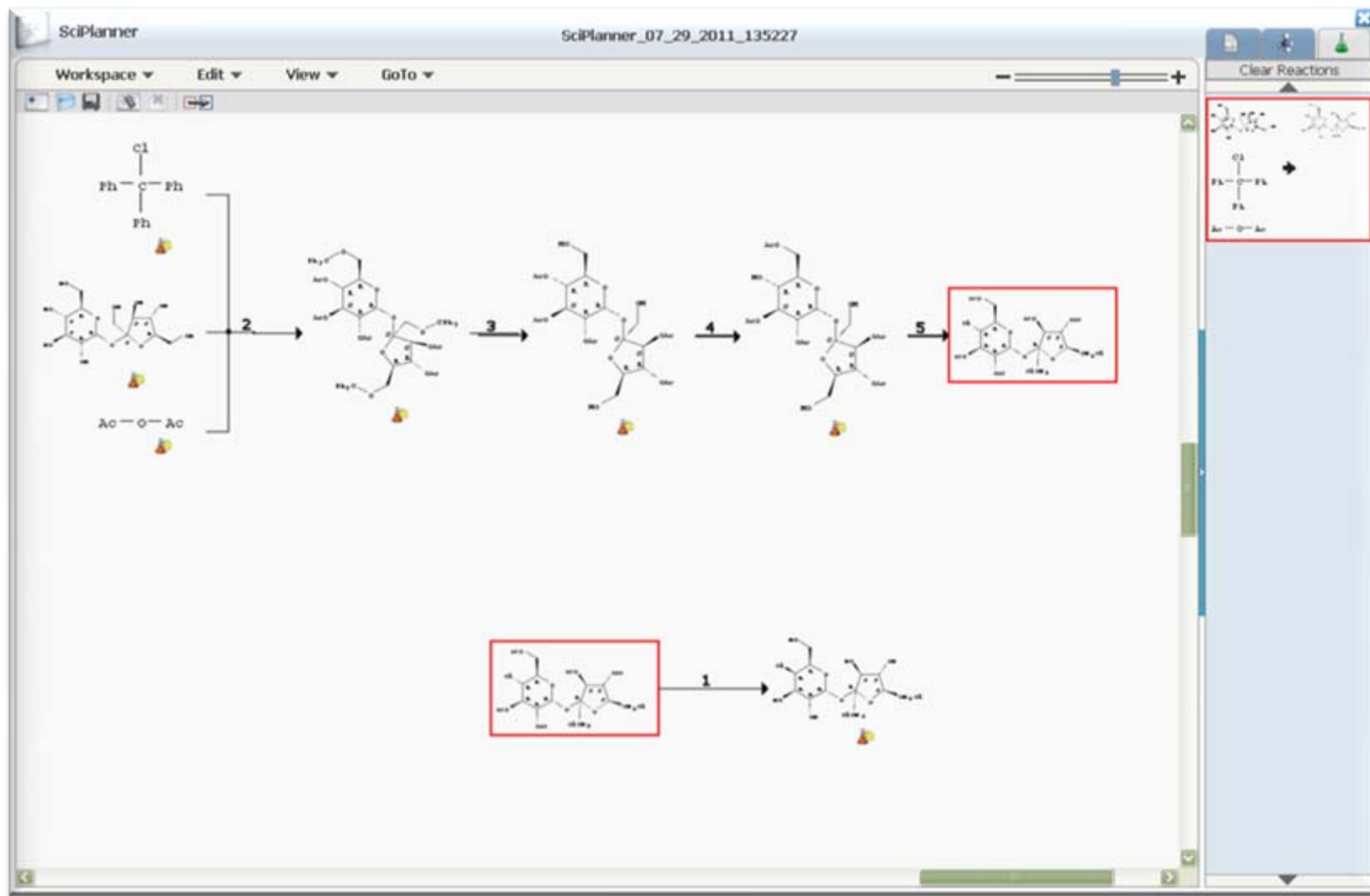
- Biodegradation of sucralose, a chlorinated carbohydrate, in samples of natural environments
By Labare, Michael P. and Alexander, Martin
From *Environmental Toxicology and Chemistry*, 12, 0730-7268, 797-804, 1993
- Artificial sweeteners as potential tracers in groundwater in urban environments
By Van Steepvoort, Dale R. et al
From *Journal of Hydrology (Amsterdam, Netherlands)*, 401, 0022-1694, 126-133, 2011
- Environmental Mass Spectrometry: Emerging Contaminants and Current Issues
By Richardson, Susan D.
From *Analytical Chemistry (Washington, DC, United States)*, 82, 0003-2700, 4742-4774, 2010
- Fate of sucralose during wastewater treatment
By Torres, Cesar I. et al
From *Environmental Engineering Science*, 28, 1057-9018, 325-332, 2011

The right sidebar contains a 'Clear Reactors' button and a diagram showing a reaction scheme with a plus sign and a minus sign, indicating the ability to add or remove reactants.

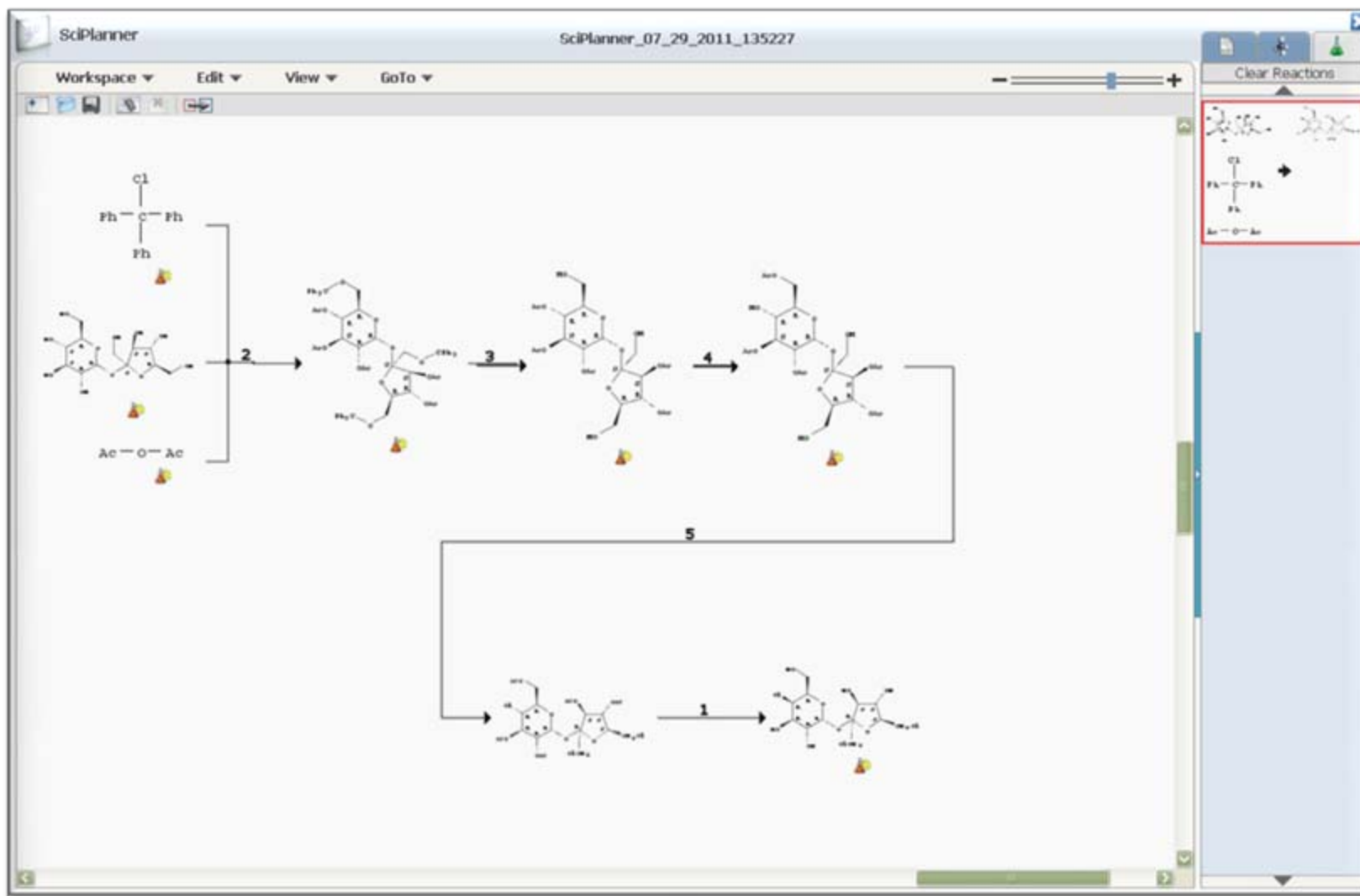
SciPlanner adds new efficiency and value to a researcher's synthetic planning



Merge multiple reactions into one synthetic pathway



Merge multiple reactions into one synthetic pathway



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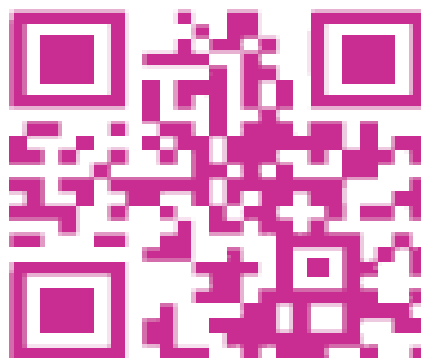
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