Project Prospect
（プロジェクト・プロスペクト）

理化学出版に意味論を導入する

リチャード・キッド

RSC | Advancing the Chemical Sciences

プロジェクト・プロスペクトの狙い

- 著者の科学的活動を保存する
- 科学をXMLとして捕捉する
- 意味を見出すために、オントロジーを応用する
- 出版プロセスに組み込む
- 読者に新しい視点を提供する
- 機械可読な化学

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意味のある検索

なぜ化学では難しいのか

- 検索
  - 無料テキストまたは所有されたテキスト
- 関連文献
  - 基準の欠如

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Introduction

The generation of bespoke pseudopeptide sequences that exhibit highly ordered secondary and tertiary structures in both solution and solid phase has developed into a highly competitive field of research in recent years, with the ability to predict the conformation of a given peptide sequence from knowledge of its primary structure an elusive goal. While much effort has been directed towards understanding the factors that control the secondary structure of α-peptides, the utility of peptides incorporating the β-amino acid structural motif has recently been investigated widely, most notably by Seebach[1] and Gellman.[2] For instance, Gellman *et al.* have shown that β-peptides derived from *trans*-2-aminocyclopentanecarboxylic acid (transpentacin) **1** adopt a helical stucture in both the solid state and in solution,[3] while Fülop *et al.* have shown that homo-oligomers of *cis*-2-aminocyclopentanecarboxylic acid (cispentacin) **2** form a sheetlike secondary structure in solution (Fig. 1).[4] The ability of mixed α,β-peptides containing both α-amino and β-amino acid derivatives to adopt a preferred conformation in solution has also been reported recently.[5]

We have shown extensively that the conjugate addition of lithiumamides derived from α-methylbenzylamine to α,β-unsaturated acceptors may be used for the asymmetric synthesis of β-amino acid derivatives.[6] This methodology has recently been utilised for the synthesis of (1*R*,2*S*,3*R*)-3-methylcispentacin **5** in >98% de and 98 ± 1% ee and (1*S*,2*S*,3*R*)-3-methyltranspentacin **7** in >98% de and 97 ± 1% ee by the kinetic resolution of *tert*-butyl (*RS*)-3-methylcyclopentene-1-carboxylate **3** with lithium (*S*)-*N*-benzyl-*N*-α-methylbenzylamide (Scheme 1).[7]

The protocol that we use to understand fully the stereoselectivity observed in these kinetic resolution reactions

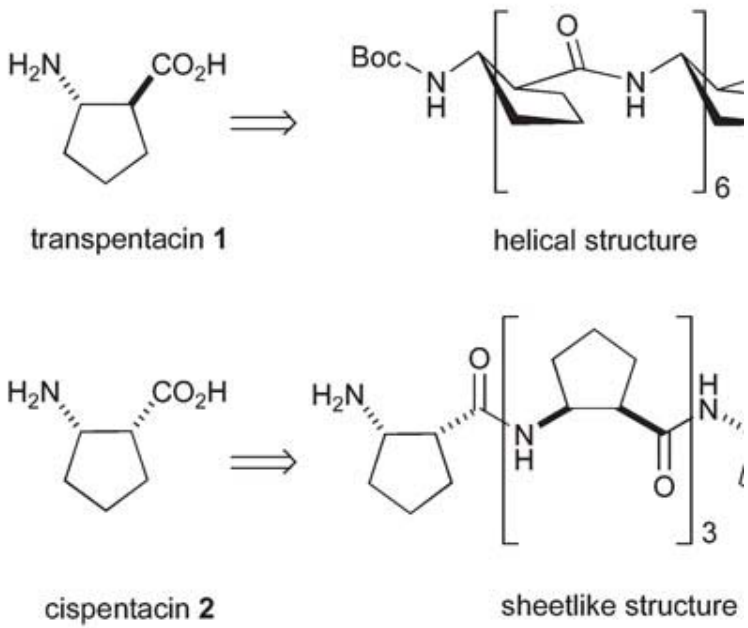

Fig. 1 Secondary structure of poly homo-pe

requires an initial evaluation of the level of offered by the chiral α,β-unsaturated ester un jugate addition, which is achieved through the a achiral lithium amide to the ester. If the α,β-uns shows high facial selectivity upon conjugate add of enantiorecognition between the chiral α,β-uns and a chiral lithium amide is evaluated throug kinetic resolution [addition of (*RS*)-ester to ar (*RS*)-lithium amide]. In this approach,[8] the ef action are eliminated, allowing the maximum st factor (*E*) for the reaction to be calculated inde reaction conversion, as it is identical to the diast observed in the reaction.[9] If high enantiorecog between the reacting partners in a mutual kine then efficient kinetic resolution may be expec

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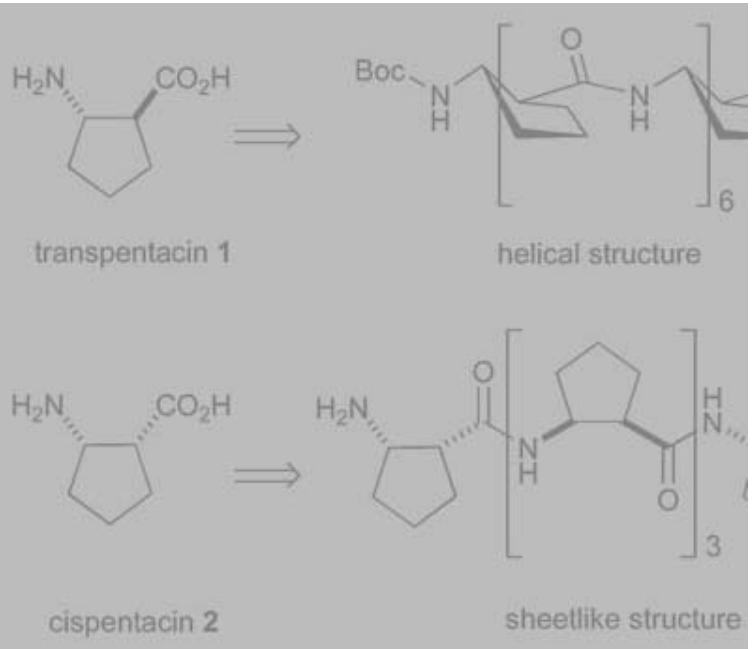

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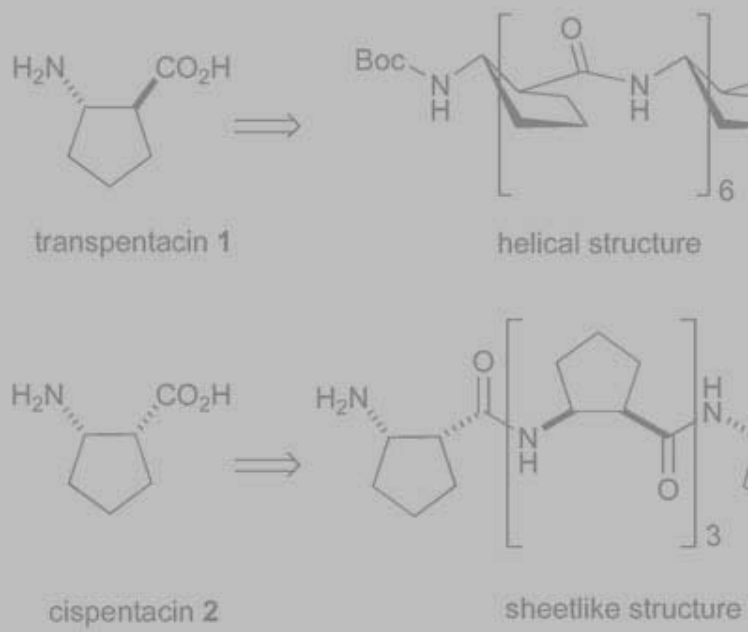

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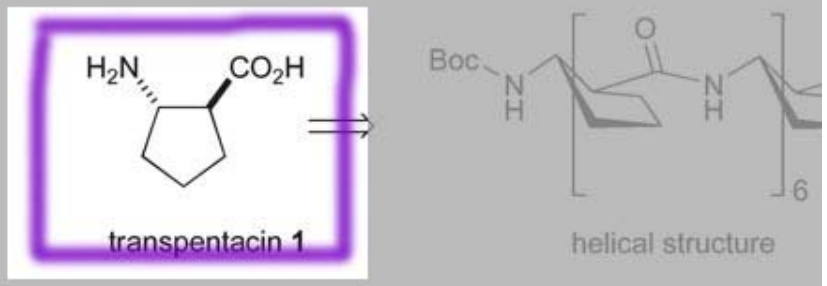

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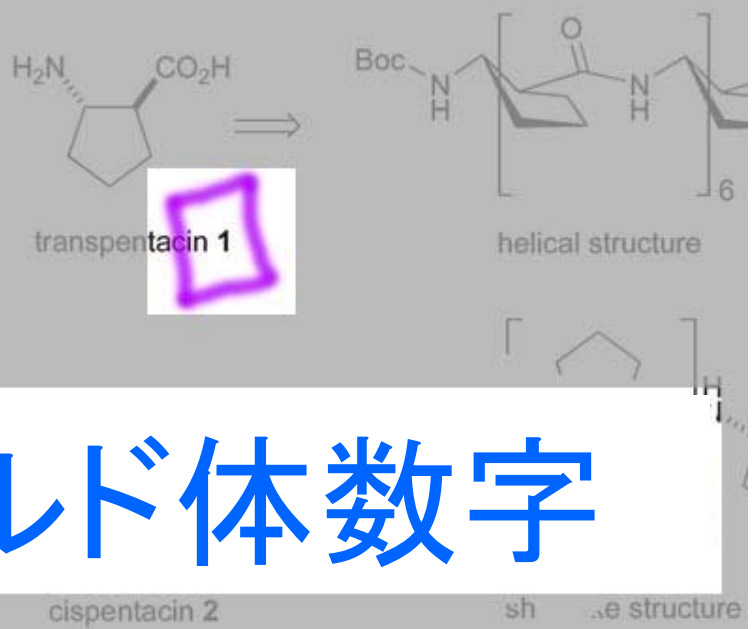

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プロスペクト･モデル

- 既存の出版物を強化する
- 既存のワークフローに直接組み込む
- 個々の製品を導入する際の問題を軽減する product

- 低分子ライブラリをマークした…
  …lysyl oxidase in zebrafish notochord morphogenesis

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方法

- 共同事業
  - ユニリーバセンター／コンピューターラボ
  - その他
- テクノロジー
  - OSCAR テキストマイニング
  - 基準
  - ワークフロー
  - RSS フィード

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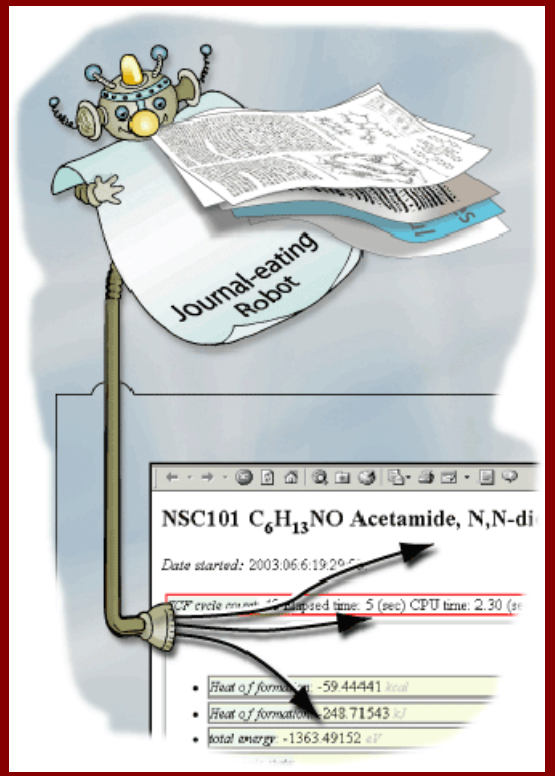
OSCAR テキストマイニング

OSCAR: Open Source Chemical Analysis Routines

- ケンブリッジ大学:
  化学(ユニリーバ・センター)
  –コンピューターラボとの共同作業
- SciBorg
- 化学の単語や短い句の構造を
  分析して構造を決定する
- テキストに構造を付与する
- 各種テーマにも応用



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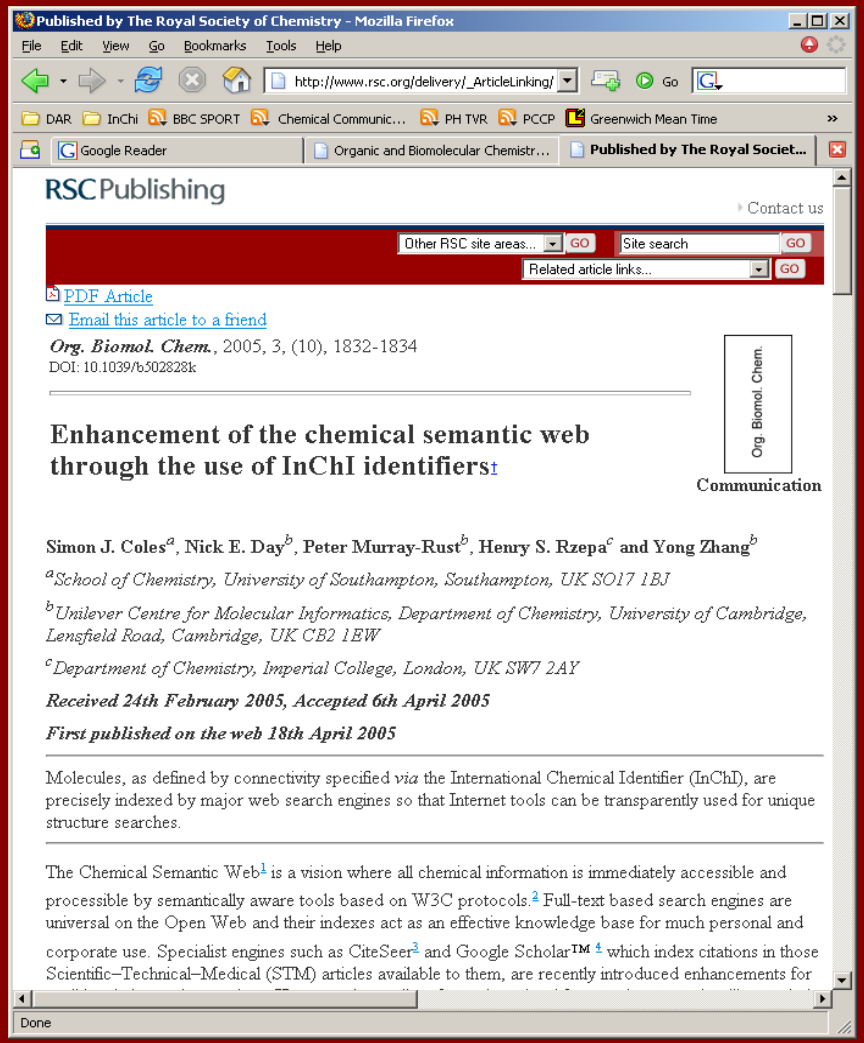
InChI

- IUPAC International Chemical Identifier
- InChI=1/C8H10N4O2/c1-10-4-9-6-5(10)7(13)12(3)8(14)11(6)2/h4H,1-3H3
- 機械可読
- InChIkey RYYVLZVUVIJVGH-UHFFFAOYAW



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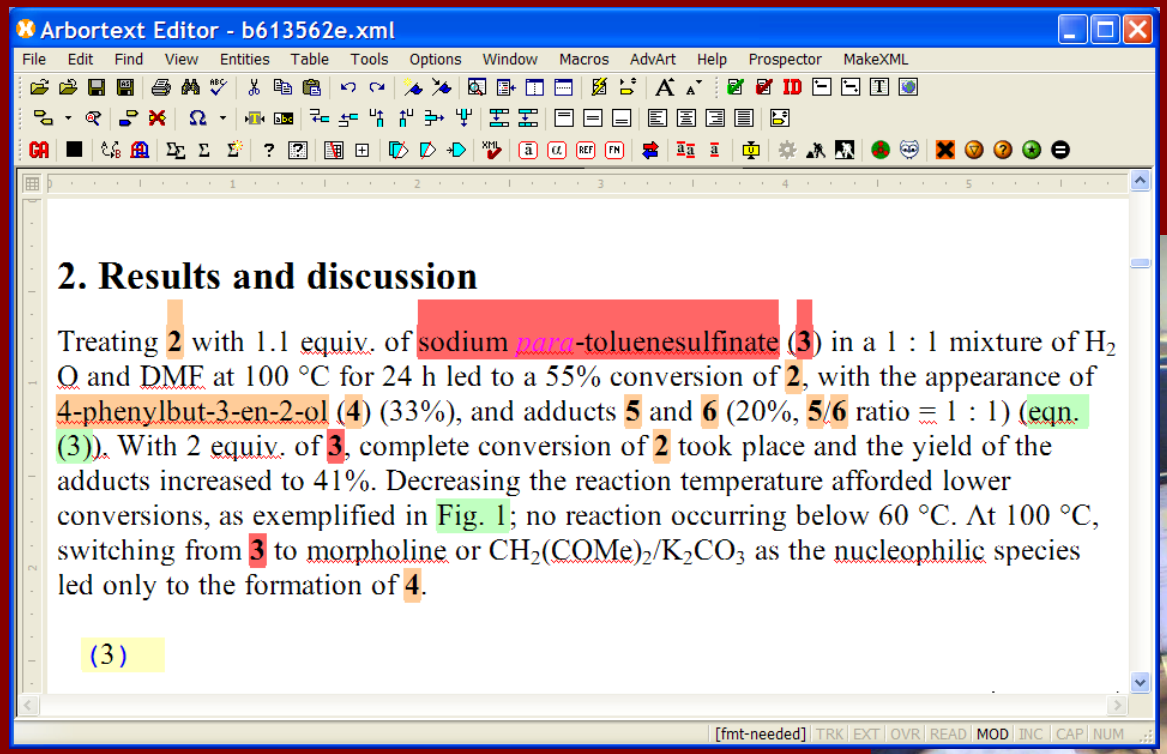
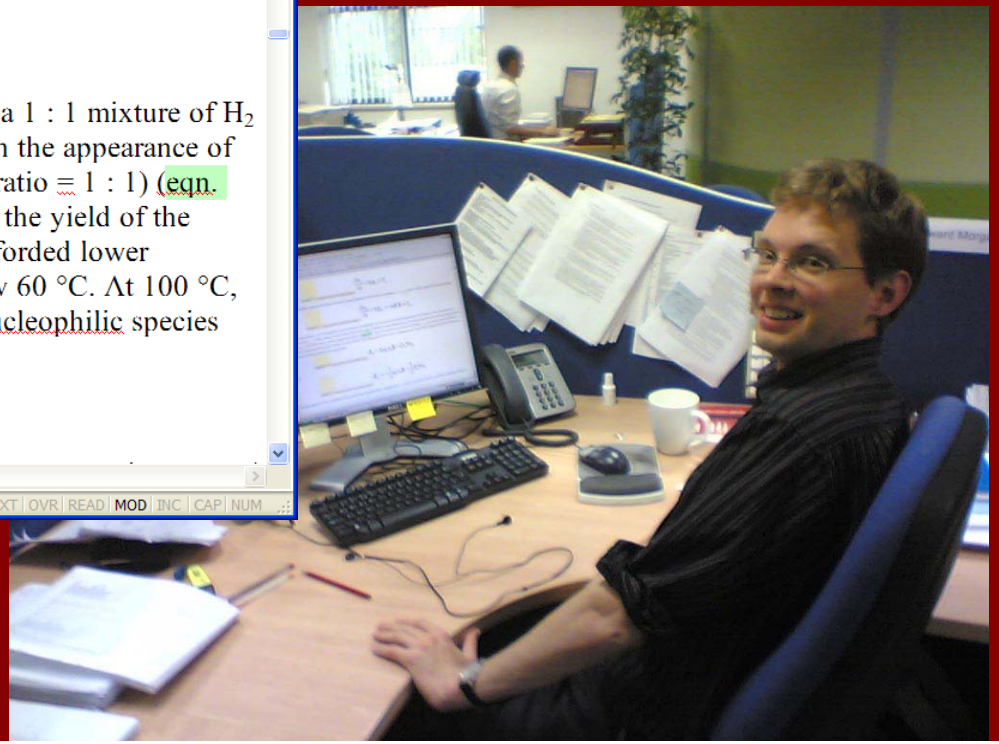
領域別の用語

- Open Biomedical Ontologies (OBO)
  - ジーンオントロジー (GO)
  - シークエンスオントロジー (SO)
  - セルオントロジー (CL)
- IUPAC ゴールド・ブック
  - 化学用語の辞書

RSC 出版プロセス

- 編集
- マイニング
- 更新と整理





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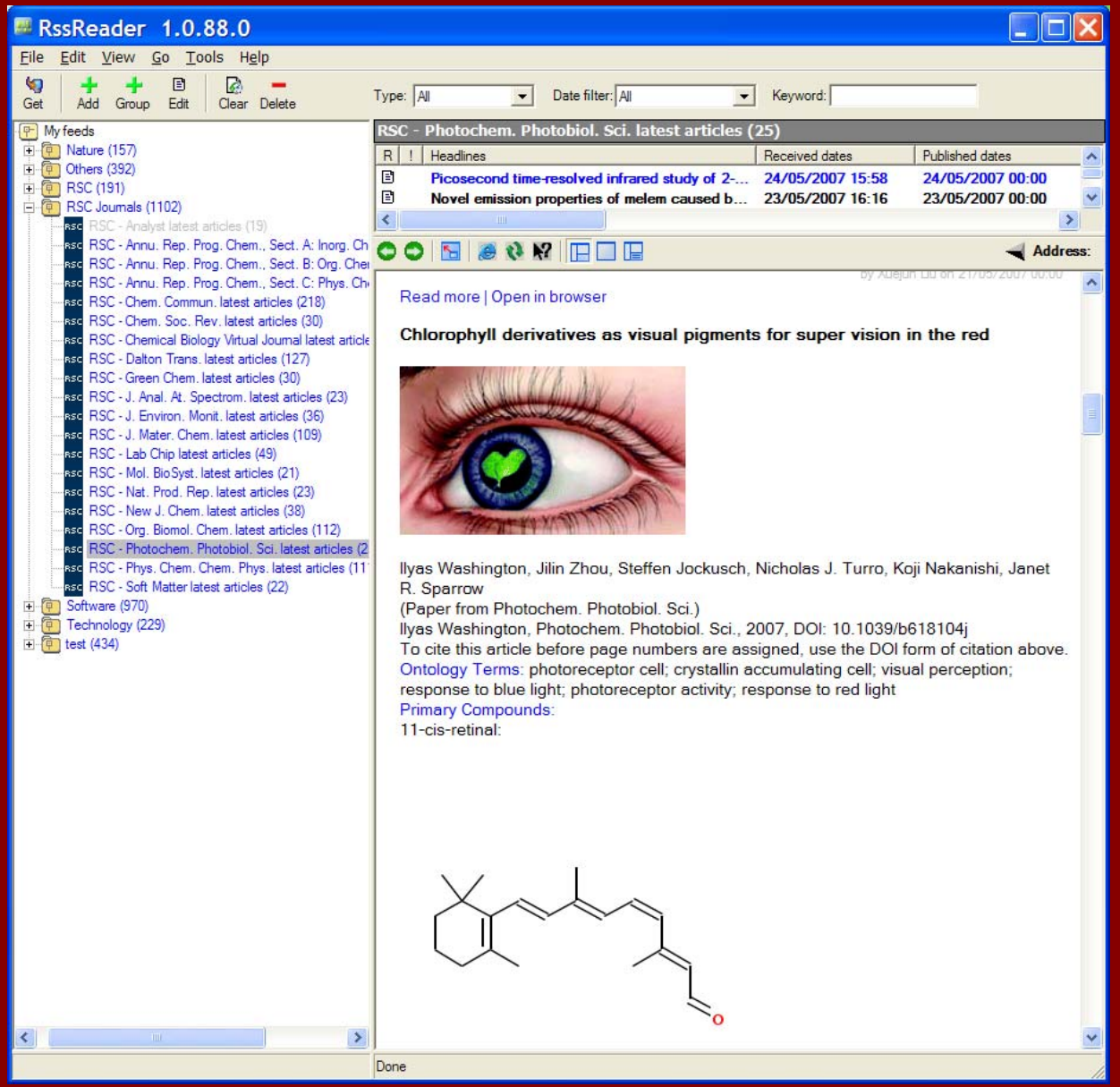
強化された RSS フィード



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問題点

- 意義のある、マニュアルの質疑応答の必要性
  - 古いデータはさらに困難
- 多くの分野におけるオントロジー開発の必要性
- 成果を最大化するための、広範囲での導入と相互リンクの必要性

データの新しい基準

- 実験的なデータ･チェッカー
  - 妥当性検証
  - 可視化
- 学会出版者のための役割

2-Methyl-2-hydroxymethyl-2,5-dihydrofuran **9** (50 mg, 0.51 mmol) was oxidised using OsO_4, TMEDA to yield the crude products [6 : 1 (*syn* : *anti*) by ^{1}H NMR]. The resulting oil was purified by flash chromatography (petrol-EtOAc, 4 : 1) to afford the pure title compound as a colourless oil (116 mg, 83%); ν_{max} (film)/cm^{-1} 2977, 2929, 1746, 1374, 1230, 1046; δ_H (300 MHz; $CDCl_3$) 5.43 (1H, q, *J* 5), 5.17 (1H, d, *J* 5), 4.26-4.09 (3H, m), 3.89 (1H, dd, *J* 10 and 5), 2.10 (6H, s), 2.08 (3H, s), 1.36 (3H, s); δ_C (75 MHz; $CDCl_3$) 170.6, 169.8, 169.5, 80.8, 76.2, 71.2, 68.9, 65.3, 22.3, 20.6, 20.4, 18.3; Found (CI) 292.1392, $C_{12}H_{22}NO_7 + NH_4$ requires 292.1396.

***anti*-2-Methyl-2-(acetoxymethyl)tetrahydrofuran *anti*-15**

2-Methyl-2-hydroxymethyl-2,5-dihydrofuran **9** (50 mg, 0.51 mmol) was oxidised using UpJohn conditions to yield the crude products [2 : 1 (*anti* : *syn*) by ^{1}H NMR]. The resulting oil was purified by flash chromatography (petrol-EtOAc, 4 : 1) to afford the product mixture as a colourless oil (110 mg, 79%) as an inseparable mixture of isomers (*anti* major compound); ν_{max} (film)/cm^{-1} 2989, 2944, 1746, 1379, 1232, 1046; δ_H (300 MHz; $CDCl_3$) 5.46-5.39 (1H, m), 5.26 (1H, d, *J* 6), 4.26-3.85 (4H, m), 2.11 (3H, s), 2.10 (6H, s), 1.26 (3H, s); δ_C (75 MHz; $CDCl_3$) 170.4, 169.8, 169.6, 81.2, 72.7, 71.9, 69.3, 67.9, 20.7, 20.5, 20.4, 18.3; Found (CI) 292.1400, $C_{12}H_{22}NO_7$ requires 292.1396,

***syn*-1,2,4-Triacetoxycyclohexane *syn*-16**

Cyclohex-3-en-1-ol **11** (50 mg, 0.51 mmol) was oxidised using OsO_4, TMEDA to yield the crude mixture of products [3 : 1 (*syn* : *anti*) by ^{1}H NMR]. The resulting oil was purified by flash chromatography (EtOAc) to afford a colourless oil (121 mg, 92%) as an inseparable mixture of isomers; mixture: ν_{max} (film)/cm^{-1} 2953, 1745, 1370, 1235, 1028; *syn*-**16** δ_H (300 MHz; $CDCl_3$) 5.17-5.11 (1H, m), 4.84-4.72 (2H, m), 2.04 (3H, s), 1.98 (3H, s), 1.86 (3H, s), 2.05-1.45 (6H, m); δ_C (75 MHz; $CDCl_3$) 170.1, 170.0, 169.9, 69.5, 69.3, 67.9, 31.4, 25.3, 24.7, 21.1, 20.9, 20.8; *anti*-**16**; δ_H (300 MHz; $CDCl_3$) 5.08-5.01 (1H, m), 4.81-4.67 (2H, m), 1.99 (9H, s), 2.05-1.45 (6H, m); δ_C (75 MHz; $CDCl_3$) 170.3, 170.2, 170.1, 69.7, 68.8, 68.6, 31.8, 25.9, 25.3, 23.6, 21.1, 20.9; mixture Found (CI) 276.1437, $C_{12}H_{22}NO_6$ requires 276.1447.

***anti*-1,2,4-Triacetoxycyclohexane *anti*-16**

Cyclohex-3-en-1-ol **11** (50 mg, 0.51 mmol) was oxidised using UpJohn conditions to yield the crude mixture of products [1 : 1 (*syn* : *anti*) by ^{1}H NMR]. The resulting oil was purified by flash chromatography (EtOAc) to afford the product mixture as a colourless oil (115 mg, 88%) as an inseparable mixture of isomers; All data are consistent with *syn*- and *anti*-**16** prepared previously.

***syn*-1,2,4,5-Tetraacetoxycyclohexane *syn*-17**

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“使い始めてすぐにわかったのは（プロジェクト・プロスペクトの）賢さだ。化合物を見ることができたり、機械可読のSMILESやInChIsがあることが素晴らしい"

“この新しいシステムには非常に感銘を受けた。多人数のコミュニティにとって非常に便利となることは確かだ”

“これは素晴らしく、またエキサイティングだ!!数分試しただけで、大きな可能性に気付いて、すぐに学生にも紹介したよ！“

“これはこのコミュニティにとって素晴らしい資源であり、またGOやSOを有効活用している。すばらしい出来だ。"

”非常に直観的かつ使い方が簡単である。論文が読者によってより魅力的なものとなるはずだ。"

“It is fantastic. I’ve just seen the future of the journal”

Ed Pentz

Executive Director, CrossRef

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何が違うのか

- テクノロジー
  - セマンティック・エンリッチメント
    - 化合物
    - オントロジー用語
  - RSSフィードの強化
- 既存のポートフォリオへの実装
  - ワークフローへ組み込み
  - 構造化された科学の可能性を示す

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RSCにおけるプロジェクト・プロスペクトの展望

- 実験データ
- 言語学
- 広範囲なリンキング
- その他の領域
- eブック、データベース、バックファイル
- ピアレビュー
- プロスペクトによるサービス

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（プロジェクト・プロスペクト）

理化学出版に意味論を導入する

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