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### 1) 1,1,4,4-Tetracyanobutadiene-Functionalized Anthracenes: Regioselectivity of Cycloadditions in the Synthesis of Small Near-IR Dyes

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* https://doi.org/10.1021/acs.orglett.1c00136
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* Published 19 Mar 2021 (early online 26 Feb 2021)
* Processed: 2021-3

Two small 1,1,4,4-tetracyanobutadiene-functionalized chromophores were obtained by careful leverage of the regioselectivity of the cycloaddition reaction of tetracyanoethylene with anthracene-ynamide derivatives, inducing either a [2 + 2] or a [4 + 2] Diels-Alder process. DFT calculations unraveled the mechanism of the [2 + 2] cycloaddition-retroelectrocyclization reaction sequence with ynamides and elucidated the differing mechanisms in the two substrates. The synthesized dyes presented panchromatic absorption extending into the near-IR and far-red/near-IR photoluminescence in the solid state up to 1550 nm.

### 2) How metallylenes activate small molecules

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* Published 28 Mar 2021 (early online 18 Feb 2021)
* Processed: 2021-3

We have studied the activation of dihydrogen by metallylenes using relativistic density functional theory (DFT). Our detailed activation strain and Kohn-Sham molecular orbital analyses have quantified the physical factors behind the decreased reactivity of the metallylene on going down Group 14, from carbenes to stannylenes. Along this series, the reactivity decreases due to a worsening of the back-donation interaction between the filled lone-pair orbital of the metallylene and the σ\*-orbital of H2, which, therefore, reduces the metallylene-substrate interaction and increases the reaction barrier. As the metallylene ligand is varied from nitrogen to phosphorus to arsenic a significant rate enhancement is observed for the activation of H2due to (i) a reduced steric (Pauli) repulsion between the metallylene and the substrate; and (ii) less activation strain, as the metallylene becomes increasingly more predistorted. Using a rationally designed metallylene with an optimal Group 14 atom and ligand combination, we show that a number of small molecules (i.e.HCN, CO2, H2, NH3) may also be readily activated. For the first time, we show the ability of our H2activated designer metallylenes to hydrogenate unsaturated hydrocarbons. The results presented herein will serve as a guide for the rational design of metallylenes toward the activation of small molecules and subsequent reactions.

### 3) Chalcogen bonds: Hierarchical ab initio benchmark and density functional theory performance study

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* Journal of Computational Chemistry
* https://doi.org/10.1002/jcc.26489
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* Published 15 Apr 2021 (early online 5 Feb 2021)
* Processed: 2021-4

We have performed a hierarchical ab initio benchmark and DFT performance study of D2Ch•••A− chalcogen bonds (Ch = S, Se; D, A = F, Cl). The ab initio benchmark study is based on a series of ZORA-relativistic quantum chemical methods [HF, MP2, CCSD, CCSD(T)], and all-electron relativistically contracted variants of Karlsruhe basis sets (ZORA-def2-SVP, ZORA-def2-TZVPP, ZORA-def2-QZVPP) with and without diffuse functions. The highest-level ZORA-CCSD(T)/ma-ZORA-def2-QZVPP counterpoise-corrected complexation energies (ΔECPC) are converged within 1.1–3.4 kcal mol−1 and 1.5–3.1 kcal mol−1 with respect to the method and basis set, respectively. Next, we used the ZORA-CCSD(T)/ma-ZORA-def2-QZVPP (ΔECPC) as reference data for analyzing the performance of 13 different ZORA-relativistic DFT approaches in combination with the Slater-type QZ4P basis set. We find that the three-best performing functionals are M06-2X, B3LYP, and M06, with mean absolute errors (MAE) of 4.1, 4.2, and 4.3 kcal mol−1, respectively. The MAE for BLYP-D3(BJ) and PBE amount to 8.5 and 9.3 kcal mol−1, respectively.

### 4) Combined cellomics and proteomics analysis reveals shared neuronal morphology and molecular pathway phenotypes for multiple schizophrenia risk genes

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* Published Mar 2021 (early online None)
* Processed: 2021-3

An enigma in studies of neuropsychiatric disorders is how to translate polygenic risk into disease biology. For schizophrenia, where > 145 significant GWAS loci have been identified and only a few genes directly implicated, addressing this issue is a particular challenge. We used a combined cellomics and proteomics approach to show that polygenic risk can be disentangled by searching for shared neuronal morphology and cellular pathway phenotypes of candidate schizophrenia risk genes. We first performed an automated high-content cellular screen to characterize neuronal morphology phenotypes of 41 candidate schizophrenia risk genes. The transcription factors Tcf4 and Tbr1 and the RNA topoisomerase Top3b shared a neuronal phenotype marked by an early and progressive reduction in synapse numbers upon knockdown in mouse primary neuronal cultures. Proteomics analysis subsequently showed that these three genes converge onto the syntaxin-mediated neurotransmitter release pathway, which was previously implicated in schizophrenia, but for which genetic evidence was weak. We show that dysregulation of multiple proteins in this pathway may be due to the combined effects of schizophrenia risk genes Tcf4, Tbr1, and Top3b. Together, our data provide new biological functions for schizophrenia risk genes and support the idea that polygenic risk is the result of multiple small impacts on common neuronal signaling pathways.

### 5) Effect of Extreme Weather Events on Contaminant Transport From Urban Run-Off to a Fjord System

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* Published Mar 2021 (early online 4 Mar 2021)
* Processed: 2021-3

Urbanization has resulted in increased contaminant run-off in densely populated areas. Climate change is expected to result in a higher frequency of extreme weather events including torrential rainfall and storms. The contaminant levels of polycyclic aromatic hydrocarbons (PAH), chlorinated paraffins (CPF) and selected metals, in a small urban river were monitored during snow-melting and rainfall events to quantify the contribution to the contamination load of receiving waters of the inner Oslo fjord, Norway. Suspended particulate matter (SPM) was characterized with respect to levels of contaminants as well as toxic response using a battery of bioassays. The contaminant flux from the river to the fjord was quantified and assessed relative to sediment data. Historic data for near-shore sediment samples from the fjord were used to document urban input. The results show a clear episodic response in contaminant load emitted from the river to the fjord. The main historic input to the fjord was found to be PAH from pyrogenic sources like coal and wood burning as well as traffic. A significant reduction in the level of PAH was observed since the 1980s. The measured flux of CPF is consistent with on-going societal use despite a ban on the use of short chain CPF imposed in Norway from 2002.

### 6) Symposium on Lactic Acid Bacteria-reading while waiting for a meeting

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* https://doi.org/10.1093/femsre/fuaa049
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* Published Mar 2021 (early online 16 Mar 2021)
* Processed: 2021-3

### 7) The proteome of granulovacuolar degeneration and neurofibrillary tangles in Alzheimer’s disease

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* Acta Neuropathologica
* https://doi.org/10.1007/s00401-020-02261-4
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* Published Mar 2021 (early online None)
* Processed: 2021-3

Granulovacuolar degeneration (GVD) is a common feature in Alzheimer’s disease (AD). The occurrence of GVD is closely associated with that of neurofibrillary tangles (NFTs) and GVD is even considered to be a pre-NFT stage in the disease process of AD. Currently, the composition of GVD bodies, the mechanisms associated with GVD and how GVD exactly relates to NFTs is not well understood. By combining immunohistochemistry (IHC) and laser microdissection (LMD) we isolated neurons with GVD and those bearing tangles separately from human post-mortem AD hippocampus (n = 12) using their typical markers casein kinase (CK)1δ and phosphorylated tau (AT8). Control neurons were isolated from cognitively healthy cases (n = 12). 3000 neurons per sample were used for proteome analysis by label free LC–MS/MS. In total 2596 proteins were quantified across samples and a significant change in abundance of 115 proteins in GVD and 197 in tangle bearing neurons was observed compared to control neurons. With IHC the presence of PPIA, TOMM34, HSP70, CHMP1A, TPPP and VXN was confirmed in GVD containing neurons. We found multiple proteins localizing specifically to the GVD bodies, with VXN and TOMM34 being the most prominent new protein markers for GVD bodies. In general, protein groups relatedto protein folding, proteasomal function, the endolysosomal pathway, microtubule and cytoskeletal related function, RNA processing and glycolysis were found to be changed in GVD neurons. In addition to these protein groups, tangle bearing neurons show a decrease in ribosomal proteins, as well as in various proteins related to protein folding. This study, for the first time, provides a comprehensive human based quantitative assessment of protein abundances in GVD and tangle bearing neurons. In line with previous functional data showing that tau pathology induces GVD, our data support the model that GVD is part of a pre-NFT stage representing a phase in which proteostasis and cellular homeostasis is disrupted. Elucidating the molecular mechanisms and cellular processes affected in GVD and its relation to the presence of tau pathology is highly relevant for the identification of new drug targets for therapy.

### 8) Not Carbon s–p Hybridization, but Coordination Number Determines C−H and C−C Bond Length

* Vermeeren, P., Zeist, W., Hamlin, T. A., Guerra, C. F., Bickelhaupt, F. M.
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* Chemistry: A European Journal
* https://doi.org/10.1002/chem.202004653
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* Published 3 Mar 2021 (early online None)
* Processed: 2021-3

### 9) How the Lewis Base F– Catalyzes the 1,3-Dipolar Cycloaddition between Carbon Dioxide and Nitrilimines

* Svatunek, D., Hansen, T., Houk, K. N., Hamlin, T. A.
* Theoretical Chemistry, Chemistry and Pharmaceutical Sciences, AIMMS
* The Journal of organic chemistry
* https://doi.org/10.1021/acs.joc.0c02963
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* Published 5 Mar 2021 (early online None)
* Processed: 2021-3

### 10) A flat embedding method for transmission electron microscopy reveals an unknown mechanism of tetracycline

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* Processed: 2021-3

Transmission electron microscopy of cell sample sections is a popular technique in microbiology. Currently, ultrathin sectioning is done on resin-embedded cell pellets, which consumes milli- to deciliters of culture and results in sections of randomly orientated cells. This is problematic for rod-shaped bacteria and often precludes large-scale quantification of morphological phenotypes due to the lack of sufficient numbers of longitudinally cut cells. Here we report a flat embedding method that enables observation of thousands of longitudinally cut cells per single section and only requires microliter culture volumes. We successfully applied this technique to Bacillus subtilis, Escherichia coli, Mycobacterium bovis, and Acholeplasma laidlawii. To assess the potential of the technique to quantify morphological phenotypes, we monitored antibiotic-induced changes in B. subtilis cells. Surprisingly, we found that the ribosome inhibitor tetracycline causes membrane deformations. Further investigations showed that tetracycline disturbs membrane organization and localization of the peripheral membrane proteins MinD, MinC, and MreB. These observations are not the result of ribosome inhibition but constitute a secondary antibacterial activity of tetracycline that so far has defied discovery.

### 11) Bismuth Amides Mediate Facile and Highly Selective Pn–Pn Radical-Coupling Reactions (Pn=N, P, As)The controlled release of well-defined radical species under mild conditions for subsequent use in selective reactions is an important and challenging task in synthetic chemistry. We show here that simple bismuth amide species [Bi(NAr2)3] readily release aminyl radicals [NAr2]. at ambient temperature in solution. These reactions yield the corresponding hydrazines, Ar2N−NAr2, as a result of highly selective N−N coupling. The exploitation of facile homolytic Bi−Pn bond cleavage for Pn−Pn bond formation was extended to higher homologues of the pnictogens (Pn=N–As): homoleptic bismuth amides mediate the highly selective dehydrocoupling of HPn

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* Angewandte Chemie - International Edition
* https://doi.org/10.1002/anie.202015514
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* Published 15 Mar 2021 (early online 14 Dec 2020)
* Processed: 2021-3

R2 to give R2Pn−PnR2. Analyses by NMR and EPR spectroscopy, single-crystal X-ray diffraction, and DFT calculations reveal low Bi−N homolytic bond-dissociation energies, suggest radical coupling in the coordination sphere of bismuth, and reveal electronic and steric parameters as effective tools to control these reactions.

### 12) Bifunctional Hydrogen Bond Donor-Catalyzed Diels–Alder Reactions: Origin of Stereoselectivity and Rate Enhancement

* Vermeeren, P., Hamlin, T. A., Bickelhaupt, F. M., Fernández, I.
* Theoretical Chemistry, AIMMS, Chemistry and Pharmaceutical Sciences, Complutense University
* Chemistry - A European Journal
* https://doi.org/10.1002/chem.202004496
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* Published 17 Mar 2021 (early online 10 Nov 2020)
* Processed: 2021-3

The selectivity and rate enhancement of bifunctional hydrogen bond donor-catalyzed Diels–Alder reactions between cyclopentadiene and acrolein were quantum chemically studied using density functional theory in combination with coupled-cluster theory. (Thio)ureas render the studied Diels–Alder cycloaddition reactions exo selective and induce a significant acceleration of this process by lowering the reaction barrier by up to 7 kcal mol−1. Our activation strain and Kohn–Sham molecular orbital analyses uncover that these organocatalysts enhance the Diels–Alder reactivity by reducing the Pauli repulsion between the closed-shell filled π-orbitals of the diene and dienophile, by polarizing the π-orbitals away from the reactive center and not by making the orbital interactions between the reactants stronger. In addition, we establish that the unprecedented exo selectivity of the hydrogen bond donor-catalyzed Diels–Alder reactions is directly related to the larger degree of asynchronicity along this reaction pathway, which is manifested in a relief of destabilizing activation strain and Pauli repulsion.

### 13) An annotation database for chemicals of emerging concern in exposome research: Environmental exposures are a key contributor to disease and premature death (Landrigan et al., 2018). Yet, only a fraction of chemicals produced in significant amounts with potential to enter the environment have sufficient information to characterize human exposure levels and toxicity.Chemicals of Emerging Concern (CECs) include a very wide group of chemicals that are suspected to be responsible for adverse effects on health, but for which very limited information is available.General information

* Lamoree, M., Hamers, T., Meijer, J., Antignac, J. P., Hutinet, S., Debrauwer, L., Covaci, A., Huber, C., von Krauss, M. K., Walker, D. I., Walker, D. I., Schymanski, E. L., Vermeulen, R., Vlaanderen, J.
* E&H: Environmental Chemistry and Toxicology, AIMMS, E&H: Environmental Health and Toxicology, Institute for Risk Assessment Sciences (IRAS), INRAE, École nationale vétérinaire, agroalimentaire et de l'alimentation, Nantes-Atlantique, UFZ – Helmholtz Centre for Environmental Research, Department of Environmental Medicine and Public Health, INRAE, Université de Toulouse, Toxicological Centre, University of Antwerp, Toxicological Center, Helmholtz Centre for Environmental Research, University of Luxembourg, Division of Environmental Epidemiology, Utrecht University
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* https://doi.org/10.1016/j.envint.2021.106511
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* Published 24 Mar 2021 (early online None)
* Processed: 2021-3

An annotation database for chemicals of emerging concern in exposome research: Environmental exposures are a key contributor to disease and premature death (Landrigan et al., 2018). Yet, only a fraction of chemicals produced in significant amounts with potential to enter the environment have sufficient information to characterize human exposure levels and toxicity.Chemicals of Emerging Concern (CECs) include a very wide group of chemicals that are suspected to be responsible for adverse effects on health, but for which very limited information is available.

### 14) The Pauli Repulsion-Lowering Concept in Catalysis

* Hamlin, T. A., Bickelhaupt, F. M., Fernández, I.
* Theoretical Chemistry, AIMMS, Chemistry and Pharmaceutical Sciences
* Accounts of Chemical Research
* https://doi.org/10.1021/acs.accounts.1c00016
* Corresponding author: None
* Published 24 Mar 2021 (early online None)
* Processed: 2021-3

### 15) Model selection reveals the butyrate-producing gut bacterium Coprococcus eutactus as predictor for language development in three-year-old rural Ugandan children

* Kort, R., Schlösser, J., Vazquez, A. R., Atukunda, P., Muhoozi, G. K., Wacoo, A. P., Sybesma, W. F., Westerberg, A. C., Iversen, P. O., Schoen, E. D.
* Molecular Cell Physiology, AIMMS
* medRxiv
* https://doi.org/10.1101/2021.03.15.21253665
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* Published 25 Mar 2021 (early online None)
* Processed: 2021-3

Introduction The metabolic activity of the gut microbiota plays a pivotal role in the gut-brain axis through the effects of bacterial metabolites on brain function and development. In this study we investigated the association of gut microbiota composition with language development of three-year-old rural Ugandan children.Methods We studied the language ability in 139 children of 36 months in our controlled maternal education intervention trial to stimulate children’s growth and development. The dataset includes 1170 potential predictors, including anthropometric and cognitive parameters at 24 months, 542 composition parameters of the children’s gut microbiota at 24 months and 621 of these parameters at 36 months. We applied a novel computationally efficient version of the all-subsets regression methodology and identified predictors of language ability of 36-months-old children scored according to the Bayley Scales of Infant and Toddler Development (BSID-III).Results The best three-term model, selected from more than 266 million models, includes the predictors Coprococcus eutactus at 24 months of age, Bifidobacterium at 36 months of age, and language development at 24 months. The top 20 four-term models, selected from more than 77 billion models, consistently include Coprococcus eutactus abundance at 24 months, while 14 of these models include the other two predictors as well. Mann-Whitney U tests further suggest that the abundance of gut bacteria in language non-impaired children (n = 78) differs from that in language impaired children (n = 61) at 24 months. While obligate anaerobic butyrate-producers, including Coprococcus eutactus, Faecalibacterium prausnitzii, Holdemanella biformis, Roseburia hominis are less abundant, facultative anaerobic bacteria, including Granulicatella elegans, Escherichia/Shigella and Campylobacter coli, are more abundant in language impaired children. The overall predominance of oxygen tolerant species in the gut microbiota of Ugandan children at the age 24 months, expressed as the Metagenomic Aerotolerant Predominance Index (MAPI), was slightly higher in the language impaired group than in the non-impaired group (P = 0.09).Conclusions Application of the all-subsets regression methodology to microbiota data established a correlation between the relative abundance of the anaerobic butyrate-producing gut bacterium Coprococcus eutactus and language development in Ugandan children. We propose that the gut redox potential and the overall bacterial butyrate-producing capacity could be factors of importance as gut microbiota members with a positive correlation to language development are mostly strictly anaerobic butyrate-producers, while microbiota members that correlate negatively, are predominantly oxygen tolerant with a variety of known adverse effects.

### 16) Do Sulfonamides Interact with Aromatic Rings?

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* Chemistry - A European Journal
* https://doi.org/10.1002/chem.202004732
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* Published 26 Mar 2021 (early online 30 Dec 2020)
* Processed: 2021-3

Aromatic rings form energetically favorable interactions with many polar groups in chemical and biological systems. Recent molecular studies have shown that sulfonamides can chelate metal ions and form hydrogen bonds, however, it is presently not established whether the polar sulfonamide functionality also interacts with aromatic rings. Here, synthetic, spectroscopic, structural, and quantum chemical analyses on 2,6-diarylbenzenesulfonamides are reported, in which two flanking aromatic rings are positioned close to the central sulfonamide moiety. Fine-tuning the aromatic character by substituents on the flanking rings leads to linear trends in acidity and proton affinity of sulfonamides. This physical-organic chemistry study demonstrates that aromatic rings have a capacity to stabilize sulfonamides via through-space NH–π interactions. These results have implications in rational drug design targeting electron-rich aromatic rings in proteins.

### 17) How Oriented External Electric Fields Modulate Reactivity

* Yu, S., Vermeeren, P., Hamlin, T. A., Bickelhaupt, F. M.
* Theoretical Chemistry, AIMMS, Chemistry and Pharmaceutical Sciences
* Chemistry: A European Journal
* https://doi.org/10.1002/chem.202004906
* Corresponding author: Hamlin, T. A.
* Published 26 Mar 2021 (early online 7 Dec 2020)
* Processed: 2021-3

A judiciously oriented external electric field (OEEF) can catalyze a wide range of reactions and can even induce endo/exo stereoselectivity of cycloaddition reactions. The Diels–Alder reaction between cyclopentadiene and maleic anhydride is studied by using quantitative activation strain and Kohn–Sham molecular orbital theory to pinpoint the origin of these catalytic and stereoselective effects. Our quantitative model reveals that an OEEF along the reaction axis induces an enhanced electrostatic and orbital interaction between the reactants, which in turn lowers the reaction barrier. The stronger electrostatic interaction originates from an increased electron density difference between the reactants at the reactive center, and the enhanced orbital interaction arises from the promoted normal electron demand donor–acceptor interaction driven by the OEEF. An OEEF perpendicular to the plane of the reaction axis solely stabilizes the exo pathway of this reaction, whereas the endo pathway remains unaltered and efficiently steers the endo/exo stereoselectivity. The influence of the OEEF on the inverse electron demand Diels–Alder reaction is also investigated; unexpectedly, it inhibits the reaction, as the electric field now suppresses the critical inverse electron demand donor–acceptor interaction.

### 18) Viral G Protein-Coupled Receptors: Attractive Targets for Herpesvirus-Associated Diseases

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* Published 1 Apr 2021 (early online 10 Mar 2021)
* Processed: 2021-4

Herpesviruses are ubiquitous pathogens that establish lifelong, latent infections in their host. Spontaneous reactivation of herpesviruses is often asymptomatic or clinically manageable in healthy individuals, but reactivation events in immunocompromised or immunosuppressed individuals can lead to severe morbidity and mortality. Moreover, herpesvirus infections have been associated with multiple proliferative cardiovascular and post-transplant diseases. Herpesviruses encode viral G protein-coupled receptors (vGPCRs) that alter the host cell by hijacking cellular pathways and play important roles in the viral life cycle and these different disease settings. In this review, we discuss the pharmacological and signaling properties of these vGPCRs, their role in the viral life cycle, and their contribution in different diseases. Because of their prominent role, vGPCRs have emerged as promising drug targets, and the potential of vGPCR-targeting therapeutics is being explored. Overall, these vGPCRs can be considered as attractive targets moving forward in the development of antiviral, cancer, and/or cardiovascular disease treatments. SIGNIFICANCE STATEMENT: In the last decade, herpesvirus-encoded G protein-coupled receptors (GPCRs) have emerged as interesting drug targets with the growing understanding of their critical role in the viral life cycle and in different disease settings. This review presents the pharmacological properties of these viral receptors, their role in the viral life cycle and different diseases, and the emergence of therapeutics targeting viral GPCRs.

### 19) Designing Rh(I)-Half-Sandwich Catalysts for Alkyne [2+2+2] Cycloadditions

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* https://doi.org/10.1055/s-0040-1707284
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* Published Apr 2021 (early online 9 Oct 2020)
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Metal-mediated [2+2+2] cycloadditions of unsaturated molecules to cyclic and polycyclic organic compounds are a versatile synthetic route affording good yields and selectivity under mild conditions. In the last two decades, in silico investigations have unveiled important details about the mechanism and the energetics of the whole catalytic cycle. Particularly, a number of computational studies address the topic of half-sandwich catalysts which, due to their structural fluxionality, have been widely employed, since the 1980s. In these organometallic species, the metal is coordinated to an aromatic ring, typically the ubiquitous cyclopentadienyl anion, C 5H 5-(Cp) or to the Cp moiety of a larger polycyclic aromatic ligand (Cp′). During the catalytic process, the metal continuously 'slips' on the ring, changing its hapticity. This phenomenon of metal slippage and its implications for the catalyst's performance are discussed in this work, referring to the most important computational mechanistic studies reported in literature for Rh(I) half-metallocenes, with the purpose of providing hints for a rational design of this class of compounds. 1 Introduction 2 Mechanism of Metal-Catalyzed Acetylene [2+2+2] Cycloaddition to Benzene and the Problem of the Indenyl Effect 2.1 Acetylene-Acetonitrile [2+2+2] Co-cycloaddition to 2-Methylpyridine: Evidence of the Indenyl Effect 2.2 Heteroaromatic Catalysts and the Evidence of a Reverse Indenyl Effect 2.3 Booth's Mechanistic Hypothesis and the Evidence of the Indenyl Effect 3 Structure-Reactivity Correlation: The Slippage-Span Model 4 Conclusions and Perspectives.

### 20) Heterologous Expression of eth

* Ho, V. Q., Verboom, T., Rong, M. K., Habjan, E., Bitter, W., Speer, A.
* Organic Chemistry, AIMMS, Molecular Microbiology, Vrije Universiteit Amsterdam
* Antimicrobial agents and chemotherapy
* https://doi.org/10.1128/AAC.01445-20
* Corresponding author: Speer, A.
* Published Apr 2021 (early online None)
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A and katG in Mycobacterium marinum Enables the Rapid Identification of New Prodrugs Active against Mycobacterium tuberculosisScreening strategies for antituberculosis compounds using Mycobacterium tuberculosis are time consuming and require biosafety level 3 (BSL3) facilities, which makes the development of high-throughput assays difficult and expensive. Mycobacterium marinum, a close genetic relative of M. tuberculosis, possesses several advantages as a suitable model for tuberculosis drug screening. However, despite the high genetic similarity, there are some obvious differences in susceptibility to some tuberculosis drugs between these two species, especially for the prodrugs ethionamide and isoniazid. In this study, we aimed to improve M. marinum as a model for antituberculosis drug identification by heterologous expression of two common drug activators, EthA and KatG. These two activators were overexpressed in M. marinum, and the strains were tested against ethionamide, isoniazid, and a library of established antimycobacterial compounds from TB Alliance to compare drug susceptibility. Both in vitro and in vivo using zebrafish larvae, these genetically modified M. marinum strains showed significantly higher susceptibility against ethionamide and isoniazid, which require activation by EthA and KatG. More importantly, a strain overexpressing both ethA and katG was potentially more susceptible to approximately 20% of the antituberculosis hit compounds from the TB Alliance library. Most of these compounds were activated by EthA in M. marinum. Four of these compounds were selected for further analysis, and three of them showed obvious EthA-dependent activity against M. tuberculosis. Overall, our developed M. marinum strains are valuable tools for high-throughput discovery of potential novel antituberculosis prodrugs.

### 21) Analysis of missense variants in the human histamine receptor family reveals increased constitutive activity of e4106.30×30k variant in the histamine h1 receptor

* Ma, X., Segura, M. A., Zarzycka, B., Vischer, H. F., Leurs, R.
* Medicinal chemistry, AIMMS
* International Journal of Molecular Sciences
* https://doi.org/10.3390/ijms22073702
* Corresponding author: Leurs, R.
* Published 1 Apr 2021 (early online None)
* Processed: 2021-4

The Exome Aggregation Consortium has collected the protein-encoding DNA sequences of almost 61,000 unrelated humans. Analysis of this dataset for G protein-coupled receptor (GPCR) proteins (available at GPCRdb) revealed a total of 463 naturally occurring genetic missense variations in the histamine receptor family. In this research, we have analyzed the distribution of these missense variations in the four histamine receptor subtypes concerning structural segments and sites important for GPCR function. Four missense variants R1273.52×52H, R13934.57×57H, R4096.29×29H, and E4106.30×30 K, were selected for the histamine H1 receptor (H1R) that were hypothesized to affect receptor activity by interfering with the interaction pattern of the highly conserved D(E)RY motif, the so-called ionic lock. The E4106.30×30 K missense variant displays higher constitutive activity in G protein signaling as compared to wild-type H1R, whereas the opposite was observed for R1273.52×52H, R13934.57×57H, and R4096.29×29H. The E4106.30×30 K missense variant displays a higher affinity for the endogenous agonist histamine than wild-type H1R, whereas antagonist affinity was not affected. These data support the hypothesis that the E4106.30×30 K mutation shifts the equilibrium towards active conformations. The study of these selected missense variants gives additional insight into the structural basis of H1R activation and, moreover, highlights that missense variants can result in pharmacologically different behavior as compared to wild-type receptors and should consequently be considered in the drug discovery process.

### 22) The Gauche Effect in XCH 2 CH 2 X Revisited

* Silva, D. R., Santos, L. A., Hamlin, T. A., Guerra, C. F., Freitas, M. P., Bickelhaupt, F. M.Pages:641-648
* Theoretical Chemistry, AIMMS, Chemistry and Pharmaceutical Sciences
* ChemPhysChem
* https://doi.org/10.1002/cphc.202100090
* Corresponding author: None
* Published 7 Apr 2021 (early online None)
* Processed: 2021-4

### 23) A Quantitative Molecular Orbital Perspective of the Chalcogen Bond

* Santos, L. A., Lubbe, S. C. C., Hamlin, T. A., Ramalho, T. C., Bickelhaupt, F. M.
* Theoretical Chemistry, AIMMS, Chemistry and Pharmaceutical Sciences
* ChemistryOpen
* https://doi.org/10.1002/open.202000323
* Corresponding author: None
* Published 17 Apr 2021 (early online None)
* Processed: 2021-4

### *24) In vitro biotransformation and evaluation of potential transformation products of chlorinated paraffins by high resolution accurate mass spectrometry*

* He, C., van Mourik, L., Tang, S., Thai, P., Wang, X., Brandsma, S. H., Leonards, P. E., Thomas, K. V., Mueller, J. F.
* E&H: Environmental Bioanalytical Chemistry, AIMMS, University of Queensland, Dongguan University of Technology
* Journal of Hazardous Materials
* https://doi.org/10.1016/j.jhazmat.2020.124245
* Corresponding author: He, C.
* Published 5 Mar 2021 (early online 10 Oct 2020)
* Processed: 2021-3

Chlorinated paraffins (CPs) are high production chemicals, which leads to their ubiquitous presence in the environment. To date, few studies have measured CPs in humans and typically at relatively low ...

### *25) Halide Perovskite-Lead Chalcohalide Nanocrystal Heterostructures*

* Imran, M., Peng, L., Pianetti, A., Pinchetti, V., Ramade, J., Zito, J., Di Stasio, F., Buha, J., Toso, S., Song, J., Infante, I., Bals, S., Brovelli, S., Manna, L.
* AIMMS, Theoretical Chemistry, Italian Institute of Technology, Shenzhen University, University of Milan - Bicocca, University of Antwerp, University of Genoa, Catholic University of the Sacred Heart
* Journal of the American Chemical Society
* https://doi.org/10.1021/jacs.0c10916
* Corresponding author: Song, J., Infante, I., Bals, S., Brovelli, S., Manna, L.
* Published 13 Jan 2021 (early online None)
* Processed: 2021-1

We report the synthesis of colloidal CsPbX3-Pb4S3Br2 (X = Cl, Br, I) nanocrystal heterostructures, providing an example of a sharp and atomically resolved epitaxial interface between a metal halide pe ...

### *26) An Environmental Dilemma for China During the COVID-19 Pandemic: The Explosion of Disposable Plastic Wastes*

* Liu, J., Vethaak, A. D., An, L., Liu, Q., Yang, Y., Ding, J.
* AIMMS, Environment and Health, Jiangnan University, Chinese Research Academy of Environmental Sciences, Nagoya University, Jiangsu Provincial Academy of Environmental Science, Deltares
* Bulletin of Environmental Contamination and Toxicology
* https://doi.org/10.1007/s00128-021-03121-x
* Corresponding author: Liu, J.
* Published Feb 2021 (early online 29 Jan 2021)
* Processed: 2021-2

Plastic pollution control has been on top of the political agenda in China. In January 2020, China announced a phased ban on the production and usage of various types of single-use plastics as a solut ...

### *27) How Lewis Acids Catalyze Ring-Openings of Cyclohexene Oxide*

* Hansen, T., Vermeeren, P., Yoshisada, R., Filippov, D. V., Van Der Marel, G. A., Codée, J. D., Hamlin, T. A.
* Chemistry and Pharmaceutical Sciences, Theoretical Chemistry, AIMMS, Leiden University
* Journal of Organic Chemistry
* https://doi.org/10.1021/acs.joc.0c02955
* Corresponding author: Hamlin, T. A.
* Published 4 Feb 2021 (early online None)
* Processed: 2021-2

We have quantum chemically studied the Lewis acid-catalyzed epoxide ring-opening reaction of cyclohexene epoxide by MeZH (Z = O, S, and NH) using relativistic dispersion-corrected density functional t ...

### *28) Analysis of recycled rubber: Development of an analytical method and determination of polycyclic aromatic hydrocarbons and heterocyclic aromatic compounds in rubber matrices*

* Skoczyńska, E., Leonards, P. E., Llompart, M., de Boer, J.
* E&H: Environmental Bioanalytical Chemistry, AIMMS, Environment and Health, University of Santiago de Compostela
* Chemosphere
* https://doi.org/10.1016/j.chemosphere.2021.130076
* Corresponding author: Skoczyńska, E.
* Published Aug 2021 (early online 23 Feb 2021)
* Processed: 2021-2

Recycled crumb rubber (CR) is rich in compounds with unrecognized toxic potency; this study aims at the development of an analytical method that would allow identification and quantification of a very ...