Organocatalysis

The term organocatalysis describes the acceleration of chemical reactions through the addition of a substoichiometric quantity of an organic compound. The interest in this field has increased spectacularly in the last few years as result of both the novelty of the concept and, more importantly, the fact that the efficiency and selectivity of many organocatalytic reactions meet the standards of established organic reactions. Organocatalytic reactions are becoming powerful tools in the construction of complex molecular skeletons.[1,2]


Recent Articles

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Asymmetric Mannich Reaction of Aryl Methyl Ketones with Cyclic Imines Benzo[e][1,2,3]oxathiazine 2,2-Dioxides Catalyzed by Cinchona Alkaloid-based Primary Amines

An asymmetric Mannich reaction of various aryl methyl ketones (acetophenone derivatives) with different substituted cyclic imine benzo[e][1,2,3]oxathiazine 2,2-dioxides has been developed using an alkaloid-derived primary amine as organocatalyst, providing benzo-fused cyclic sulfamidate N-heterocycles with 85-98% ee.


Nitroxy1-Radical-Catalyzed Oxidative Coupling of Amides with Silylated Nucleophiles through N-Halogenation

A halo to make them shine: A high-yielding nitroxy1-radical-catalyzed oxidative coupling reaction between amines protected with an electron-withdrawing group and silylated nucleophiles proceeded through the activation of N-halogenated amides by the nitroxy1-radical catalyst to give imines. The N-halogenated amide intermediates were generated in situ from amides by treatment with a halogenation reagent (see scheme).


Heteroatom Tuning of Bimolecular Criegee Reactions and Its Implications

Gas-phase reactions: The calculated barriers for the bimolecular reactions of Criegee intermediates and H2X inversely correlate with the bond strength of X–H bond of H2X or directly correlate with the first pKₐ value of H2X. Thus, it is not only the substitutions of Criegee intermediates but also the properties of the heteroatom in H2X that play a crucial role in determining the reactivity.

Sequential NHC-Catalyzed Reaction of Enals and Cyclic Aryldiene-1,3-Diones: Synthesis of Tricyclic Chromenones and Related Compounds.

N-heterocyclic carbene (NHC) catalyzed synthesis of highly functionalized pyrano[3,2-c]chromene-2,5-dione derivatives, pyrano[3,2-c]quinoline-2,5(6H)-dione derivatives and pyrano[4,3-b]pyran-2,5-dione derivatives with potential biological activities is reported. The reaction occurs via a Knoevenagel condensation and NHC-catalyzed enolate addition in one pot.

[Communication]
Vijay Nair, JAGADEESH KRISHNAN, SNEHA MATHEW, ANJANA JAYAPRAKASH P, SASIDHAR B. S., MAYADEVI T. S., SURESH E.

Carbon Dioxide Based N-Formylation of Amines Catalyzed by Fluoride and Hydroxide Anions

I've got anion you: A simple approach for the N-formylation of aliphatic and aromatic amines with CO$_2$ and hydrosilane reducing agents at room temperature and atmospheric pressure is described. Fluoride and hydroxide salts efficiently catalyze the reaction, principally through activation of the hydrosilanes. Using n-Bu$_4$NF as a simple ammonium salt catalyst, the N-formylated products are obtained in excellent yields with high selectivities.

[Communication]
Martin Hulla, Felix D. Bobbink, Shoubhik Das, Paul J. Dyson
ChemCatChem, September 26, 2016, DOI: 10.1002/cctc.201601027. Read article

Iodoalkyne-Based Catalyst-Mediated Activation of Thioamides through Halogen Bonding

Building relationships: An iodoalkyne bearing a pentafluorophenyl group was found to be effective in the catalytic activation of thioamides through halogen bonding. The thus activated thioamides reacted with 2-aminophenol to produce benzoxazoles in good yield. Mechanistic studies provided concrete evidence that this catalytic activation is based on halogen bonding.

[Communication]
Akinobu Matsuzawa, Shihito Takeuchi, Kazuyuki Sugita
Chem. Asian J., September 21, 2016, DOI: 10.1002/asia.201601130. Read article

Organocatalyzed Assembly of Chlorinated Quaternary Stereogenic Centers

The catalytic asymmetric construction of chiral quaternary stereocenters is always a continuous area of research in organic chemistry. In this sense, when a chlorine atom takes part in a quaternary stereocenter, the difficulty of its synthesis increases along with the significance of the resulting products. This is true, not only because of the intrinsic interest of such chlorinated molecules, but also because they are considered as highly valuable chiral building blocks in organic synthesis, as they can be easily converted to more complex molecules by a simple SN2 displacement. Among the different strategies followed to create chlorinated quaternary stereogenic centers, organocatalysis has played a pivotal role during the last decade. In this review, a comprehensive analysis of such organocatalyzed transformations is presented.

[Focus Review]
Melania Gómez-Martínez, Diego A. Alonso, Isidro M. Pastor, Gabriela Guillena, Alejandro Baeza


In this paper, the density functional theory (DFT) has been employed to investigate the detailed mechanisms, origin of chemo- and stereoselectivity, and role of catalyst for the reaction of enals with nitroalkenes catalyzed by N-heterocyclic carbene (NHC). The calculated results disclose that the reaction contains seven steps, i.e., the nucleophilic attack on the -unsaturated aldehyde by NHC, the [1, 2]-proton transfer for the formation of Breslow intermediate, the -protonation for...
affording enolate intermediate, the nucleophilic addition on the Re/Si face of enolate by the nitroalkenes, the [1, 5] proton transfer, the ring-closure process, and the regeneration of NHC. The addition on the Re/Si face of enolate is identified to be the stereocontrolling step, in which the chiral centers including -carbon of enals and -carbon of nitroalkenes are formed. Moreover, the reaction pathway leading to the RR-configured product has the lowest Gibbs free energy barrier, which is in agreement with the experimental observation. Furthermore, the analyses of electrophilic and nucleophilic Parr functions and global reactivity indexes (GRIs) have been performed to explore the origin of chemoselectivity and the role of catalyst. This theoretical work would provide valuable insights for the rational design of more effective organocatalyst for this kind of reactions with high stereoselectivities.

Linjie Zheng, Donghui Wei, Yang Wang, Yan Qiao
Chem. Asian J., September 08, 2016, DOI: 10.1002/asia.201601022. Read article

Kinetically Controlled α-Selective O-Glycosylation of Phenol Derivatives Using 2-Nitroglycals by a Bifunctional Chiral Thiourea Catalyst

The highly α-selective organocatalytic glycosylation of phenol derivatives using 2-nitroglycals has been developed. The stereoselectivity of this reaction was kinetically controlled by a bifunctional thiourea catalyst, and was applied to synthesis of glycopeptides.

Keisuke Yoshida, Yohei Kanoko, Kenichi Takao

Facile Preparation of Flavinium Organocatalysts

The green route: α(5)-Ethylated flavinium organocatalyst can be readily prepared without using any hazardous chemicals or inert atmosphere as previously required. This work breaks the limited application of flavinium oxidation catalysts in both laboratory and industrial synthesis.

Yukihiro Arakawa, Takahiro Oonishi, Takahiro Kohda, Keiji Minagawa, Yasushi Imada
ChemSusChem, August 24, 2016, DOI: 10.1002/cssc.201600846. Read article

Promotion of Organic Reactions by Non-Benzenoid Carbocyclic Aromatic Ions

Demelza J. M. Lyons, Reece D. Crocker, Marcus Blümel, Thanh Vinh Nguyen

Synthesis of Diheteroatomic Five-Membered Heterocyclic Compounds from α,β-Unsaturated Aldehydes

Channel 5: This Focus Review summarizes recent methods for the synthesis of five-membered N,N-, N,O-, and N,S-heterocycles based on the transformations of 2-alkenals. A multitude of catalytic and technological novelties, such as asymmetric metal- and organocatalysis, one-pot multicomponent reactions that proceed through domino, cascade, or tandem sequences, and microwave activation, have been used to afford a diverse range of products.

N. A. Keiko, N. V. Vchislo

Mass Spectrometric Back Reaction Screening of Quasi-Enantiomeric Products as a Mechanistic Tool

Observing back and forth: Mass spectrometric back reaction screening of quasi-enantiomeric products may serve as a valuable tool for examining the mechanism of an enantioselective catalytic process. By comparing the results from the forward and back reaction, direct evidence for the involvement of a catalytic intermediate in the enantioselective step can be obtained. The potential of this method is demonstrated for various organocatalytic asymmetric reactions.

Patrick G. Isenegger, Andreas Pfaltz
The Chemical Record, July 15, 2016, DOI: 10.1002/tcr.201600072. Read article

Organocatalytic [3+2] Cycloadditions of Barbiturate-Based Olefins with 3-Isothiocyanato Oxindoles: Highly Diastereoselective and Enantioselective Synthesis of Dispirobarbiturates
N-Heterocyclic Carbene-Catalyzed Synthesis of Multi-Substituted Benzenes from Enals and o-Cyano-\(\beta\)-methyleneones

An Atropisomerically Enforced Phosphoric Acid for Organocatalytic Asymmetric Reactions

Catalytic Efficiency of Primary \(\beta\)-Amino Alcohols and Their Derivatives in Organocatalysis

Novel Base-Free Catalytic Wittig Reaction for the Synthesis of Highly Functionalized Alkenes

The First Enantioselective Organocatalytic Synthesis of 3-Spiro-\(\alpha\)-Alkyldiene-\(\gamma\)-Butyrolactone Oxindoles
An innovative and flexible methodology catalyzed by bifunctional chiral thioureas was developed to react β-nitro oxindoles with aldehydes (see scheme). This approach allows the first enantioselective synthesis of 3-spiro-α-alkylidene-γ-butyro lactone oxindoles 3 with the aim of merging two potentially bioactive structural motifs: the spirooxindole and the α-alkylidene-γ-butyro lactone.


Chiral Triazoles in Anion-Binding Catalysis: New Entry to Enantioselective Reissert-Type Reactions

Against the elements: A family of chiral triazoles has been introduced as innovative C-H bond-based hydrogen donors for anion-binding catalysis. Contrary to the believed inefficiency of the low polarized C-H bonds for promoting organocatalysis, these structures proved to be competitive with respect to the more established N-H-type hydrogen donors in enantioselective Reissert-type reactions.


Acetaldehyde: A Small Organic Molecule with Big Impact on Organocatalytic Reactions

Utility of acetaldehyde: Acetaldehyde has recently received a great deal of attention as the simplest enolizable carbonyl compound because of its versatile applications in the synthesis of poly(vinyl alcohol), unnatural amino acids, and medicine (see graphic). This Minireview summarizes a methodologically diverse approach to the synthesis of target molecules by outlining a diverse array of reactions such as aldol, Mannich, Michael, and NHC-catalyzed reactions.


The Resurgence of the Highly Ylidic N-Heterocyclic Olefins as a New Class of Organocatalysts

One carbon better: N-Heterocyclic olefins, the alkylidene derivatives of the prevalent N-heterocyclic carbenes, have recently emerged as efficient promoters for CO₂ fixation and polymerization reactions. Their extraordinarily strong Lewis/Bronsted basicity suggests great potential as a new class of organocatalysts for a broad range of reactions in synthetic chemistry.


Whither Organic Synthesis?