

Which Of The Following Cross Couplings Of An Enolate

Unlocking the Potential of Enolate Cross Couplings in Organic Synthesis

Every now and then, a topic captures people's attention in unexpected ways. One such fascinating subject in the realm of organic chemistry is the cross coupling of enolates. Enolates, being versatile intermediates, play a pivotal role in the construction of carbon-carbon bonds, which are fundamental to building complex molecules.

What Are Enolates?

Enolates are resonance-stabilized anions derived from carbonyl compounds such as ketones, aldehydes, and

esters. They are generated by deprotonation at the alpha position relative to the carbonyl group. Because of their nucleophilic character, enolates can participate in a variety of reactions, including alkylation, Michael additions, and importantly, cross coupling reactions.

Understanding Cross Coupling Reactions

Cross coupling reactions are a cornerstone of modern synthetic organic chemistry. These reactions enable the formation of new carbon-carbon bonds by coupling two different partners in the presence of metal catalysts such as palladium, nickel, or copper. The classic examples include Suzuki, Negishi, and Stille couplings, each utilizing specific organometallic reagents.

Which Cross Couplings Are Applicable to Enolates?

When we consider enolates as coupling partners, several cross coupling strategies come into play. Among the most effective are the Suzuki-Miyaura, Negishi, and Kumada couplings, adapted to incorporate enolate derivatives or equivalents. The

question often arises: which of the following cross couplings of an enolate is optimal under given conditions?

1. Suzuki-Miyaura Couplings of Enolates

The Suzuki reaction employs organoboron reagents and palladium catalysts. When combined with enolates or their derivatives such as enol triflates, it facilitates the formation of α -substituted carbonyl compounds with high selectivity and functional group tolerance. This methodology is prized for its mild conditions and environmental friendliness.

2. Negishi Couplings Involving Enolates

Negishi coupling utilizes organozinc reagents, which can be generated from enolate precursors. The reaction is known for its excellent stereoselectivity and compatibility with a variety of functional groups. However, the sensitivity of organozinc reagents to moisture and air requires careful handling.

3. Kumada Couplings and Enolates

Kumada coupling involves organomagnesium reagents (Grignard reagents) and palladium or nickel catalysts. While powerful, this approach can be limited by the reactivity of Grignard reagents toward sensitive functional groups present in enolate substrates.

4. Stille and Hiyama Couplings

Although less common with enolates, Stille (organostannanes) and Hiyama (organosilanes) couplings can be employed under specific conditions. Their utility depends on the availability of suitable enolate derivatives and the compatibility with catalysts.

Challenges and Considerations

Cross coupling of enolates requires careful consideration of reaction conditions, catalyst choice, and substrate stability. Enolates are inherently reactive and prone to side reactions such as self-condensation or protonation. Protecting groups, temperature control, and choice of base are critical to achieving high yields and selectivity.

Applications in Synthesis

The ability to perform cross coupling reactions on enolates expands the synthetic toolbox for constructing complex molecules, including natural products and pharmaceuticals. It allows chemists to introduce diverse substituents at the alpha position of carbonyl compounds, enabling the fine-tuning of molecular properties.

Conclusion

In summary, the cross coupling of enolates represents a dynamic and versatile area of organic synthesis. By understanding which coupling reactions are compatible with enolates and optimizing conditions accordingly, chemists can harness these transformations to build increasingly complex and functional molecules with precision.

Understanding Cross Couplings of Enolates: A Comprehensive Guide

In the realm of organic chemistry, enolates play a crucial role in various synthetic transformations. One of the most significant reactions involving enolates is cross-coupling. This process allows for the formation

of new carbon-carbon bonds, which is essential in the synthesis of complex molecules. In this article, we will delve into the world of cross-couplings of enolates, exploring the different types, mechanisms, and applications.

What are Enolates?

Enolates are resonance-stabilized carbanions that can be generated from carbonyl compounds such as ketones and aldehydes. They are highly nucleophilic and can participate in a variety of reactions, including alkylation, acylation, and cross-coupling. The formation of enolates typically involves the deprotonation of a carbonyl compound using a strong base like lithium diisopropylamide (LDA).

Types of Cross-Couplings

Cross-coupling reactions involve the formation of a new carbon-carbon bond between two different organic fragments. When it comes to enolates, several types of cross-couplings can be performed, each with its unique characteristics and applications.

Stille Cross-Coupling

The Stille cross-coupling reaction involves the

coupling of an enolate with an organotin compound. This reaction is highly versatile and can be used to synthesize a wide range of complex molecules. The reaction is typically catalyzed by palladium compounds and proceeds under mild conditions.

Suzuki-Miyaura Cross-Coupling

The Suzuki-Miyaura cross-coupling reaction involves the coupling of an enolate with an organoboron compound. This reaction is particularly useful for the synthesis of biaryl compounds, which are important in the pharmaceutical industry. The reaction is catalyzed by palladium compounds and proceeds under mild conditions.

Negishi Cross-Coupling

The Negishi cross-coupling reaction involves the coupling of an enolate with an organozinc compound. This reaction is highly selective and can be used to synthesize a wide range of complex molecules. The reaction is typically catalyzed by palladium compounds and proceeds under mild conditions.

Mechanisms of Cross-Couplings

The mechanisms of cross-coupling reactions involving

enolates are complex and involve several steps. The first step typically involves the formation of an enolate, which is then coupled with an organometallic compound. The reaction is catalyzed by a transition metal, such as palladium, which facilitates the formation of the new carbon-carbon bond.

Applications of Cross-Couplings

Cross-coupling reactions involving enolates have a wide range of applications in organic synthesis. They are used in the synthesis of complex natural products, pharmaceuticals, and materials. The ability to form new carbon-carbon bonds makes these reactions invaluable in the synthesis of complex molecules.

Conclusion

In conclusion, cross-couplings of enolates are a powerful tool in organic synthesis. They allow for the formation of new carbon-carbon bonds, which is essential in the synthesis of complex molecules. Understanding the different types, mechanisms, and applications of these reactions is crucial for any chemist looking to synthesize complex molecules.

Analytical Perspectives on Cross Couplings of Enolates: Mechanisms, Challenges, and Advancements

The chemistry of enolates and their cross coupling reactions has been an area of sustained research interest, given the importance of forming carbon-carbon bonds in a selective and efficient manner. This article delves into the current state of knowledge surrounding the cross coupling of enolates, assessing the mechanisms, the catalytic systems employed, and the strategic considerations that inform their application.

Background and Mechanistic Insights

Enolates, generated typically by the deprotonation of α -protons adjacent to carbonyl groups, serve as ambident nucleophiles with a high propensity for C-C bond formation. Cross coupling reactions involving enolates require the formation of organometallic species or their analogs that can participate in palladium-, nickel-, or copper-catalyzed processes. The key mechanistic steps include oxidative addition, transmetallation, and reductive

elimination, each of which may be influenced by the nature of the enolate and coupling partner.

Comparative Analysis of Cross Coupling Reactions

Among the suite of cross coupling reactions, Suzuki-Miyaura couplings have gained prominence due to their mild reaction conditions and broad functional group tolerance. Enolates can be converted to enol triflates or boronate esters, which act as coupling partners in this reaction. The mildness of the conditions ensures minimal side reactions and high stereochemical integrity.

Conversely, Negishi couplings, involving organozinc enolate equivalents, offer excellent control over stereochemistry and reactivity. However, the preparation of organozinc species often requires stringent anhydrous conditions and can be limited by functional group compatibility.

Kumada couplings, while effective in certain contexts, are less commonly employed with enolates due to the high reactivity of Grignard reagents, which can lead to side reactions such as enolate protonation and undesired nucleophilic attack.

Catalyst Selection and Ligand Effects

The catalytic system is pivotal in dictating the efficiency and selectivity of enolate cross couplings. Palladium catalysts remain the workhorse, often modified by specially tailored phosphine ligands which influence oxidative addition rates and reductive elimination steps. Nickel catalysts have also emerged as viable alternatives, particularly for coupling less reactive electrophiles.

Challenges in Enolate Cross Coupling

Several intrinsic challenges arise when coupling enolates. Their high nucleophilicity and basicity can undermine catalyst stability and selectivity. Additionally, competing side reactions such as aldol condensations or polymerizations are frequent concerns. Strategies to mitigate these issues include the use of masked enolate equivalents, controlled addition techniques, and judicious solvent and base selection.

Applications and Future Directions

Cross coupling of enolates has facilitated the synthesis of a wide array of complex molecules, from natural product analogs to pharmaceuticals with fine-

tuned bioactivity. The ongoing development of more robust catalysts and milder conditions promises to expand the substrate scope and functional group compatibility. Furthermore, enantioselective variants of these couplings are an exciting frontier, enabling access to chiral centers with high fidelity.

Conclusion

The cross coupling of enolates is a nuanced and evolving field. Through a detailed understanding of mechanism, catalyst design, and reaction conditions, chemists are progressively overcoming limitations to unlock new synthetic possibilities. Continued innovations in this area are poised to have significant impacts on both academic research and industrial applications in organic synthesis.

Investigating the Cross-Couplings of Enolates: An In-Depth Analysis

The cross-coupling of enolates has emerged as a cornerstone in modern organic synthesis, enabling the formation of complex molecular architectures. This article delves into the intricacies of these reactions, examining their mechanisms, applications, and the challenges faced by researchers in this field.

The Evolution of Enolate Chemistry

The use of enolates in organic synthesis dates back several decades, with early work focusing on their role in alkylation and acylation reactions. The advent of cross-coupling reactions, however, has expanded the utility of enolates significantly. These reactions allow for the formation of new carbon-carbon bonds, which is crucial in the synthesis of complex natural products and pharmaceuticals.

Mechanistic Insights

The mechanisms of cross-coupling reactions involving enolates are complex and multifaceted. The reaction typically begins with the formation of an enolate, which is then coupled with an organometallic compound. The role of the transition metal catalyst, often palladium, is pivotal in facilitating the formation of the new carbon-carbon bond. Recent studies have shed light on the electronic and steric factors that influence the selectivity and efficiency of these reactions.

Challenges and Limitations

Despite the significant advancements in enolate cross-coupling reactions, several challenges remain.

One of the primary challenges is the selectivity of the reaction. Enolates can exist in different tautomeric forms, and the reaction conditions can influence the selectivity of the coupling. Additionally, the compatibility of the reaction with various functional groups is a critical consideration. Researchers are actively working to develop new catalysts and reaction conditions that can overcome these limitations.

Future Directions

The future of enolate cross-coupling reactions looks promising, with ongoing research aimed at developing more efficient and selective catalysts. The integration of computational chemistry and artificial intelligence is also expected to play a significant role in the design of new reactions and catalysts. Furthermore, the exploration of sustainable and environmentally friendly reaction conditions is a growing area of interest.

Conclusion

In conclusion, the cross-coupling of enolates represents a powerful tool in organic synthesis. The ongoing research in this field is aimed at overcoming

the current challenges and expanding the applications of these reactions. As our understanding of the mechanisms and factors influencing these reactions deepens, the potential for their use in the synthesis of complex molecules continues to grow.

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Questions & Answers About which of the following cross couplings of an enolate

No	Question	Answer
1	What is the role of enolates in cross coupling reactions?	Enolates act as nucleophilic partners that enable the formation of carbon-carbon bonds during cross coupling reactions, typically through their participation as organometallic equivalents or derivatives.

2	Which cross coupling methods are most commonly used with enolates?	Suzuki-Miyaura, Negishi, and Kumada couplings are among the most common methods adapted for cross coupling involving enolates.
3	Why are Suzuki-Miyaura couplings preferred for enolate cross coupling?	Because they proceed under mild conditions, tolerate a variety of functional groups, and use relatively stable organoboron reagents, making them suitable for sensitive enolate substrates.
4	What challenges do chemists face when performing cross coupling of enolates?	Challenges include controlling side reactions such as aldol condensation, managing the high reactivity and basicity of enolates that can affect catalyst stability, and ensuring selectivity.
5	How do catalyst and ligand choice affect enolate cross coupling efficiency?	Catalysts and ligands influence key steps like oxidative addition and reductive elimination, affecting the reaction rate, selectivity, and tolerance to functional groups in enolate cross coupling.
6	Can cross coupling of enolates be done enantioselectively ?	Yes, ongoing research is developing enantioselective cross coupling protocols for enolates, allowing the formation of chiral centers with high selectivity.

7	Are organozinc reagents compatible with enolate cross coupling?	Organozinc reagents used in Negishi couplings can be compatible, offering good stereocontrol, though they require stringent anhydrous conditions.
8	What strategies help minimize side reactions during enolate cross coupling?	Using masked enolate equivalents, optimized bases, controlled reaction temperatures, and appropriate solvents can reduce side reactions.
9	Is Kumada coupling widely used with enolates?	Kumada coupling is less frequently used with enolates due to the high reactivity of Grignard reagents, which can lead to side reactions.
10	What are potential applications of enolate cross coupling in synthesis?	Enolate cross coupling is valuable for synthesizing α -substituted carbonyl compounds, natural products, pharmaceuticals, and complex organic molecules with precise functionalization.

1 1	What are the primary types of cross-coupling reactions involving enolates?	The primary types of cross-coupling reactions involving enolates include Stille cross-coupling, Suzuki-Miyaura cross-coupling, and Negishi cross-coupling. Each of these reactions involves the coupling of an enolate with a different type of organometallic compound, facilitated by a transition metal catalyst.
1 2	How are enolates typically formed in cross-coupling reactions?	Enolates are typically formed by the deprotonation of a carbonyl compound using a strong base, such as lithium diisopropylamide (LDA). This process generates a resonance-stabilized carbanion that can participate in various reactions, including cross-coupling.
1 3	What role does the transition metal catalyst play in enolate cross-coupling reactions?	The transition metal catalyst, often palladium, plays a crucial role in facilitating the formation of the new carbon-carbon bond. It coordinates with the enolate and the organometallic compound, enabling the coupling reaction to proceed under mild conditions.

1 4	What are some of the challenges faced in enolate cross-coupling reactions?	Some of the challenges faced in enolate cross-coupling reactions include selectivity issues due to the different tautomeric forms of enolates, compatibility with various functional groups, and the development of more efficient and selective catalysts.
1 5	How can computational chemistry and artificial intelligence contribute to the development of enolate cross-coupling reactions?	Computational chemistry and artificial intelligence can contribute to the development of enolate cross-coupling reactions by aiding in the design of new catalysts and reaction conditions. These tools can help predict the outcomes of reactions and optimize the conditions for maximum efficiency and selectivity.
1 6	What are some of the applications of enolate cross-coupling reactions in the pharmaceutical industry?	Enolate cross-coupling reactions are used in the synthesis of complex natural products and pharmaceuticals. The ability to form new carbon-carbon bonds makes these reactions invaluable in the synthesis of biaryl compounds, which are important in the pharmaceutical industry.

1 7	What are the future directions in the field of enolate cross-coupling reactions?	The future directions in the field of enolate cross-coupling reactions include the development of more efficient and selective catalysts, the integration of computational chemistry and artificial intelligence, and the exploration of sustainable and environmentally friendly reaction conditions.
1 8	How do electronic and steric factors influence the selectivity and efficiency of enolate cross-coupling reactions?	Electronic and steric factors play a significant role in the selectivity and efficiency of enolate cross-coupling reactions. The electronic properties of the enolate and the organometallic compound can influence the reactivity and selectivity of the reaction. Steric factors, such as the size and shape of the substituents, can also affect the approach of the reactants and the outcome of the reaction.

19	What are some of the sustainable and environmentally friendly reaction conditions being explored for enolate cross-coupling reactions?	Some of the sustainable and environmentally friendly reaction conditions being explored for enolate cross-coupling reactions include the use of green solvents, such as water or ionic liquids, and the development of catalysts that are less toxic and more recyclable. Additionally, the use of renewable energy sources and the minimization of waste are also areas of interest.
20	How can the integration of computational chemistry and artificial intelligence enhance the understanding of enolate cross-coupling reactions?	The integration of computational chemistry and artificial intelligence can enhance the understanding of enolate cross-coupling reactions by providing insights into the electronic and steric factors that influence the reactivity and selectivity of the reactions. These tools can also help predict the outcomes of reactions and optimize the conditions for maximum efficiency and selectivity.

artificial intelligence in chemistry, carbon carbon bond formation, carbon-carbon bond formation, catalyst ligand effects, computational chemistry, cross-coupling reactions, enolate chemistry, enolate cross coupling, kumada coupling enolates, negishi coupling enolates, negishi cross-coupling, organic synthesis, organic synthesis techniques,

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This shift allows readers to engage with Which Of The Following Cross Couplings Of An Enolate content without the physical constraints traditionally associated with printed materials.

The digital nature of Which Of The Following Cross Couplings Of An Enolate eBooks makes distribution fast and efficient, enabling instant access to updated information without the delays associated with print publishing.

The modular design of Which Of The Following Cross

Couplings Of An Enolate eBooks allows selective reading.

Ultimately, Which Of The Following Cross Couplings Of An Enolate eBooks represent an efficient, scalable, and sustainable approach to continuous learning.

Readers value Which Of The Following Cross Couplings Of An Enolate eBooks for clarity and organization.

Which Of The Following Cross Couplings Of An Enolate eBooks align with modern digital productivity systems.

Many learners prefer Which Of The Following Cross Couplings Of An Enolate eBooks because they reduce physical storage requirements.

Which Of The Following Cross Couplings Of An Enolate eBooks support offline access, enabling uninterrupted learning without constant internet connectivity.

The modular design of Which Of The Following Cross Couplings Of An Enolate eBooks allows readers to focus on specific sections.

Which Of The Following Cross Couplings Of An Enolate eBooks reduce dependency on continuous internet access.

Centralized information reduces redundancy and confusion.

Extended focus improves comprehension and retention.

Which Of The Following Cross Couplings Of An Enolate eBooks allow readers to engage deeply with subjects.

Sharing Which Of The Following Cross Couplings Of An Enolate

Sharing Which Of The Following Cross Couplings Of An Enolate with others can be a positive way to spread knowledge, encourage learning, and build communities around shared interests. However, responsible and legal sharing is essential to respect copyright laws and support the authors and publishers who create valuable content.

Understanding what can and cannot be shared helps prevent legal issues and ensures ethical use of digital materials.

In general, only free, open-access, or public domain versions of Which Of The Following Cross Couplings Of An Enolate may be shared freely. Public domain works are no longer protected by copyright and can be distributed without restrictions. Many classic

texts, government publications, and educational resources fall into this category. Trusted platforms such as public libraries and reputable digital archives clearly label content that is legally shareable.

For copyrighted or paid editions of *Which Of The Following Cross Couplings Of An Enolate*, direct file sharing is usually prohibited. Instead of sending copies, it is best to share official purchase links, publisher pages, or authorized platforms where others can obtain the book legally. Recommending a book through legitimate channels supports content creators and ensures that readers receive accurate and complete versions.

Many eBook platforms provide built-in sharing features that allow limited access, previews, or recommendations without violating copyright. Some services even support temporary lending or family sharing within defined rules. Always review the platform's terms of use before sharing any content related to *Which Of The Following Cross Couplings Of An Enolate*.

Ethical considerations when sharing

Beyond legal requirements, ethical considerations

play an important role. Sharing unauthorized copies can harm authors and publishers by reducing potential income and discouraging future content creation. Supporting legal distribution ensures that high-quality Which Of The Following Cross Couplings Of An Enolate materials continue to be produced and updated. Ethical sharing builds trust and sustainability within reading and learning communities.

Finding Reviews

Reading reviews is one of the most effective ways to choose the best edition of Which Of The Following Cross Couplings Of An Enolate. With many versions, formats, and publishers available, reviews help readers avoid low-quality or poorly formatted editions and focus on content that meets their expectations.

Online bookstores often feature customer reviews and ratings that provide insights into readability, formatting quality, and overall satisfaction. Paying attention to detailed reviews can reveal common issues such as missing pages, poor editing, or compatibility problems with certain devices. Reviews that mention specific strengths or weaknesses are especially useful when selecting a digital version of

Which Of The Following Cross Couplings Of An Enolate.

Community-driven platforms such as Goodreads, Reddit, and specialized forums offer additional perspectives. These communities allow readers to discuss content in depth, compare editions, and share personal experiences. Recommendations from experienced readers or subject-matter enthusiasts can be particularly valuable when choosing educational or technical Which Of The Following Cross Couplings Of An Enolate materials.

Professional reviews from blogs, academic journals, or reputable websites can also provide objective evaluations. These reviews often focus on content accuracy, relevance, and usefulness, making them helpful for students and professionals who rely on reliable information.

Evaluating review credibility

Not all reviews carry the same level of reliability. When reading reviews, consider the reviewer's background, level of detail, and consistency with other feedback. Multiple reviews highlighting similar strengths or weaknesses usually indicate a genuine

pattern. Avoid relying solely on extreme opinions and instead look for balanced assessments that discuss both pros and cons of the Which Of The Following Cross Couplings Of An Enolate edition.

Using Audiobooks

Audiobooks offer an alternative way to experience Which Of The Following Cross Couplings Of An Enolate content and are increasingly popular among modern readers. Instead of reading text, users listen to narrated versions, allowing them to engage with content while performing other tasks. Audiobooks are especially useful during commuting, exercising, or completing routine activities.

Platforms such as Audible, Google Audiobooks, Apple Books, and Scribd offer professionally narrated audiobooks of many Which Of The Following Cross Couplings Of An Enolate titles. These versions often feature high-quality narration, clear pronunciation, and structured pacing that enhances understanding. Some audiobooks also include chapter navigation, bookmarks, and playback speed controls for added convenience.

For public domain works, platforms like LibriVox

provide free audiobooks narrated by volunteers.

While narration quality may vary, LibriVox remains a valuable resource for accessing classic or open-access versions of Which Of The Following Cross Couplings Of An Enolate without cost. Listening to samples before committing to a full audiobook can help ensure a comfortable listening experience.

Audiobooks are particularly beneficial for auditory learners or individuals with visual impairments. They also help reduce screen time, making them a healthy alternative for extended content consumption.

However, audiobooks may not be ideal for detailed study that requires frequent referencing, highlighting, or visual analysis.

Combining audiobooks with text

Many readers find value in combining audiobooks with digital or printed text. Listening while following along in the text can improve comprehension and retention. Others use audiobooks for initial exposure and then refer to the text version of Which Of The Following Cross Couplings Of An Enolate for deeper study. This multi-format approach maximizes flexibility and learning efficiency.

Tracking Progress

Tracking reading progress is a powerful way to stay motivated and organized when engaging with *Which Of The Following Cross Couplings Of An Enolate*.

Monitoring progress helps readers set goals, manage time effectively, and reflect on what they have learned. Whether reading for leisure, study, or professional development, tracking tools enhance accountability and consistency.

Apps such as Goodreads, StoryGraph, and LibraryThing allow users to log books, track reading status, write reviews, and set annual or monthly reading goals. These platforms also offer personalized recommendations based on reading history, making it easier to discover related *Which Of The Following Cross Couplings Of An Enolate* materials.

For readers who prefer a more customized approach, spreadsheets or note-taking apps can serve as effective tracking tools. Creating a simple reading log that includes dates, chapters completed, key notes, and personal reflections helps organize learning and maintain focus. Digital notes can be linked directly to highlighted sections within *Which Of The Following Cross Couplings Of An Enolate* for easy reference.

Using tracking for study and research

For academic or professional purposes, tracking progress goes beyond simple completion. Recording insights, questions, and references while reading Which Of The Following Cross Couplings Of An Enolate creates a structured knowledge base that can be revisited later. This approach supports deeper understanding and improves long-term retention of information.

Tracking tools also help identify patterns in reading habits, such as preferred formats or optimal reading times. Understanding these patterns allows readers to adjust their routines for better productivity and enjoyment.

Community engagement and motivation

Sharing progress within reading communities can increase motivation and accountability. Many platforms allow users to join reading challenges, discussion groups, or book clubs centered around specific topics or genres. Engaging with others who are also reading Which Of The Following Cross Couplings Of An Enolate fosters discussion, insight exchange, and a sense of shared purpose.

However, sharing progress should always respect privacy preferences. Users can choose what information to make public and what to keep personal. Balanced participation ensures that tracking remains a supportive tool rather than a source of pressure.

Final thoughts on sharing and managing Which Of The Following Cross Couplings Of An Enolate

Responsible sharing, informed selection, and effective tracking are key aspects of enjoying Which Of The Following Cross Couplings Of An Enolate in the digital age. By respecting copyright, relying on trusted reviews, exploring audiobooks, and monitoring reading progress, readers can create a well-rounded and ethical reading experience. These practices not only enhance personal understanding but also contribute to a sustainable and supportive reading ecosystem built around high-quality Which Of The Following Cross Couplings Of An Enolate content.