

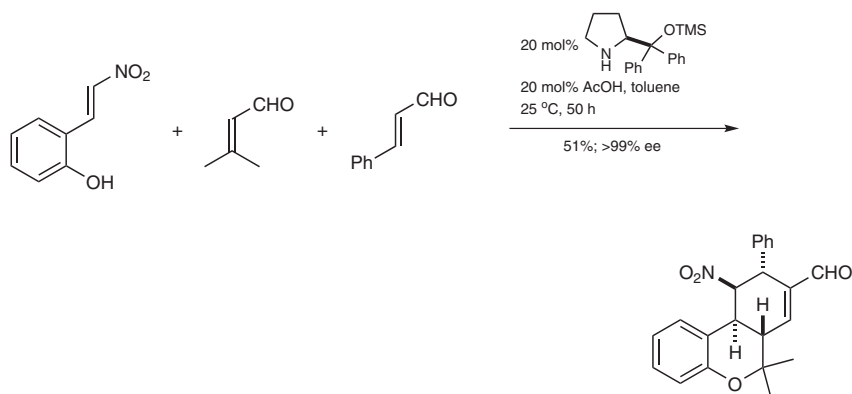
Abstracts

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2.1.1 Michael Addition as the Key Step

J. Rodriguez, D. Bonne, Y. Coquerel, and T. Constantieux

This chapter focuses on multicomponent reactions involving an α,β -unsaturated compound as an electrophilic component and in which a Michael addition is a key step during the process. The Michael addition step can be either the starting point or a late event in the domino sequence. These reactions are extremely powerful processes, allowing the synthesis of diverse, valuable carbocyclic, heterocyclic, or acyclic scaffolds.



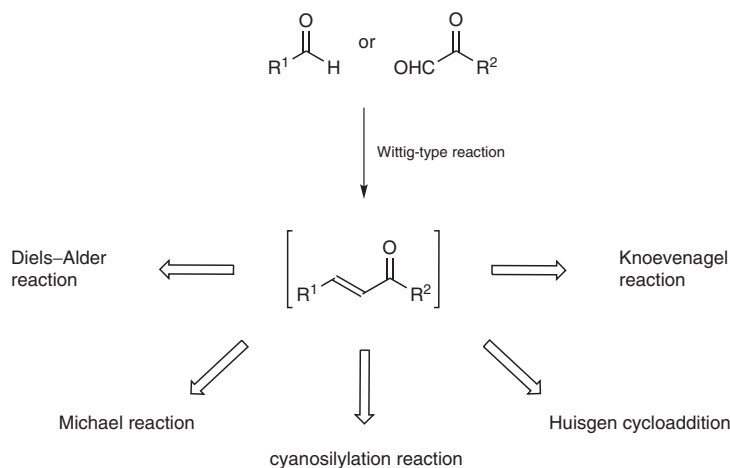
Keywords: α,β -unsaturated compounds • Michael addition • domino reactions • carbocycles • heterocycles • stereoselective synthesis

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2.1.2 In Situ Generation of the α,β -Unsaturated Carbonyl Component by Wittig-Type Reaction

N. S. Alavijeh, E. Ghabraie, and S. Balalaie

This chapter describes various multicomponent reactions (MCRs) involving in situ generated α,β -unsaturated carbonyl compounds formed by Wittig-type reactions.

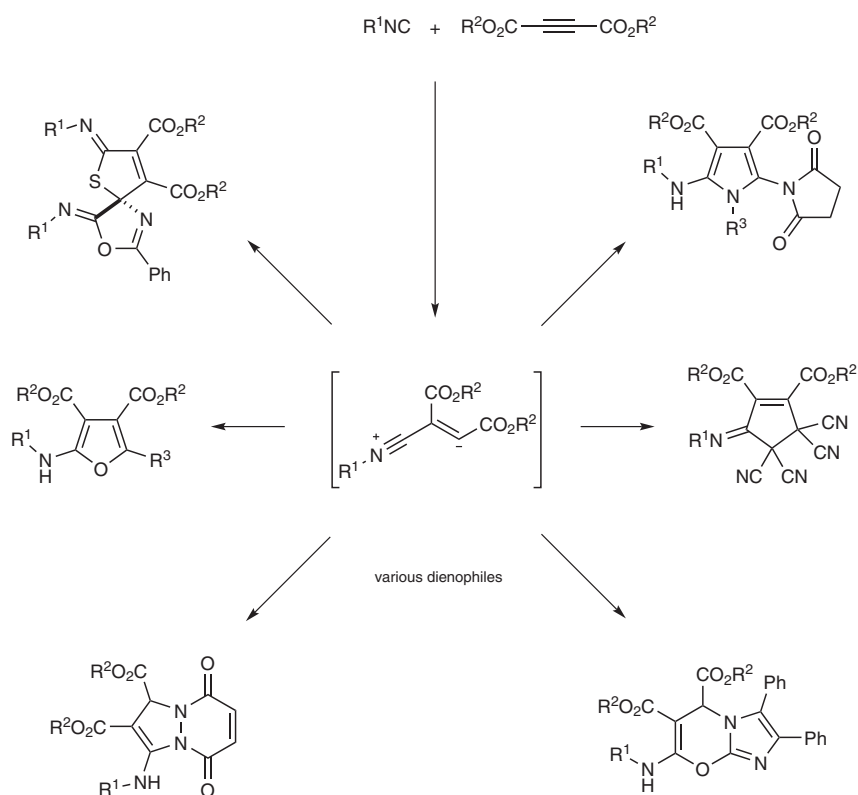


Keywords: Diels–Alder reaction · Horner–Wadsworth–Emmons reaction · Knoevenagel condensation · Michael addition · multicomponent reaction · unsaturated carbonyl compounds · Wittig reaction

2.1.3 With Isocyanide Participation

A. Shaabani, A. Sarvary, and S. Shaabani

Isocyanide-based multicomponent reactions represent a very important synthetic method for the synthesis of heterocyclic compounds with potential biological and medicinal activities. The nucleophilic property of isocyanides makes them a popular reactant class for the development of novel multicomponent reactions. One of the isocyanide-based multicomponent reaction approaches involves the generation of a dipolar intermediate by the addition of isocyanides to electron-deficient α,β -unsaturated carbonyl compounds such as dialkyl acetylenedicarboxylates; the dipolar intermediate can then be captured efficiently by various dipolarophiles such as CH-, NH-, and OH-acids, electron-deficient alkenes, and imines to form diverse cycloadducts.

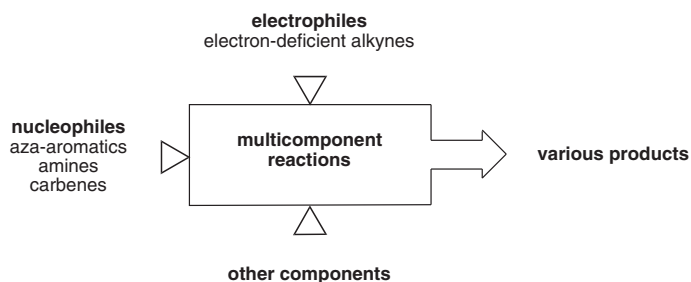


Keywords: isocyanides · α,β -unsaturated carbonyl compounds · dialkyl acetylenedicarboxylates · dipolar intermediates · dipolarophiles · heterocycles

2.1.4 Electron-Deficient Alkynes as Electrophiles

A. Shaabani, A. Sarvary, and S. Shaabani

This chapter describes multicomponent reactions involving electron-deficient alkynes as electrophiles. The main focus is the addition of nucleophiles such as aza-aromatics, amines, and carbenes to electron-deficient alkynes in the presence of various suitable components such as CH-, NH-, and OH-acids, carbonyl and imine compounds, and electron-deficient alkenes. These multicomponent reactions result in the synthesis of various heterocyclic and open-chain organic products.

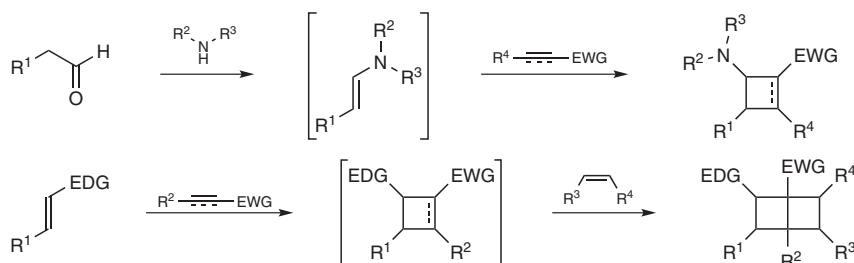


Keywords: electron-deficient alkynes · carbonyl compounds · electrophile · nucleophile · heterocycles · cyclization

2.1.5 [2 + 2] Cycloaddition as the Key Step

K. Takasu

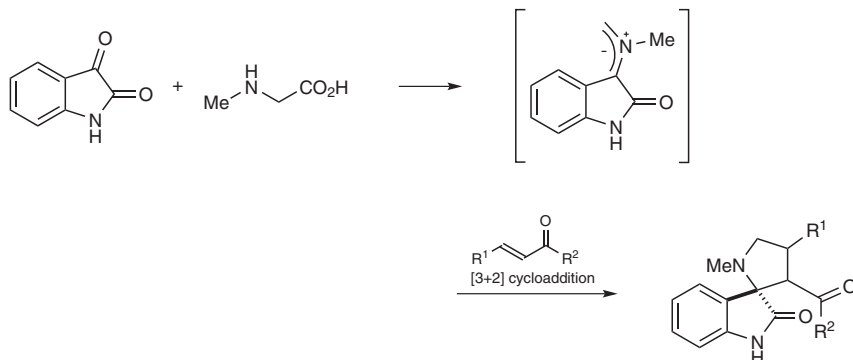
This chapter covers multicomponent reactions involving the thermal [2 + 2] cycloaddition of electron-rich alkenes, such as enamines, silyl enol ethers, allylsilanes, or styrenes, with electron-deficient alkenes or alkynes. In one strategy, the process affords multisubstituted and/or polycyclic four-membered carbocycles in a single operation. In another, the multicomponent reaction utilizes the [2 + 2] cycloadduct as an intermediate for further transformation.



Keywords: allylsilanes · cycloaddition · cyclobutanes · cyclobutenes · enamines · silyl enol ethers · styrenes

2.1.6 [3+2] Cycloaddition as the Key Step*R. Raghunathan and S. Purushothaman*

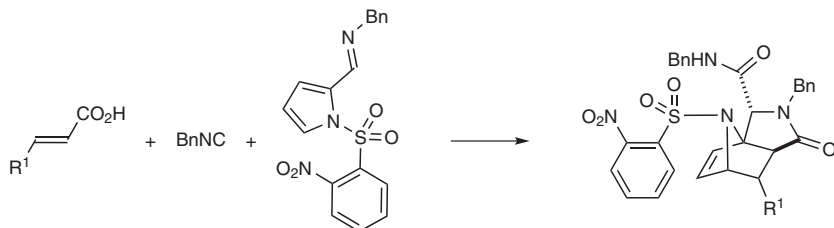
α,β -Unsaturated carbonyl compounds, which act as dipolarophiles in [3+2]-cycloaddition reactions with azomethine ylides, have been used for the highly regio- and stereoselective construction of heterocycles such as spiro-fused pyrrolidines. Azomethine ylides generated from isatin (1*H*-indole-2,3-dione) and cyclic and acyclic α -amino acids are considered to be important 1,3-dipoles, since their cycloaddition to α,β -unsaturated carbonyl compounds leads to the formation of spiro[indoline-3,2'-pyrrolidin]-2-ones, which form the basic building units of several natural and biologically active compounds.



Keywords: azomethine ylides · [3+2]-cycloaddition reactions · 1,3-dipoles · spiro-fused pyrrolidines · stereoselective synthesis · α,β -unsaturated carbonyl compounds

2.1.7 [4+2] Cycloaddition as the Key Step*M. C. Elliott and D. H. Jones*

α,β -Unsaturated carbonyl compounds are widely used as dienes and as dienophiles in [4+2] cycloadditions. This review covers those cycloaddition reactions in which a multicomponent reaction is used either in the formation of the α,β -unsaturated carbonyl compound or for the assembly of the final product. The review is organized according to the role of the carbonyl component (diene or dienophile) and whether it is introduced as a reagent or formed during the reaction.

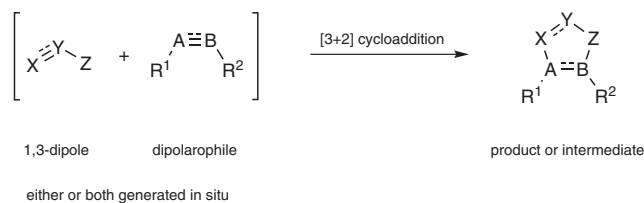


Keywords: alkenation · asymmetric synthesis · [4+2] cycloaddition · cyclohexenes · Diels–Alder reaction · diketones · enals · enones · isoindoles · Knoevenagel condensation · oxazoles · pyridines

2.2.1 [3+2] Cycloaddition

S. G. Modha and E. V. Van der Eycken

The cycloaddition reaction of a 1,3-dipole and a dipolarophile, commonly known as the [3+2]-cycloaddition reaction, has become well established over the years. Multicomponent reactions involving a [3+2] cycloaddition as the key step conveniently generate diversely substituted heterocycles. In contrast to Section 2.1.6, the focus here is on reactions not involving α,β -unsaturated carbonyl compounds.

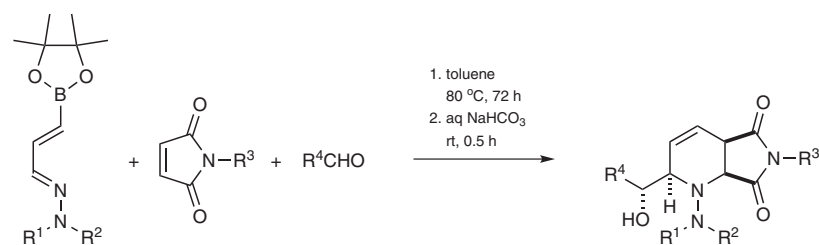


Keywords: alkynes · α -amino acids · azides · carbenes · dipolar cycloaddition · isoxazoles · nitrile oxides · nitrones · pyrroles · triazoles · ylides

2.2.2 [4+2] Cycloaddition

L. G. Voskressensky and A. A. Festa

The Diels–Alder reaction, with its diverse and extremely rich synthetic potential, is a powerful protocol in synthetic strategies toward natural and unnatural carbo- and heterocycles. This chapter describes multicomponent reaction sequences in which a [4+2]-cycloaddition reaction is a key step. In contrast to Section 2.1.7, the focus here is on cycloaddition reactions not involving α,β -unsaturated carbonyl compounds. Examples are described both where the [4+2] cycloaddition is the first step in the multicomponent sequence and where the [4+2] cycloaddition is a later step in the sequence, with the requisite diene and/or dienophile being formed in the initial steps.

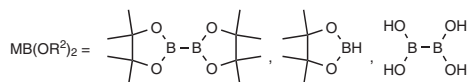


Keywords: Diels–Alder reaction · cycloaddition · dienes · heterodienes · dienophiles · carbocycles · heterocycles · allylboration · hydrovinylation · Povarov reaction · Knoevenagel reaction

2.3 Boron-Mediated Multicomponent Reactions

K. J. Szabó

Organoboronates are important reagents in modern synthetic applications. However, some organoboronates are unstable or difficult to purify. A possible solution is to perform organic transformations with in situ generated organoboronates. The organoboronates react selectively with many substrates, such as carbonyl compounds (allylation reactions) or organohalides (Suzuki–Miyaura coupling). Furthermore, synthesis of organoboronates and the subsequent transformations can be easily combined in the same reaction vessel. This chapter presents examples of these reactions including generation of organoboronates from simple prefunctionalized substrates (such as alcohols) and via C–H functionalization processes.



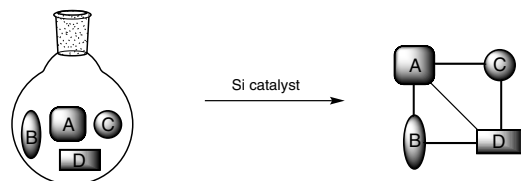
catalyst = Ir, Rh, Ru, or Pd complex; X = OH, OCOR⁴, Cl, Br, H

Keywords: homogeneous catalysis · C–B bond formation · allylation · Suzuki–Miyaura coupling · selectivity

2.4 Silicon-Mediated Multicomponent Reactions

J.-P. Wan

Silicon reagents are commonly employed in organic synthesis as catalysts or promoters because of their availability and versatile catalytic activity. Some typical silicon reagents, such as trimethylsilyl halides (where the halide is chlorine or iodine) or trimethylsilyl trifluoromethanesulfonate, are known to be capable of acting as Lewis acids, Brønsted acids (upon hydrolysis), and water scavengers. This section presents an overview of the particularly broad application of silicon reagents in multicomponent reactions. Silicon-mediated multicomponent processes that lead to both cyclic and acyclic products are summarized.

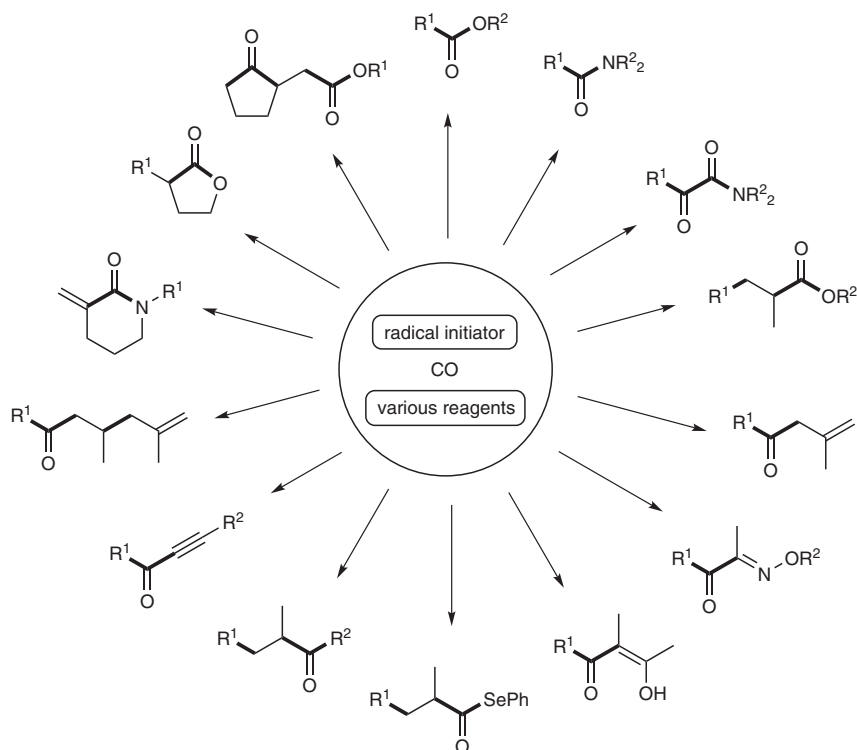


Keywords: Biginelli reactions · cyclization reactions · 1,3-dicarbonyl compounds · imidazoles · pyridine synthesis · quinoxalines · silicon reagents · tetrahydropyridinones · 1,3-thiazines

2.5 Free-Radical-Mediated Multicomponent Reactions Involving Carbon Monoxide

A. Fusano and I. Ryu

This review describes free-radical-mediated multicomponent reactions leading to a variety of carbonyl compounds, such as ketones, esters, amides, and the related cyclic carbonyl compounds, with introduction of carbon monoxide as the carbonyl function. All reactions are carried out in a single vessel using a stainless steel autoclave with a glass liner, and are therefore one-pot synthetic processes.



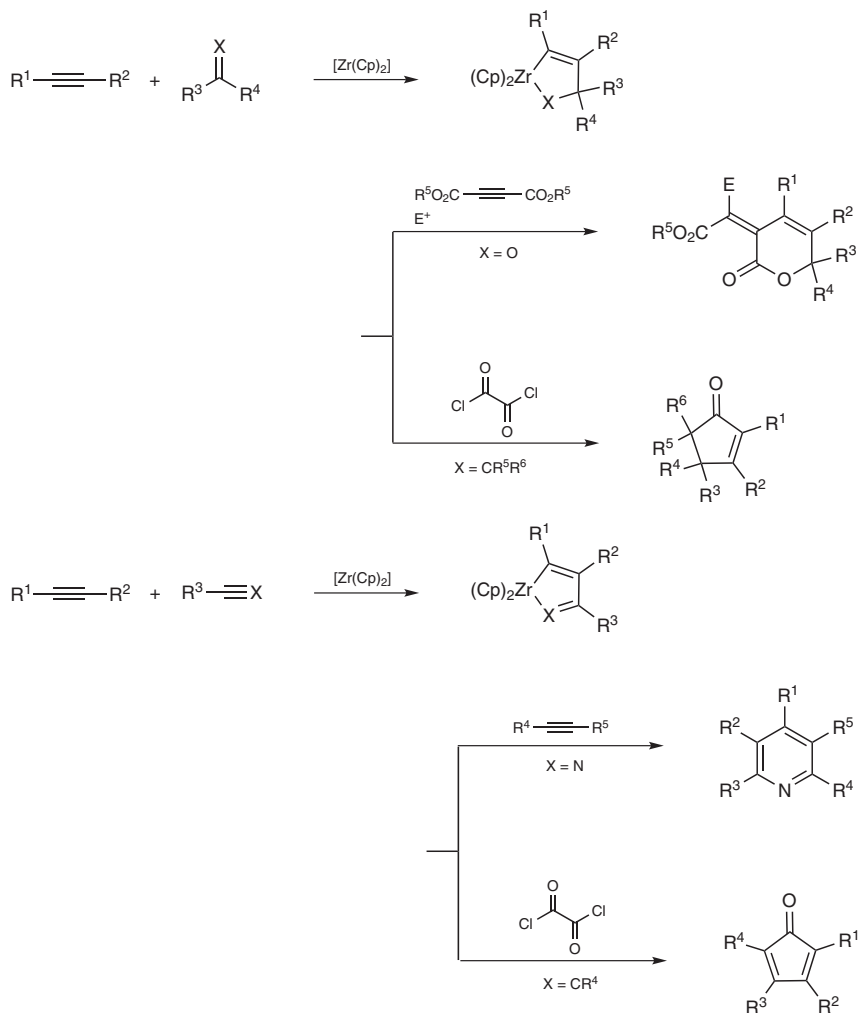
— = newly formed bond

Keywords: alkyl halides • carbon monoxide • carbonylation • carbonyl compounds • C—C bond formation • multicomponent reactions • radical addition • radical cyclization • radical reactions

2.6.1 Stoichiometric Metal Participation

C. Xi and C. Chen

Multicomponent reactions (MCRs) make possible the rapid synthesis of molecular libraries that have a high degree of structural diversity. Metal-mediated multicomponent reactions are particularly interesting as they give access to processes that occur with high chemo-, regio-, and stereoselectivity with excellent functional group tolerance. For example, reductive coupling of two unsaturated compounds on reduced zirconocene affords a variety of zirconacycles, which react with electrophiles to form various carbo- and heterocycles.



Keywords: carbene complexes · chemoselectivity · C–M bonds · main group metals · metallacycles · regioselectivity · stereoselectivity · stoichiometric reactions · transition metals

2.6.2 Catalytic Metal Participation*B. A. Arndtsen and J. Tjutrins*

Transition-metal-catalyzed multicomponent reactions are of great utility in organic synthesis. These transformations exploit the reactivity of metal catalysts to both activate simple substrates toward reactions, and control how they react, thereby allowing the assembly of structurally complex products in an efficient fashion via the coupling of simple building blocks. This chapter highlights a number of important examples of such transformations, with a focus on those that lead to formation of three or more bonds, from substrates that are both widely available and easily tuned.



Keywords: transition-metal catalysis • heterocycles • carbonylation reactions • reductive couplings • cycloadditions • cross-coupling reactions • 1,3-dipolar cycloaddition