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Base-mediated *C*-vinylation of ketones with alkynes: synthesis of β,γ-ethylenic ketones and their synthetic applications

Elena Yu. Schmidt, Nadezhda V. Semenova, Boris A. Trofimov*

A.E.Favorsky Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences, 664033 Irkutsk, Russian Federation

This review summarizes the latest advances in the chemistry of β,γ-ethylenic ketones, which have emerged over the last decade as valuable synthetic building blocks to create molecules of high complexity and diversity. This family of multifunctional γ-aryl-β,γ-ethylenic ketones has now become accessible owing to the discovery and systematic development of a new general $C(sp^3)–C(sp^2)$ bond-forming reaction, namely superbase-mediated *C*-vinylation of ketones with alkynes. In the context of the Favorsky reaction (the addition of acetylenic carbanions to the carbonyl group of ketones), this discovery represents a chemical paradox in the form of temperature-controlled inversion of electrophilicity and nucleophilicity of acetylenes and ketones. Various transformations of β,γ-ethylenic ketones: nucleophilic addition reactions, inverse-electron-demand Diels–Alder reactions, reactions involving a carbonyl group followed by transformations of functionalized adducts, *etc*. are discussed. The review also highlights the cascade reactions, in which the *in situ* formed β,γ-ethylenic ketones, are key intermediates in the synthesis of various highly functionalized carbo- and heterocyclic systems.
The bibliography includes 102 references.
Keywords: alkynes, ketones, ethylenic ketones, carbocycles, heterocycles, superbases, vinylation.

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1. Introduction

The aim of this review is to draw attention of the synthetic community to the synthesis of functionalized unsaturated carbo- and heterocyclic systems and to promote further research in this area on the platform of diverse transformations of β,γ-ethylenic ketones. The latter have rapidly gained status as multifaceted reaction partners due to the discovery in 2010 and systematic development of the new $C(sp^3)–C(sp^2)$ bond-forming reaction, representing superbase-catalyzed *C*-vinylation of ketones with alkynes. These compounds now occupy a prominent position in the toolkit of organic chemistry. The advantages of the reaction that leads to this family of β,γ-ethylenic ketones include its generality (it covers a practically inexhaustible range of ketones and diversely substituted aryl- and hetarylacetylenes), its high regio- and stereoselectivity, the availability and simplicity of transition-metal-free promoting systems (KOH/DMSO or KOBu^t/DMSO).

Despite significant progress in recent years in the study of β,γ-ethylenic ketones, a comprehensive survey of their rich chemistry is still lacking. Meanwhile, these newly accessible β,γ-ethylenic ketones are employed extensively in numerous chemical transformations, including the nucleophilic addition to various electrophiles, often accompanied by the cascade

E.Yu.Schmidt. Doctor of Chemical Sciences, Chief Researcher at the A.E.Favorsky Irkutsk Institute of Chemistry.
E-mail: LSCHMIDT@irioch.irk.ru
Current research interests: nucleophilic reactions of acetylenes involving superbases as reactants and catalysts, heterocyclic chemistry.
N.V.Semenova. Candidate of Sciences in Chemistry, Senior Researcher at the A.E.Favorsky Irkutsk Institute of Chemistry.
E-mail: nadya@irioch.irk.ru
Current research interests: organic synthesis based on the reaction of acetylene in superbasic media, heterocyclic chemistry.
B.A.Trofimov. Full Member of the Russian Academy of Sciences, Professor and Head of Research at the A.E.Favorsky Irkutsk Institute of Chemistry.
E-mail: boris_trofimov@irioch.irk.ru
Current research interests: organic synthesis based on acetylene and its derivatives, the chemistry of heterocyclic compounds, superbasic catalysis.

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cyclizations; asymmetric inverse-electron-demand Diels–Alder reaction; the formation of the corresponding functionalized adducts of the carbonyl group (*e.g.*, reactions with hydroxylamine, hydrazine, guanidine, *etc*.) and their further cyclizations; the cascade processes triggered by the nucleophilic addition of ketones to alkynes, in which the *in situ* generated β,γ-ethylenic ketones play a pivotal role as key intermediates in the synthesis of various practically important products.

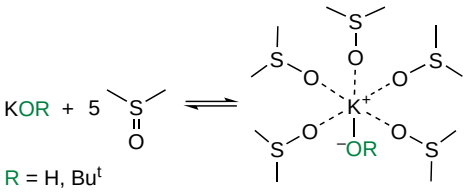
2. Background of the discovery

For more than a century, the base-mediated *C*-vinylation of ketones with terminal alkynes was considered impossible because it was known that, in the presence of bases, the ketones react with alkynes to produce tertiary propargyl alcohols or diols (classic Favorsky reaction).[1–3] This reaction has found wide application in both fine organic synthesis (vitamins, carotenoids, fragrance materials, isoprene and isoprenoids, drugs)[4–8] and industry (isoprene rubbers, surfactants, corrosion inhibitors, adjuvants for pesticides),[9] and has therefore been thoroughly studied.

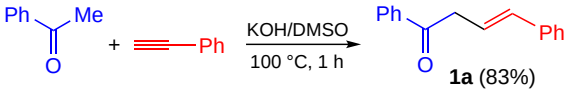
It should be emphasized that until 2010, no example of ketone addition (as *C*-nucleophiles) to a carbon-carbon triple bond in the presence of bases had been reported. The reasons why this issue had not arisen were of an experimental and theoretical nature. From an experimental perspective, it was common knowledge that acetylenic carbanions would aggressively attack an electrophilic carbonyl group (at room temperature or below) to form *O*-centred propargyl anions or the corresponding alkali metal alkoxides. Another reason was the understanding that acetylenic carbanions, partially present in the reaction mixture, cannot be attacked by nucleophiles (enolate anions). Theoretically, it was widely accepted that the carbanionic form of enolate anions was thermodynamically unfavorable compared to the *O*-centered one.[10]

However, the fact that Favorsky tertiary propargyl alcohols dissociate back into the starting ketones and alkynes when heated with bases (*retro*-Favorsky reaction) has not been considered.[11–14] Therefore, at elevated temperatures, the enolizable ketones can add to alkynes. It should also be taken into consideration that enolizable ketones are usually much more acidic than alkynes (by about 4 units of p*K*a, ~25 (Ref. 15) and ~29,[16,17] respectively) and hence, in basic media, the enolate-anions prevail whereas the ionization of alkynes is suppressed, that is to say, alkynes are mostly present in the reaction mixture in the non-ionized form. Thus, at elevated temperatures, conditions actually arise for the formation of the ketone adducts to the triple bond of alkynes. It is noteworthy that all the aforementioned processes and effects are more pronounced in strongly basic (superbasic) media,[18] which we systematically exploit to dramatically accelerate classic reactions of acetylenes[19,20] and to discover new ones.[21,22] For these purposes, the superbasic compositions of the type MOR/polar complexing nonhydroxylic solvent (M = Na, K, R = H, Alkyl) have been successfully used. The most universal and convenient systems are KOH/DMSO and KOBu^t/DMSO, which ensure the p*K*a values of 25–35.[23,24] According to the quantum chemical calculations, in these compositions, the potassium cation is coordinated with hydroxide or alkoxide anion and five molecules of DMSO (Scheme 1)[25–27] which makes RO^- anions more basic as they are separated from the cation by the solvent.

Scheme 1



Scheme 2



In light of the above rationale, one might expect the addition of deprotonated ketones to alkynes to be feasible. Indeed, our experiments confirmed this: when acetophenone was allowed to contact with phenylacetylene in the KOH/DMSO system at 100°C for 1 h, (*E*)-1,4-diphenyl-3-buten-1-one **1a**, a representative of γ-aryl-β,γ-ethylenic ketones, was isolated in 83% yield (Scheme 2).[28]

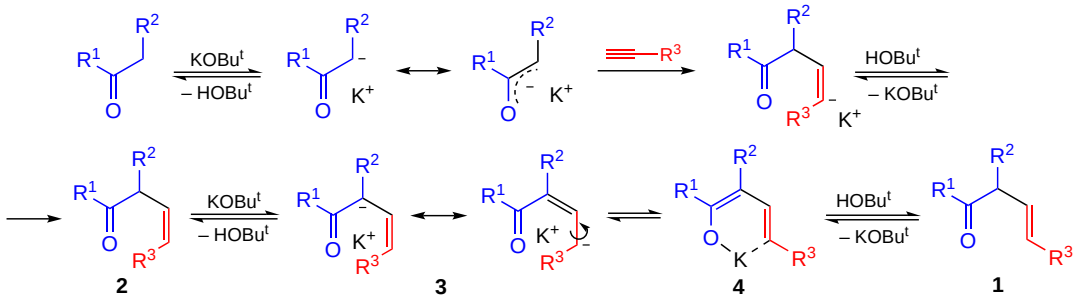
This was the discovery of the base-mediated *C*-vinylation of ketones with alkynes.

3. Characteristic features of *C*-vinylation of ketones with alkynes

This reaction appeared to be a general one, covering aliphatic, cycloaliphatic (including macrocyclic), aromatic, condensed aromatic, and heteroaromatic ketones, as well as various aryl and hetaryl alkynes.[28,29] Later,[30] the KOBu^t/DMSO system was found to be more versatile and convenient than KOH/DMSO and other superbasic systems. This allowed the *C*-vinylation of ketones to be carried out in a shorter time (30 min). Consequently, a wide variety of the corresponding β,γ-ethylenic ketones **1** became readily accessible right away.

The discovered reaction, involving the addition of the enolate-anions to terminal alkynes, should follow the classic nucleophilic *trans*-addition rule[31] to afford *Z*-adducts **2** (Scheme 3). The later, apparently, tend to undergo the *Z*→*E* isomerization in their deprotonated form **3**, wherein a free

Scheme 3



R^1 = Alk, Ar, Het; R^2 = H, Alk, Ar; R^1–R^2 = $(CH_2)_n$; R^3 = Ar, Het

rotation of the aryl group (R^3) around the former double bond is allowed. The driving force of such an isomerization may be the chelation of the potassium cation with the participation of the carbonyl group and the arylethenyl moiety in the six-π-electron quasi-aromatic dienolates **4**, which fixe the *E*-configuration.

Importantly, the adducts of ketones to alkynes, (*E*)-γ-aryl-β,γ-ethylenic ketones **1**, are by virtue substituted styrenes. This means that despite the possibility of its migration towards the carbonyl group to form α,β-ethylenic isomers, the double bond remains conjugated with the aryl moiety (R^3 in Scheme 3). This stereo- and regioselective synthesis of β,γ-ethylenic ketones **1** results from the energetically more favourable conjugation of the double bond with aryl substituent rather than with the carbonyl function that was supported by quantum chemical calculations.[30]

The efficient straightforward transition metal-free *C*-vinylation of ketones with terminal alkynes using inexpensive starting materials under operationally simple conditions makes β,γ-ethylenic ketones **1** an easily accessible class of compounds, which represent valuable reagents due to their multifaceted reactivity. The unusual stability of these β,γ-ethylenic ketones, which are not prone of transforming into α,β-isomers, substantially extends the application potential of these new synthetic building blocks.

Before the above *C*-vinylation of ketones with alkynes become the public knowledge,[28–30] a number of syntheses of β,γ-ethylenic ketones were known, particularly those employing allyl-[32,33] or alkenylmetals,[34,35] oxidation of homoallylic alcohols,[36,37] ruthenium-catalyzed hydroacylation of dienes,[38,39] dimerization/hydration of aryl acetylenes catalyzed by [Cp*Ru(NCMe)$_3^+$PF$_6^-$]/*p*-TSA (Cp* is pentamethylcyclopentadienyl, TSA is *p*-toluenesulfonic acid).[40] A common approach to the synthesis of β,γ-ethylenic ketones is the acylation of olefins,[41–43] but this is complicated by the prototropic migration of the double bond, which gives rise to conjugated α,β-ethylenic isomers. Relatively accessible β,γ-ethylenic ketones were prepared by allylation of acyl chlorides,[44–47] however these protocols were characterized[48] as having limited applications since they are tedious and time-consuming.

It is no surprise that none of these methods allowed β,γ-ethylenic ketones to become popular synthons in organic synthesis. As mentioned above, a fundamental cause of this is the easy transformation of β,γ-ethylenic ketones into their α,β-isomers, which are usually thermodynamically more stable, and which often occurs in the course of the process. At the same time, most β,γ-ethylenic ketones of type **1** synthesized according to Scheme 3, are stable with respect to the migration of the double bond, because it is in a stronger conjugation with the aromatic moiety than with the carbonyl group.

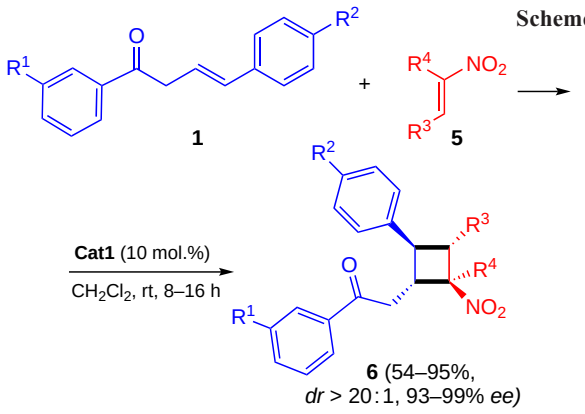
4. γ-(Het)aryl-β,γ-ethylenic ketones in organic synthesis

The three different reaction centers of ketones **1** (carbonyl function, double bond and α-CH active group) promise these compounds to have a rich and intriguing chemistry. Overall, the β,γ-ethylenic ketones **1**, synthesized by the base-mediated *C*-vinylation of ketones with aryl alkynes, have all the prerequisites to become versatile synthons in current organic synthesis.

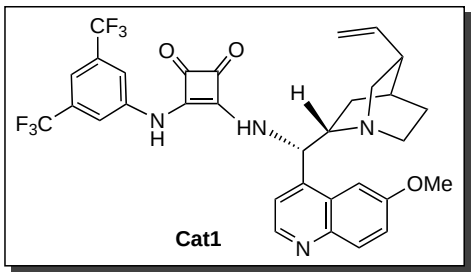
4.1. Synthesis of carbocyclic compounds

The chiral squaramide (**Cat1**)-catalyzed regio-, diastereo-, and enantioselective double Michael addition of β,γ-ethylenic

Scheme 4



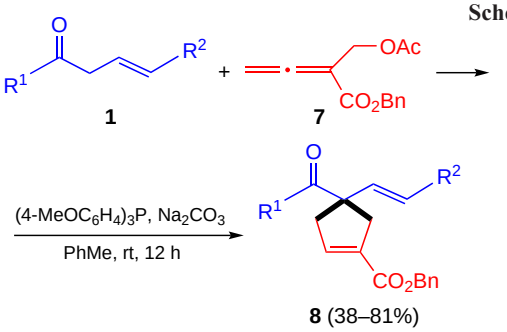
R^1 = H, Cl, Br; R^2 = H, MeO, F;
R^3 = Bu^n, Ph, PhCH$_2$CH$_2$, 4-MeOC$_6$H$_4$, 4-FC$_6$H$_4$, 2-ClC$_6$H$_4$, 4-ClC$_6$H$_4$, 2-BrC$_6$H$_4$, 3-BrC$_6$H$_4$, 4-BrC$_6$H$_4$, 4-O$_2$NC$_6$H$_4$;
R^4 = Me, Et; Cat is catalyst, *dr* is diastereomeric ratio, *ee* is enantiomeric excess



ketones **1** to nitro alkenes **5** was achieved (Scheme 4).[†,49] This cascade reaction provided pentasubstituted cyclobutanes **6** bearing four contiguous stereocentres in good yields with a diastereomeric ratio of >20:1 and high enantioselectivities. The reaction starts with the addition of the γ-CH group of ethylenic ketone **1** to nitroolefin with subsequent cyclization involving the β-carbon atom of the same ketone to form the [2+2] cycloaddition adducts.

The tertiary phosphine-catalyzed [4+1] annulation of β,γ-ethylenic ketones **1** with β′-acetoxy allenoate **7** was reported.[50] In this reaction, the β,γ-ethylenic ketones serve as α-C,α-C′-bisnucleophiles. The reaction proceeds in toluene at room temperature using (4-MeOC$_6$H$_4$)$_3$P as a catalyst and Na$_2$CO$_3$ as a base to afford functionalized cyclopentenes **8** in moderate to good yields (Scheme 5).[50]

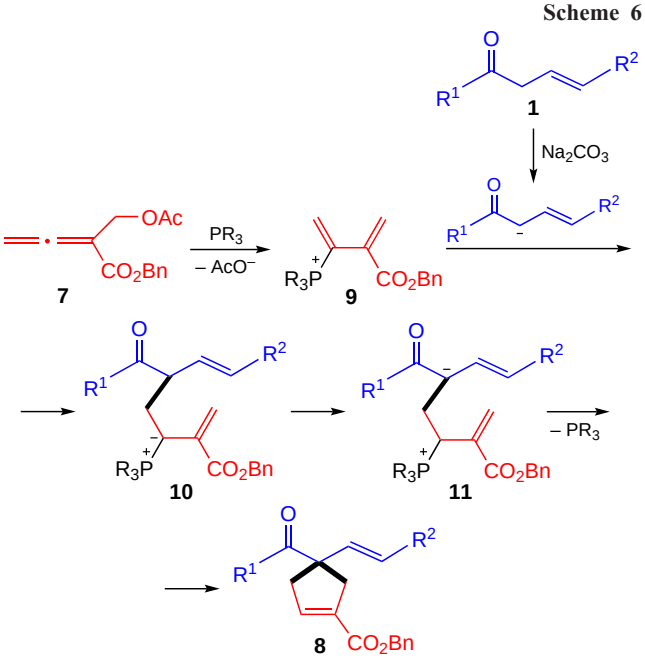
Scheme 5



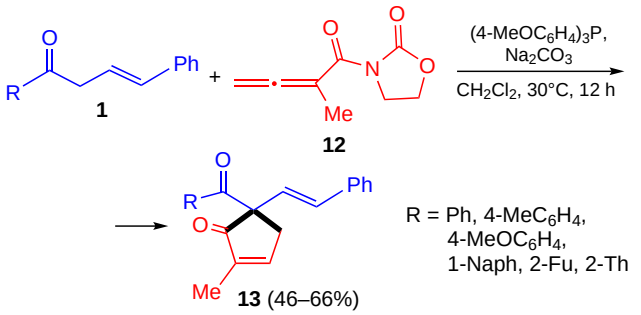
R^1 = Me, Ph, 2-BrC$_6$H$_4$, 3-MeC$_6$H$_4$, 4-MeC$_6$H$_4$, 3-MeOC$_6$H$_4$, 4-MeOC$_6$H$_4$, 4-FC$_6$H$_4$, 4-ClC$_6$H$_4$, 4-BrC$_6$H$_4$, 2-Naph, 2-Fu, 2-Th;
R^2 = Ph, 2-Naph; Naph is naphthyl, Fu is furyl, Th is thienyl

[†] Hereinafter, the C–C bonds formed during the reaction are highlighted with bold black lines.

Scheme 6



Scheme 7

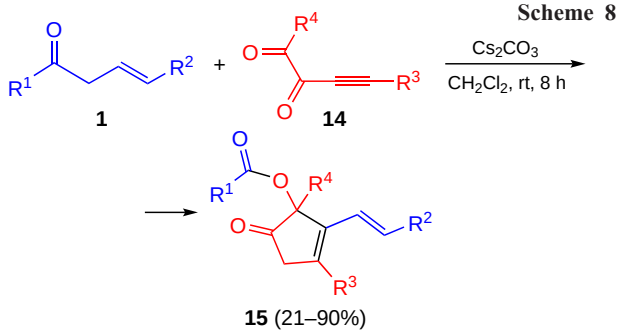


Apparently, this annulation involves the nucleophilic attack of deprotonated ketones **1** at the vinyl phosphonium intermediate **9** to form zwitterionic adducts **10** (Scheme 6).[50] Next, the intermediate zwitterions **11** undergo cyclization to afford cyclopentenes **8** and regenerate the phosphine catalyst.

A similar $(4\text{-MeOC}_6H_4)_3P$-catalyzed [4+1] annulation of β,γ-ethylenic ketones **1** with allenyl imide **12** was implemented to furnish substituted 2-cyclopent-2-en-1-ones **13** (Scheme 7).[51]

In the presence of $CaCO_3$, β,γ-ethylenic ketones **1** undergo a cascade reaction with alkynyl 1,2-diketones **14** to give 2-acyloxycyclopent-3-enones **15** (Scheme 8),[52] which are key units in a variety of natural products and pharmaceutically active compounds.[53]

Scheme 8

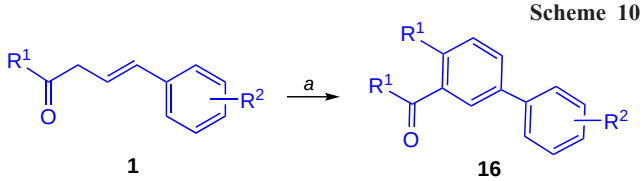


R^1 = Me, Ph, 4-MeC_6H_4, 3-ClC_6H_4, 4-BrC_6H_4;
R^2 = Ph, 4-MeC_6H_4, 4-ClC_6H_4;
R^3 = $n\text{-C}_6H_{13}$, Ph, 4-EtC_6H_4, 3-ClC_6H_4,4-ClC_6H_4, 3-Th;
R^4 = Et, Ph, 4-MeC_6H_4, 4-MeOC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4

This process starts with the addition of deprotonated ketones **1** to alkynyl 1,2-diketones **14** followed by aldol-type intramolecular cyclization and the C–C bond cleavage (Scheme 9).[52]

Upon heating in the KOBu^t/DMSO (100°C, 4 h)[54] or Cs_2CO_3/dioxane (90°C, 13 h)[55] systems, β,γ-ethylenic ketones **1** smoothly convert to acylated terphenyls **16**, which are actually dimers of ketones **1** without the substituted toluene moiety (Scheme 10).

Scheme 10

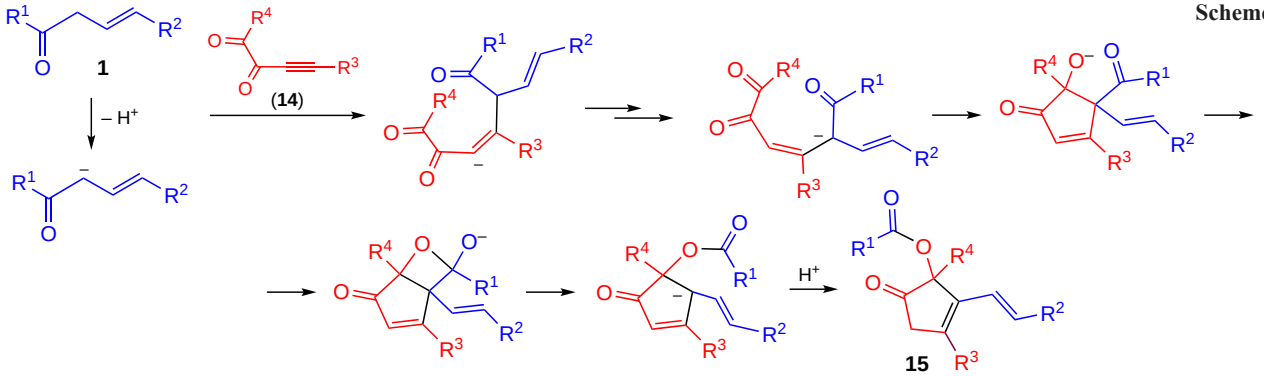


(*a*) KOBu^t/DMSO or Cs_2CO_3/dioxane;
R^1 = Ph, 4-MeC_6H_4, 3-MeOC_6H_4, 4-MeOC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, $3,4\text{-(MeO)}_2C_6H_3$, 2-Th;
R^2 = H, 4-Me, 4-Et, 4-Ph, 4-MeO, 4-EtO, $3,4\text{-(MeO)}_2$, 4-F, 4-Cl, 2-Br-4,5-$(MeO)_2$

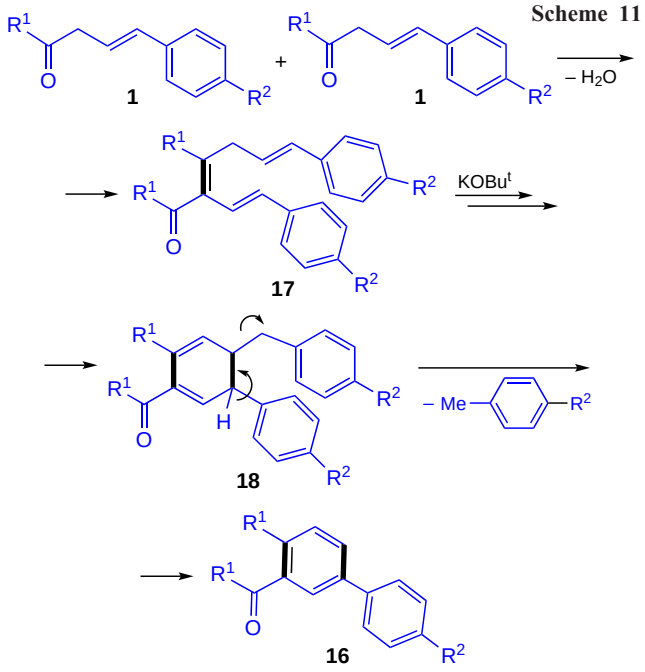
Dimerization of β,γ-ethylenic ketones **1** proceeds *via* a crotonic condensation. The resulting trienes **17** then undergo base-catalyzed cyclization to dihydrobenzenes **18** (Scheme 11). The latter then undergo aromatization *via* the elimination of methyl aromatics from the dihydrobenzene moiety. The final stage of this cascade sequence was confirmed experimentally.

The synthesis of acyl terphenyls **16** including complex polyaromatic systems **16a**–**c** (important building blocks for materials science)[56–58] was performed *via* base-promoted *C*-vinylation of acetyl(het)arenes with aryl alkynes in a one-pot manner without isolating intermediate β,γ-ethylenic ketones **1** (Scheme 12).[59]

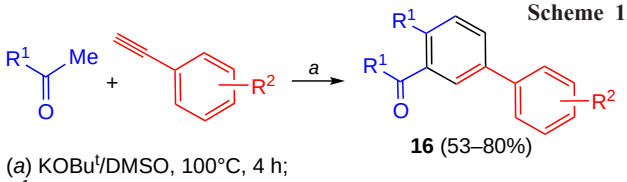
Scheme 9



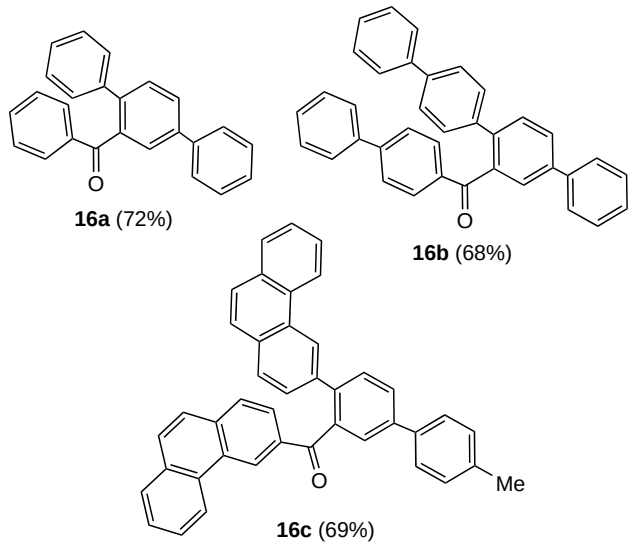
Scheme 11



Scheme 12



(*a*) KOBu^t/DMSO, 100°C, 4 h;
R^1 = Ph, 4-MeC_6H_4, 4-FC_6H_4, 4-PhC_6H_4, phenanthren-2-yl, 2-Th;
R^2 = H, 4-Me, 4-Ph, 3-F



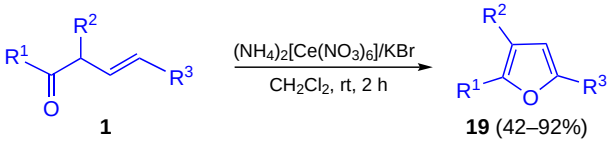
4.2. Synthesis of heterocyclic compounds

4.2.1. Synthesis of oxygen heterocycles

The formation of 2,5-disubstituted furans **19** from the *in situ* generated β,γ-ethylenic ketones **1** was first described by the reaction of acetophenone or 2-acetylnaphtalene with 2-nitrophenyl acetylene in the presence of the KOH/DMSO system (Scheme 13).[28] Here, the intermediate dienolates **20** undergo cyclization to dihydrofurans **21**, which are further oxidized (probably by the NO_2 moiety) to give furans **19** (see Scheme 13).

Subsequently, various 2,5-di(het)aryl substituted furans **19** were synthesized through the oxidative cyclization of ketones **1** in the presence of $(NH_4)_2[Ce(NO_3)_6]$/KBr oxidizing composition (Scheme 14).[60]

Scheme 14



R^1= Ph, 4-MeC_6H_4, 4-PhC_6H_4, 4-MeOC_6H_4, 4-FC_6H_4, 2-Naph, 2-Fu, 2-Th; R^2 = H, Me; R^3= Ph, 4-EtC_6H_4, 4-FC_6H_4

A chiral dipeptide-phosphonium salt (**Cat2**)-catalyzed regio- and stereoselective reaction of β,γ-ethylenic ketones **1** with 2-nitroindoles, 2-nitrobenzofurans, and 2-nitrobenzothiophenes afforded three types of dihydrofuro-fused [2,3-*b*]-hetarene systems **22** in high yields and with excellent stereoselectivities (Scheme 15).[61]

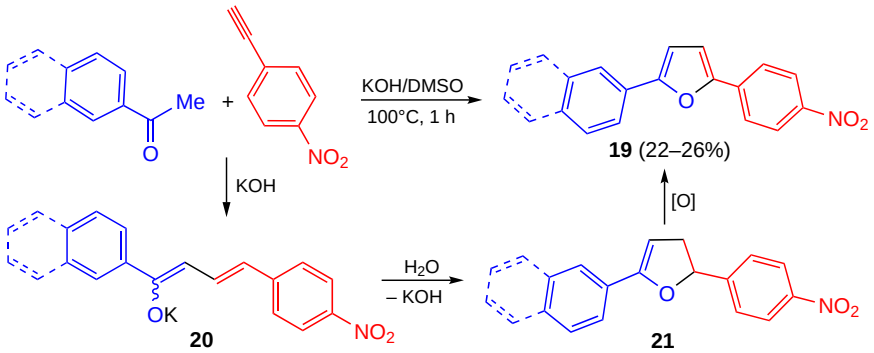
This reaction cascade involves a nucleophilic attack of deprotonated ketones **1** on the 2-nitro substituted heterocycle followed by the intramolecular substitution of the nitro group by the *O*-centered anion of intermediates **23** (Scheme 16).[61]

In the presence of the 1,4-diazabicyclo[2.2.2]octane (DABCO)/Cs_2CO_3 catalytic dyad (DABCO is 1,4-diazabicyclo[2.2.2]octane), β,γ-ethylenic ketones **1** undergo the [3+3] annulation with allenyl imides **24** providing tetrasubstituted 2-pyranones **25**, in generally high yields (Scheme 17).[51]

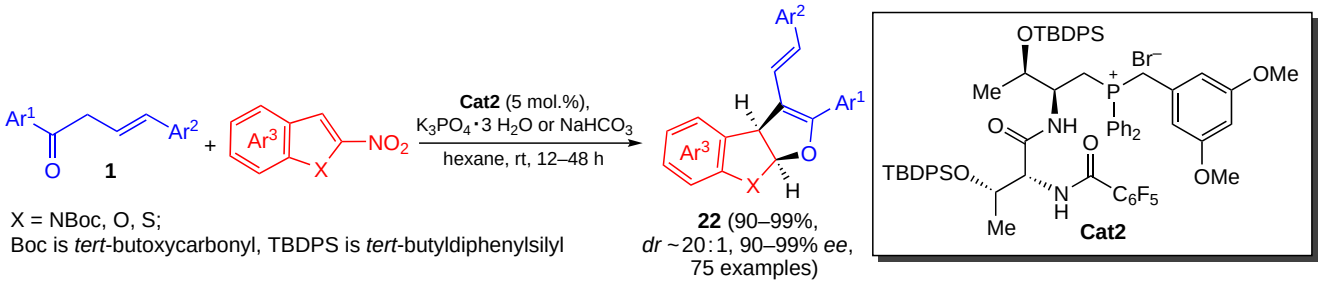
The reaction is initiated by the addition of DABCO to allenyl imides **24** with the release of the 2-oxazolidinyl anion and generation of adducts **26**.[51] Then, these adducts **26** are attacked by deprotonated β,γ-ethylenic ketone **1** leading to zwitterionic intermediates **27** (Scheme 18). After that, the latter eliminates DABCO to produce ketenyl derivatives **28**. Intramolecular nucleophilic addition into enolates **29**, isomerization, and protonation finalize the process.

The organocatalytic reaction of β,γ-ethylenic ketones **1** with hydroxynitroolefins **30** provided access to functionalized tetrahydropyrans **31** (Scheme 19).[62] High diastereo- (>20:1 *dr*)

Scheme 13

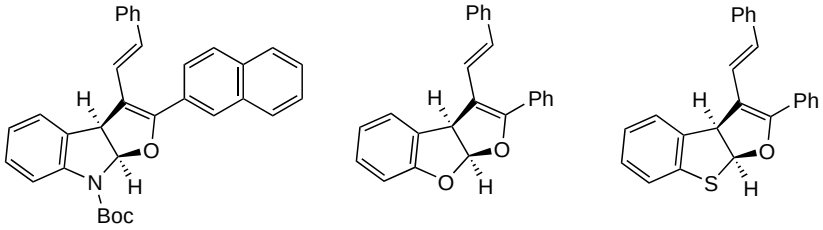


Scheme 15



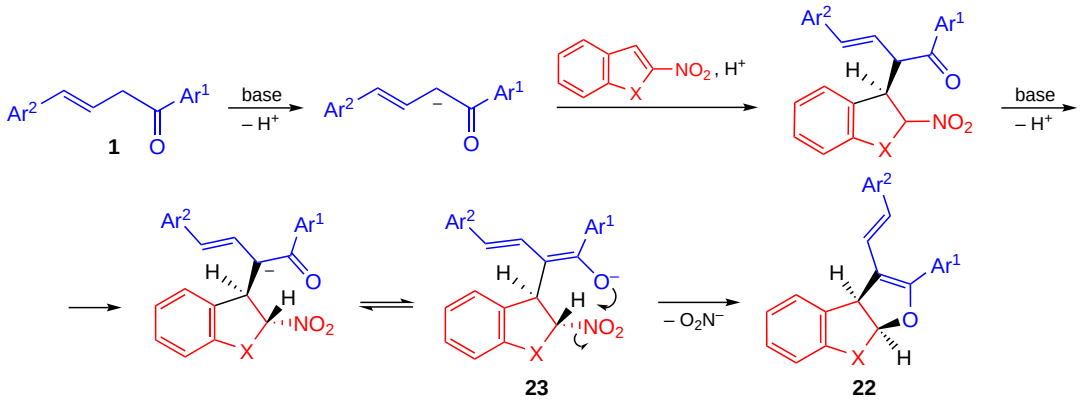
X = NBoc, O, S;
Boc is *tert*-butoxycarbonyl, TBDPS is *tert*-butyldiphenylsilyl

22 (90–99%, *dr* ~20:1, 90–99% *ee*, 75 examples)

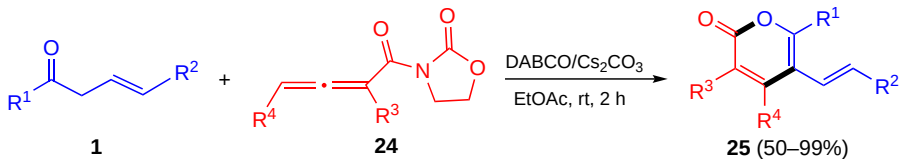


22a (95%, 99% *ee*) **22b** (95%, 99% *ee*) **22c** (90%, 94% *ee*)

Scheme 16

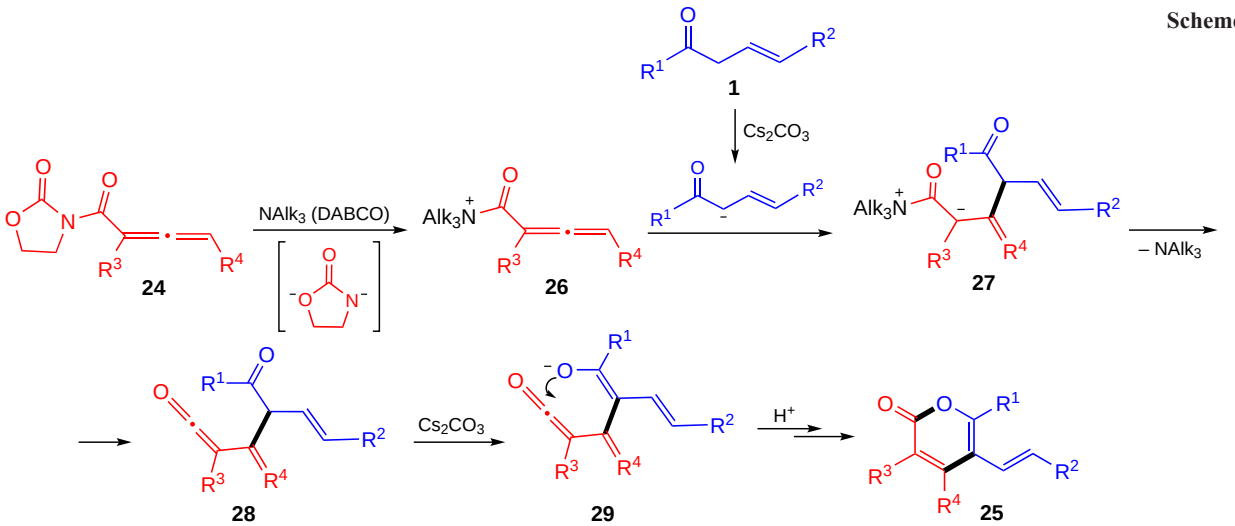


Scheme 17

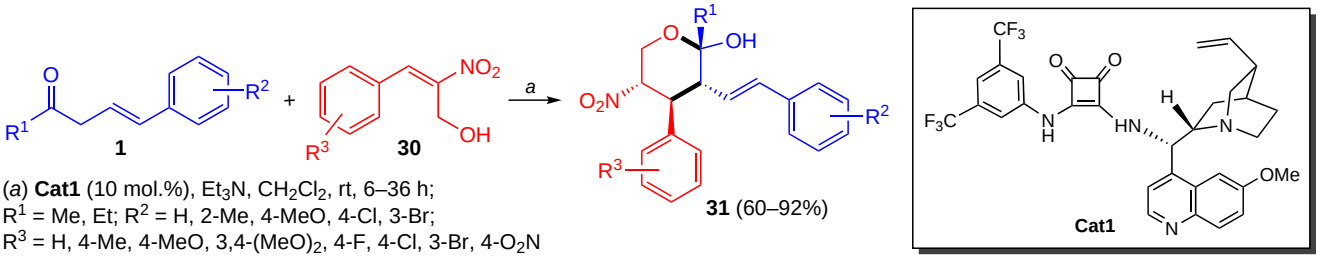


R^1 = Me, Ph, 3-MeC_6H_4, 3-ClC_6H_4, 4-MeC_6H_4, 4-n-$C_5H_{11}C_6H_4$, 4-MeOC_6H_4, 4-FC_6H_4, 1-Naph, 2-Fu, 2-Th;
R^2 = Ph, 4-MeOC_6H_4, 4-FC_6H_4, 4-ClC_6H_4;
R^3 = H, Me; R^4 = Me, Et, Bn

Scheme 18



Scheme 19



(*a*) **Cat1** (10 mol.%), Et_3N, CH_2Cl_2, rt, 6–36 h;
R^1 = Me, Et; R^2 = H, 2-Me, 4-MeO, 4-Cl, 3-Br;
R^3 = H, 4-Me, 4-MeO, 3,4-$(MeO)_2$, 4-F, 4-Cl, 3-Br, 4-O_2N

and enantioselectivities (in most cases, 93–97% *ee*) were achieved using a bifunctional squaramide (**Cat1**)/Et_3N catalytic pair. Mechanistically, this cascade reaction involves the initial addition of the deprotonated ketones **1** to nitroolefin **31** followed by cyclization involving the carbonyl carbon atom.[62] Synthetic applications of tetrahydropyran products **31** were demonstrated by their transformation to a series of polycyclic compounds, including the euroticin B[63] analogue.

Polycondensed pyrans of higher complexity (functionalized 1,3-dioxolochromans **33**) were assembled stereoselectively by the chiral phosphonium salt (**Cat3**)-catalyzed reaction of β,γ-ethylenic ketones **1** with *ortho*-quinone methides **32** (Scheme 20).[64]

The reaction proceeds *via* the prototropic isomerization/deprotonation of β,γ-ethylenic ketones **1** and the addition of γ-carbanions **34** thus formed to the activated double bond of *ortho*-quinone methide **32** followed by the intramolecular addition of *O*-centered anions **35** to the β-carbon atom of the ethylenic ketone counterpart (Scheme 21).[64]

The synthesis of 1,3-dioxolochromans **33** was also realized *via* the asymmetric domino oxidation/annulation of β,γ-ethylenic ketones **1** with 2-alkenyl phenols **36** (precursors of *ortho*-quinone methides **32**). The process employed silver oxide as the oxidant and the same chiral phosphonium salt **Cat3** as catalyst (Scheme 22). This modified synthesis is highly efficient, affording polycondensed pyrans **33** in high yields, and with good diastereo- and enantioselectivities.[64]

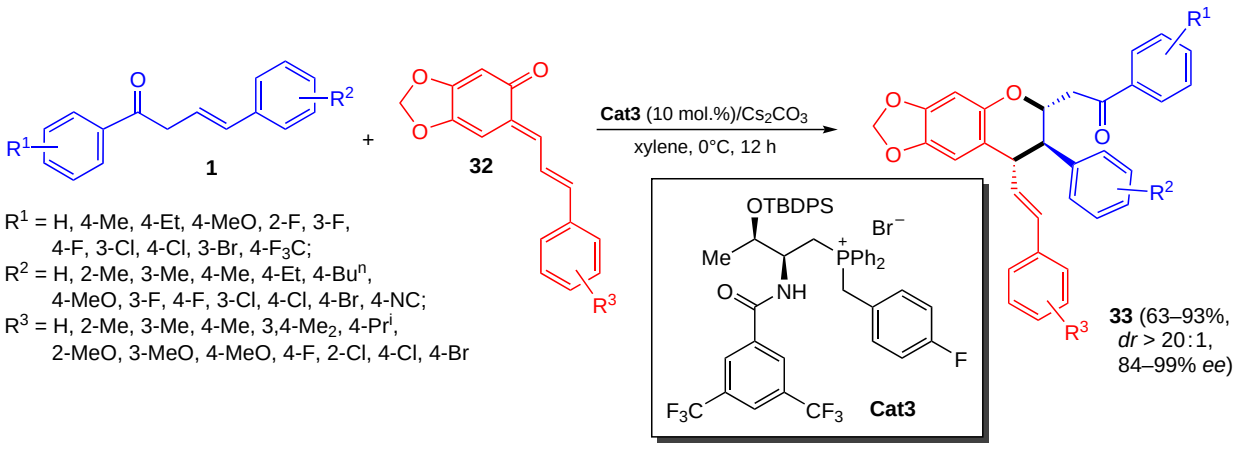
An asymmetric organocatalytic cascade reaction of fluorine-containing β,γ-ethylenic ketones **1** with α,β-unsaturated ketoesters **37** leading to fluorinated chiral pyrans **38** under mechanochemical activation was accomplished (Scheme 23).[65]

In the first step of pyrans **38** assembly, dienolates of β,γ-ethylenic ketones add to ketoester **37** (Scheme 24). The pyrane ring is then formed by the intramolecular addition of *O*-centered anions of intermediates **39** to the activated double bond. The quinine organocatalyst binds preferentially only dienolate and thus antiperiplanar arrangement in the transition state is preferred leading to (*S*,*S*,*S*)-configured pyrans **38**.

β,γ-Ethylenic ketones **1** find a wide application as dienophiles in the asymmetric inverse-electron-demand Diels–Alder reaction with various functionalized dienes. This universal strategy ensures the synthesis of pharmaceutically valuable richly functionalized pyran derivatives.

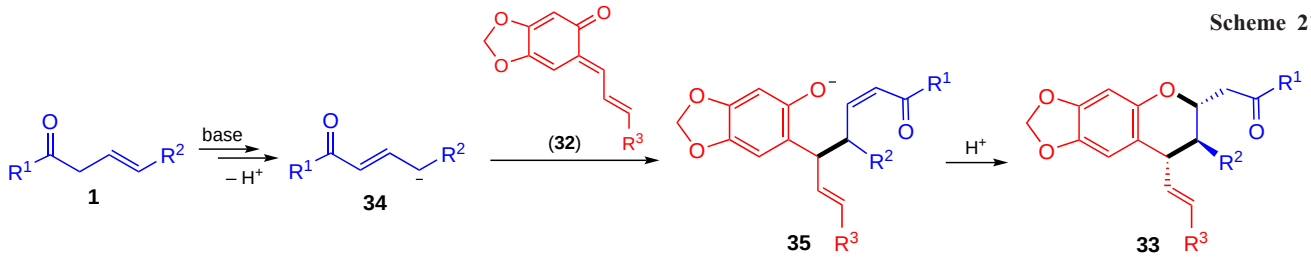
Along this line, the Diels–Alder reaction of β,γ-ethylenic ketones **1** and alkenyl 1,2-diketones **40** in the presence of a chiral bifunctional thiourea catalyst **Cat5** provides highly functionalized dihydropyrans **41** bearing three consecutive

Scheme 20

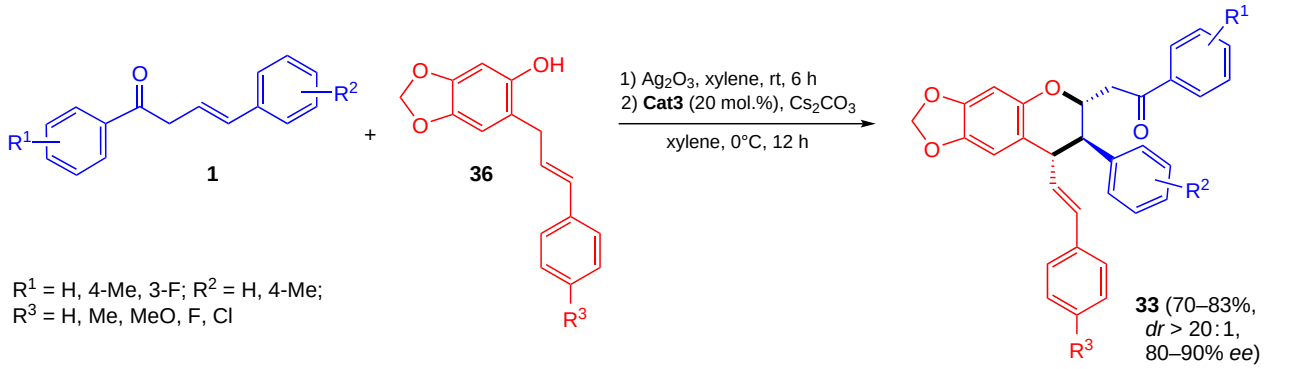


R^1 = H, 4-Me, 4-Et, 4-MeO, 2-F, 3-F, 4-F, 3-Cl, 4-Cl, 3-Br, 4-F_3C;
R^2 = H, 2-Me, 3-Me, 4-Me, 4-Et, 4-Bu^n, 4-MeO, 3-F, 4-F, 3-Cl, 4-Cl, 4-Br, 4-NC;
R^3 = H, 2-Me, 3-Me, 4-Me, 3,4-Me_2, 4-Pr^i, 2-MeO, 3-MeO, 4-MeO, 4-F, 2-Cl, 4-Cl, 4-Br

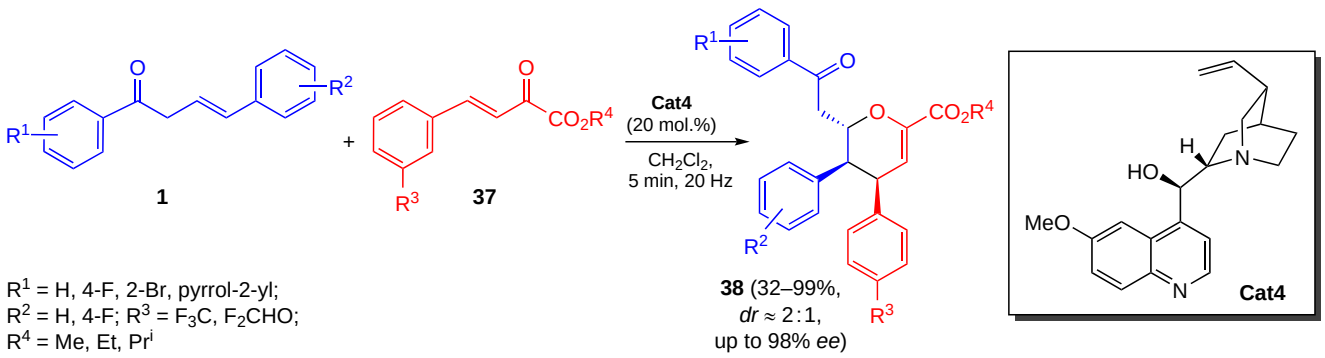
Scheme 21

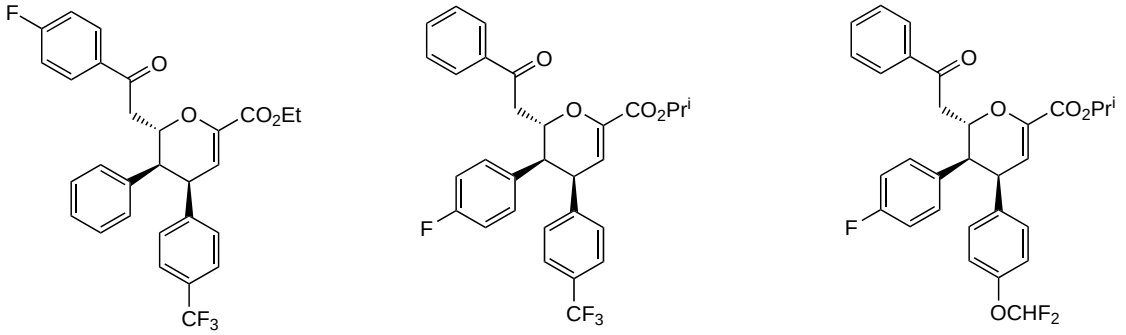


Scheme 22

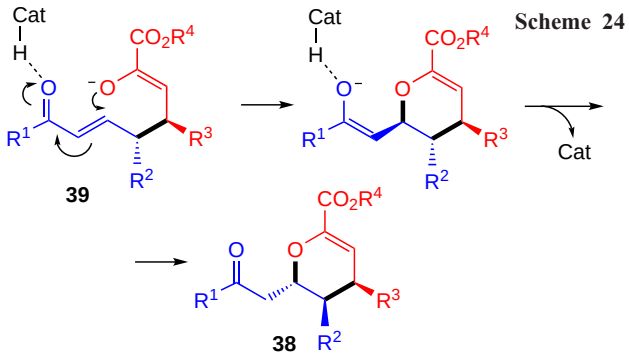


Scheme 23





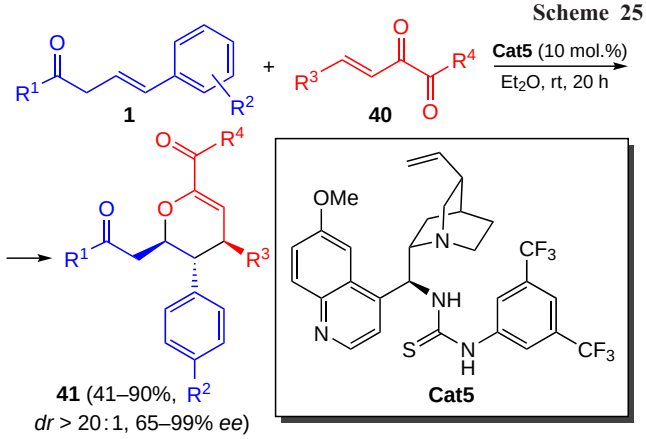
Scheme 24



stereocentres with good to excellent enantioselectivities (Scheme 25).[66]

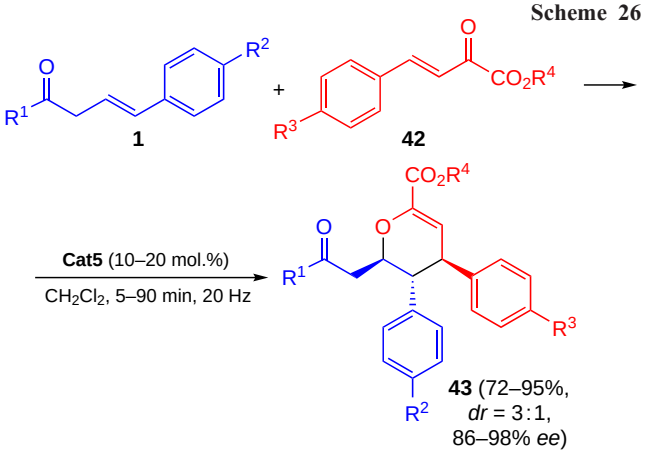
A similar transformation of β,γ-ethylenic ketones **1** with unsaturated keto esters **42**, promoted by the same bifunctional thiourea catalyst **Cat5** under mechanochemical activation, affords tetrasubstituted chiral dihydropyrane derivatives **43** (Scheme 26).[67]

Scheme 25



R^1 = Me, Bu^t, Ph, 4-MeC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4;
R^2 = H, 4-Et, 4-EtO, 3-F, 4-Cl;
R^3 = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-FC_6H_4, 4-ClC_6H_4, 3,4-$Cl_2C_6H_3$, 2-Fu;
R^4 = Me, Ph, 4-$Bu^tC_6H_4$, 2-$MeOC_6H_4$, 4-$MeOC_6H_4$, 4-ClC_6H_4, 4-BrC_6H_4

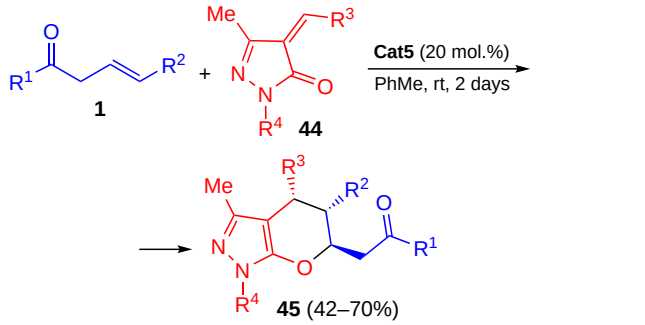
Scheme 26



R^1 = Ph, 4-MeC_6H_4, 2-Fu, 2-Th, 1-methylpyrrol-2-yl;
R^2 = H, Me, MeO; R^3 = H, MeO, Cl, Br; R^4 = Me, Et, Bn

The catalyst **Cat5** was successfully employed in the [4+2] cycloaddition of β,γ-ethylenic ketones **1** with alkylidene pyrazolones **44** to produce tetrahydropyrano[2,3-*c*]pyrazoles **45** with high diastereo- and enantioselectivities and in moderate to good yields (Scheme 27).[68]

Scheme 27



R^1 = Ph, 4-MeC_6H_4, 3-MeOC_6H_4, 3-FC_6H_4, 3-ClC_6H_4, 3-BrC_6H_4, 4-FC_6H_4, 3-ClC_6H_4, 1-Naph, 2-Fu, 2-Th;
R^2 = 4-MeOC_6H_4, 4-FC_6H_4, 4-ClC_6H_4; R^3 = H, Me; R^4 = Me, Et, Bn

The catalyst **Cat5** was found to be effective in the enantioselective inverse-electron-demand oxa-Diels–Alder reaction of β,γ-ethylenic ketones **1** with 5-alkenyl thiazolones **46** to afford highly functionalized pyrano[2,3-*d*]thiazoles **47** with excellent enantioselectivity (Scheme 28).[69]

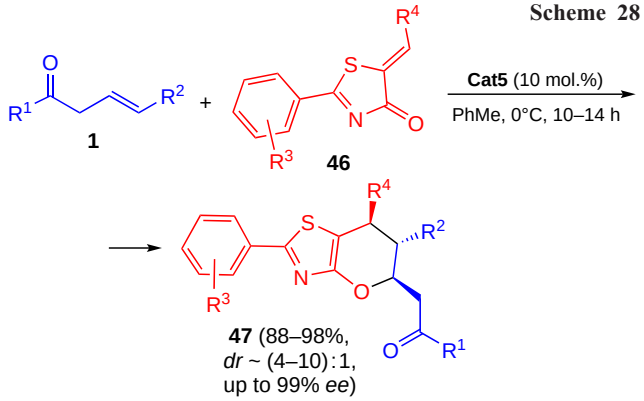
Enantioenriched 3,4′-pyranyl spirooxindole derivatives **48** bearing three contiguous chiral centres were synthesized *via* the chiral bifunctional squaramide (**Cat6**)-catalyzed asymmetric inverse-electron-demand oxa-Diels-Alder reaction of structurally diverse β,γ-ethylenic ketones **1** and β,γ-unsaturated α-keto esters **49** (Scheme 29).[70]

The asymmetric inverse-electron-demand Diels–Alder reaction between ketones **1** and unsaturated α-ketoamides **50** assisted by a chiral bifunctional Zn-ProPhenol catalyst **Cat7** leads to various biologically important dihydropyrans **51** in good yields and with good stereoselectivity (Scheme 30).[71]

In the presence of the DBU/DMSO system (DBU is 1,8-diazabicyclo[5.4.0]undec-7-ene), β,γ-ethylenic ketones **1** react with β-phenyl ethenesulfonyl fluoride **52** to afford γ-alkenylated δ-sultones **53** in close to quantitative yields (Scheme 31).[72]

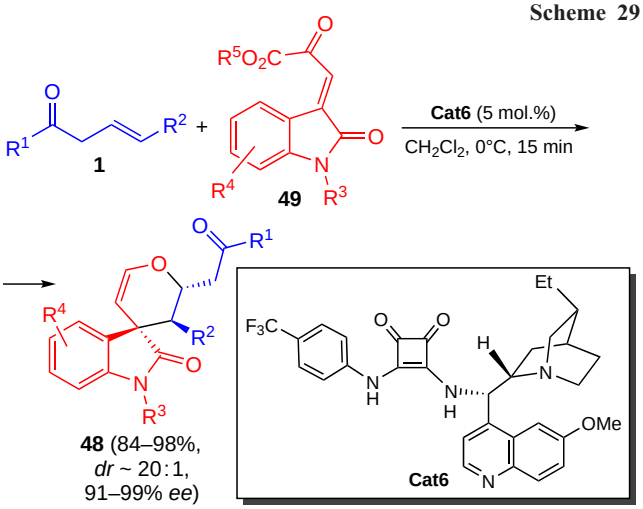
The formation of δ-sultones **53** (Scheme 32)[72] is initiated by the Michael addition of deprotonated ketones **1** to the double bond of ethenesulfonyl fluoride **52**. Subsequent 1,3-prototropic

Scheme 28



R^1 = Me, Ph, 4-n-$C_5H_{11}C_6H_4$, 2-MeC_6H_4, 3-MeC_6H_4, 4-MeOC_6H_4, 3-ClC_6H_4;
R^2 = Ph, 3-MeC_6H_4, 4-MeC_6H_4, 2-MeOC_6H_4, 3-MeOC_6H_4, 4-ClC_6H_4, 3-Th;
R^3 = H, 4-MeO, 3-Cl, 4-F, 4-Cl;
R^4 = Ph, 2-MeC_6H_4, 2-MeOC_6H_4, 2-FC_6H_4, 2-BrC_6H_4, 3-MeC_6H_4, 3-ClC_6H_4, 3-BrC_6H_4, 4-Bu^tC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 4-$O_2NC_6H_4$, 4-NCC_6H_4, 3,4-$F_2C_6H_3$, 2-Fu

Scheme 29



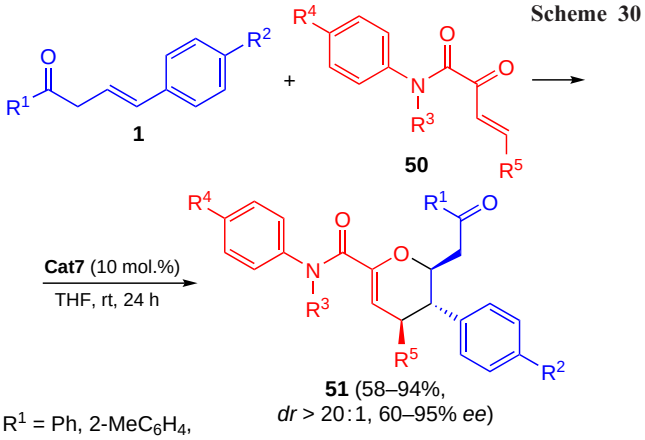
R^1 = Me, Ph, 4-MeOC_6H_4, 4-FC_6H_4, 4-BrC_6H_4, 2-Naph;
R^2 = Ph, 4-MeC_6H_4, 3-FC_6H_4, 4-FC_6H_4, 4-ClC_6H_4;
R^3 = Me, Bn, All, 4-Br$C_6H_4CH_2$;
R^4 = H, 5-Me, 5-MeO, 5-F, 5-Cl, 6-Cl, 5-Br;
R^5 = Me, Et; All is allyl

shift/enolization generates intermediates **54**, which undergo an intramolecular nucleophilic substitution of the fluorine atom to produce the final δ-sultones **53**.

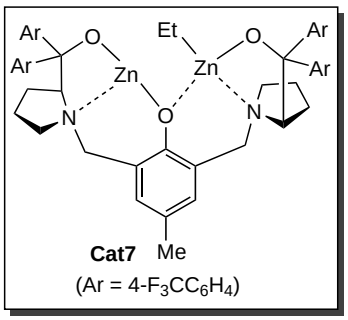
The *in situ* generated β,γ-ethylenic ketones **1**, the adducts of 2-fluorophenylacetylenes and various ketones, are converted to functionalized benzo[*b*]oxepines **55** in moderate to high yields *via* an intramolecular nucleophilic substitution of the fluorine atom by an enolate anion (Scheme 33).[73] This methodology features a wide substrate scope and a high functional group tolerance.

A special group of diastereoisomerically pure β,γ-ethylenic ketones **57** with a dihydropyran moiety was obtained by the base-mediated reaction of 2-acetyl-3,4-dihydropyrans **56** with aryl alkynes. These ketones undergo acid-catalyzed (in the presence of NH_4Cl) stereoselective cyclization to dienyl bicyclic structures **58** (Scheme 34),[74] which are closely related to naturally abundant DOBCO molecules (6,8-dioxabicyclo[3.2.1]-

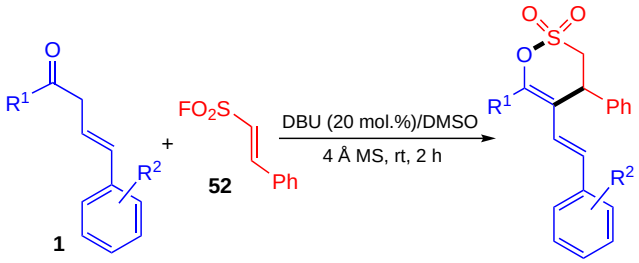
Scheme 30



R^1 = Ph, 2-MeC_6H_4, 3-MeC_6H_4, 4-MeC_6H_4, 3-$MeOC_6H_4$, 4-$MeOC_6H_4$, 3-ClC_6H_4, 4-ClC_6H_4, 4-FC_6H_4, 4-BrC_6H_4, 2-Naph, 2-Th;
R^2 = H, Me, Et, MeO, F, Cl, Br;
R^3 = Me, Et, Ph; R^4 = H, Me, MeO, F, Cl, Br;
R^5 = Ph, 4-MeC_6H_4, 3,4-$Me_2C_6H_3$, 4-FC_6H_4, 4-ClC_6H_4, 3-BrC_6H_4, 4-BrC_6H_4, 1-Naph, 2-Naph, 2-Th

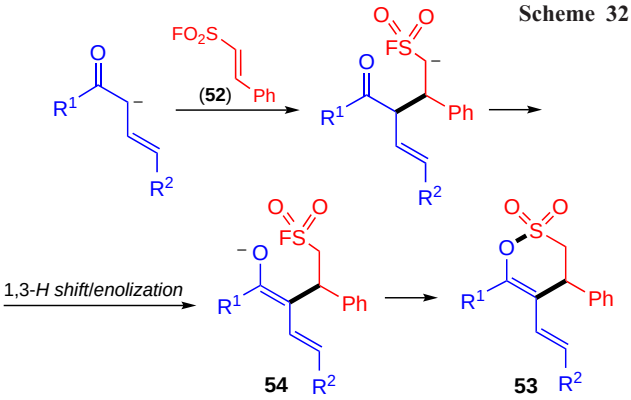


Scheme 31

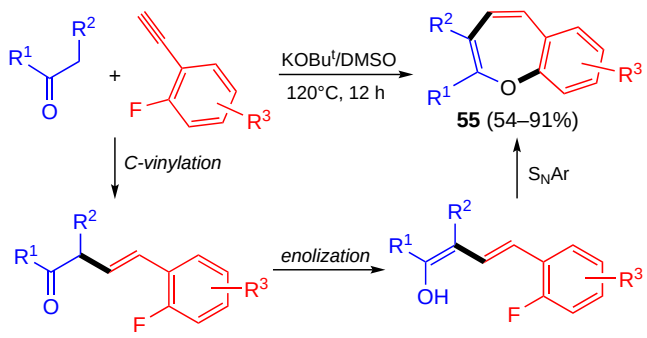


R^1 = Me, Ph; R^2 = H, 2-Cl, 3-Cl, 4-Cl;
MS is molecular sieves

Scheme 32



Scheme 33



R^1 = Me, Et, Pr^i, Bu^n, cyclo-C_3H_5, Bn, Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-FC_6H_4, 4-ClC_6H_4,4-$F_3CC_6H_4$, 4-$Me_2NC_6H_4$, 3,4-$Me_2C_6H_3$, 2-Fu, 2-Th, 2-Naph;
R^2 = H, Me, Bn, Ph, 3-MeC_6H_4, 4-MeC_6H_4, 2-$MeOC_6H_4$, 3-$MeOC_6H_4$, 4-$MeOC_6H_4$, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 2-Fu, 2-Py; R^1–R^2 = $(CH_2)_4$,$(CH_2)_5$, $(CH_2)_6$;
R^3 = 4-Me, 5-Me, 4-CN, 4-Cl, 3-Br; Py is pyridyl

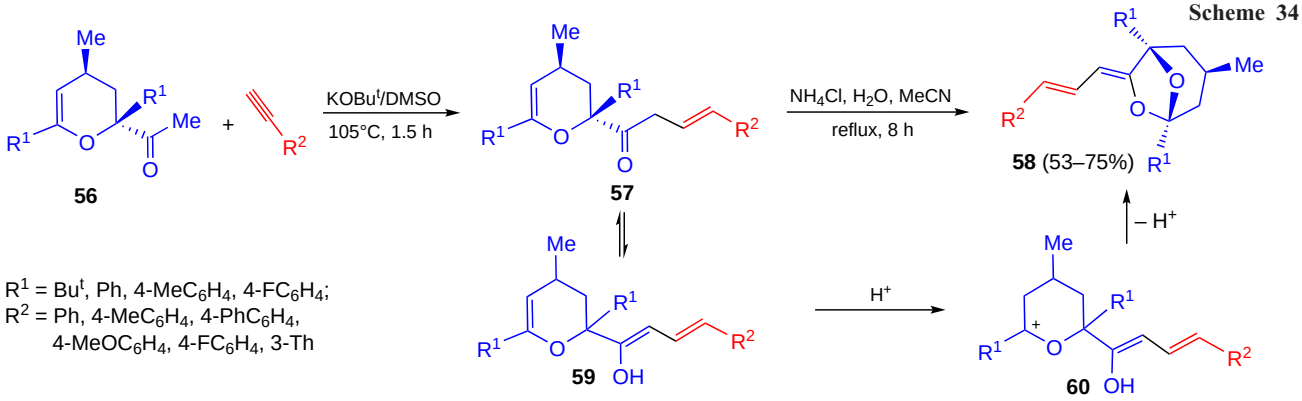
octanes).[75] The cyclization involves protonation of the enol form of ketones **59** followed by intramolecular cyclization of carbocations **60** (see Scheme 34).[74] The diastereoselectivity of the ring-closing reaction is predetermined by the cyclic structure of the starting ketones **57**, in which the hydroxyl group attacks position 6 of the pyran ring only from the axial direction, leading to a single configuration of this carbon atom.

4.2.2. Synthesis of nitrogen heterocycles

The reaction between oximes of β,γ-ethylenic ketones **61** (prepared from ketones **1** and hydroxylamine hydrochloride) with acetylene was successfully used for the stereoselective synthesis of 3-styryl-1*H*-pyrroles **62** and 1-vinyl-3-styrylpyrroles **63** (Scheme 35).[76]

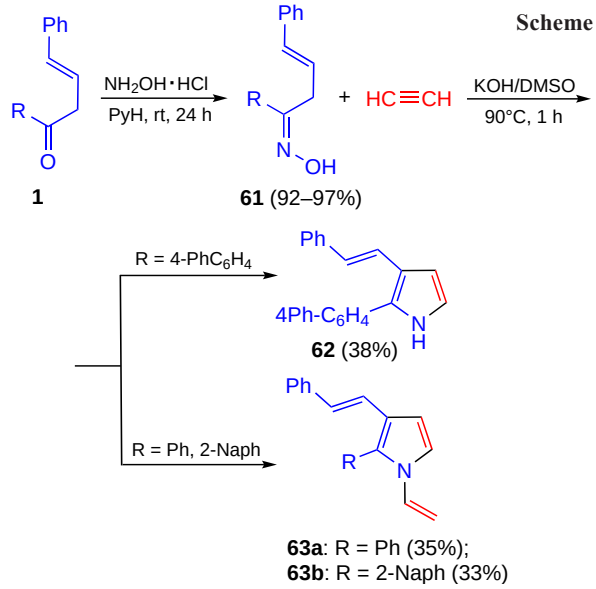
The pyrrole synthesis[77,78] begins with the *O*-vinylation of oximes **61** with acetylene (Scheme 36). This is followed by a cascade sequence involving a 1,3-prototropic shift in *O*-vinyloximes **64**, a 3,3-sigmatropic rearrangement of intermediate dialkenylhydroxylamines **65**, the cyclization of

Scheme 34



R^1 = Bu^t, Ph, 4-MeC_6H_4, 4-FC_6H_4;
R^2 = Ph, 4-MeC_6H_4, 4-PhC_6H_4, 4-$MeOC_6H_4$, 4-FC_6H_4, 3-Th

Scheme 35



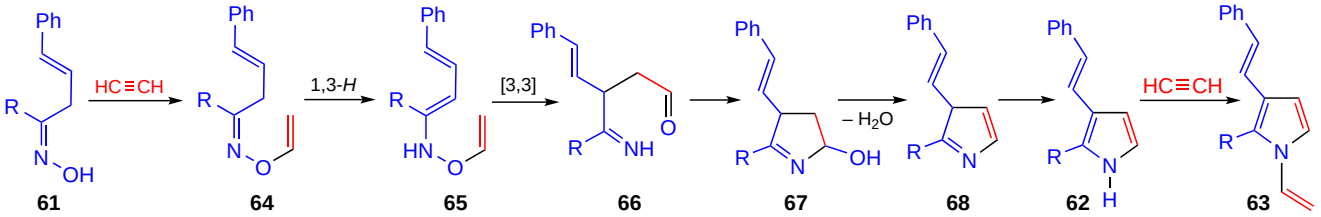
iminoaldehydes **66**, the dehydration of hydroxypyrrolines **67**, and aromatization of 3*H*-pyrroles **68**.

The annulation of substituted β,γ-ethylenic ketones **1** with unsaturated cyclic imines **69** *via* the inverse-electron-demand hetero-Diels–Alder reaction stereoselectively afforded the polycondensed heterocyclic systems, *viz.*, tetrahydrobenzofuro-[3,2-*b*]pyridine-substituted systems **70** (Scheme 37).[79] The reaction was realized under organocatalytic (**Cat8**) conditions and proceeded in a highly stereo- and site-selective manner.

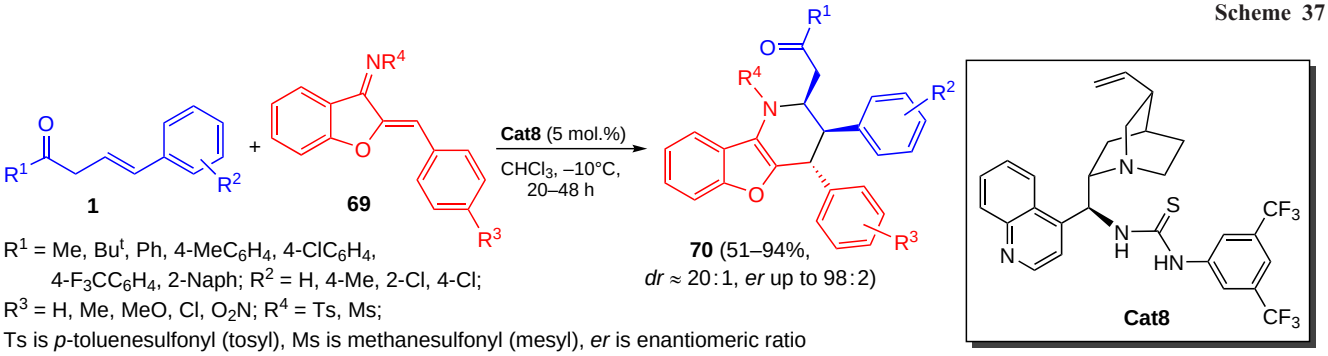
The base-promoted *C*-vinylation of ketones with electron-deficient acetylenes (alkynones), which leads to the formation of 1,5-diketones **71**, was used in the preparation of Kröhnke pyridines[80–82] (2,4,6-triarylpyridines).[83] The methodology tolerates diversely substituted ketones and alkynones, enabling the synthesis of a variety of 2,4,6-triarylpyridines **72**, including tetrasubstituted and fused ones, in good to excellent yields (Scheme 38).

The one-pot synthesis of substituted pyridines **72** involves the nucleophilic addition of ammonia (generated from NH_4Cl) to a one carbonyl function of the *in situ* formed unsaturated

Scheme 36

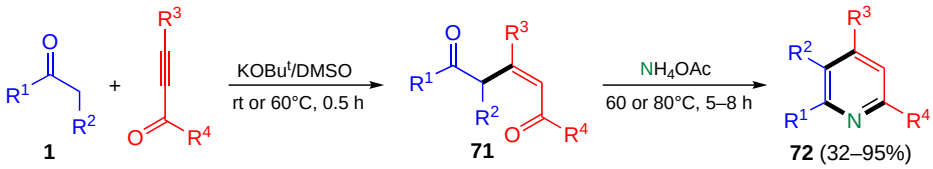


Scheme 37

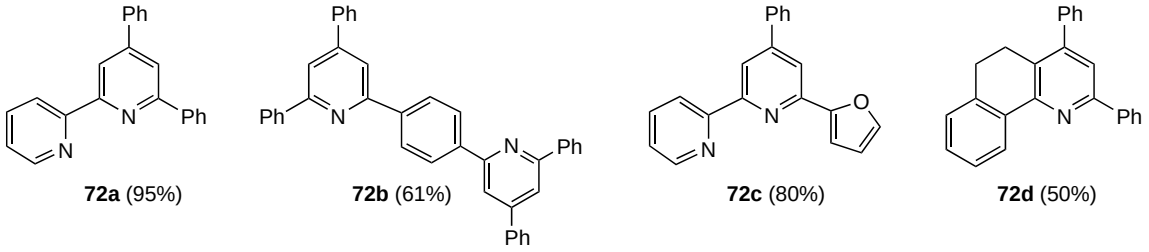


R^1 = Me, Bu^t, Ph, 4-MeC_6H_4, 4-ClC_6H_4, 4-F_3CC_6H_4, 2-Naph; R^2 = H, 4-Me, 2-Cl, 4-Cl; R^3 = H, Me, MeO, Cl, O_2N; R^4 = Ts, Ms;
Ts is *p*-toluenesulfonyl (tosyl), Ms is methanesulfonyl (mesyl), *er* is enantiomeric ratio

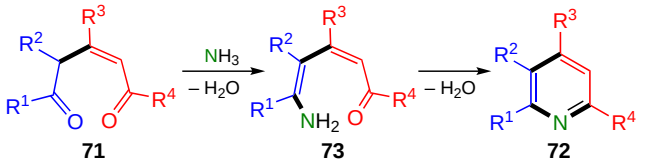
Scheme 38



R^1 = Bu^t, Ph, 4-MeC_6H_4, 4-MeOC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 4-F_3CC_6H_4, 2-Fu, 2-Th, 2-Py, ferrocenyl; R^2 = H, Me, Et; R^1–R^2 = $(CH_2)_4$; R^3 = cyclo-C_6H_{11}, Ph, 4-MeC_6H_4, 3-MeOC_6H_4, 3-FC_6H_4, 3-Th; R^4 = Ph, 4-MeC_6H_4, 4-MeOC_6H_4, 4-ClC_6H_4, 2-Fu, 2-Th, 3-Py



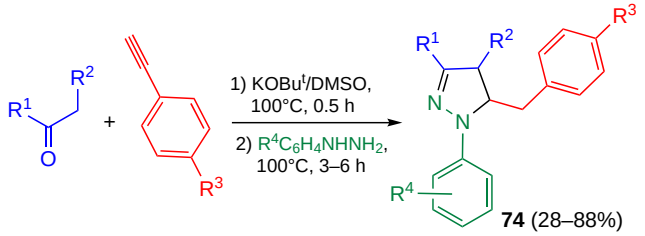
Scheme 39



1,5-diketones **71**, followed by the intramolecular cyclization of intermediate amines **73** involving the second carbonyl group and elimination of a water molecule (Scheme 39).[83]

The simple straightforward one-pot synthesis of diversely substituted 4,5-dihydropyrazoles **74** *via* the reaction of β,γ-ethylenic ketones **1** with aryl hydrazines was achieved. Ketones **1** were generated *in situ* by the *C*-vinylation of the starting ketones with alkynes in the presence of KOBu^t/DMSO system (Scheme 40).[84]

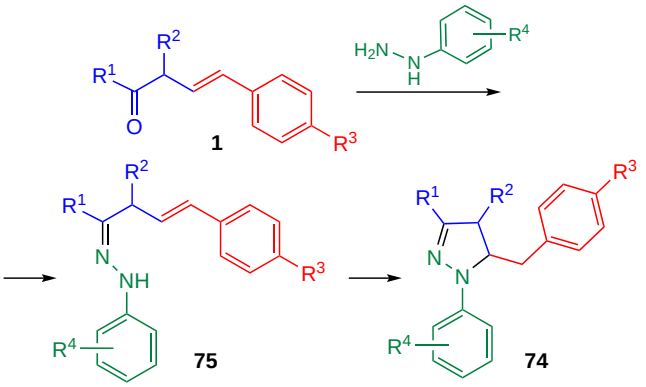
Scheme 40



R^1 = Et, Ph, 2-MeC_6H_4, 4-MeC_6H_4, 2-MeOC_6H_4, 4-MeOC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, 4-PhC_6H_4, 2-Naph, 2-Fu, 2-Th, 2-Py;
R^2 = H, Me, Et; R^3 = H, Et; R^4 = H, 4-MeO, 3-Cl

The reaction involves the formation of hydrazones **75**, which undergo intramolecular cyclization (Scheme 41).[84]

Scheme 41

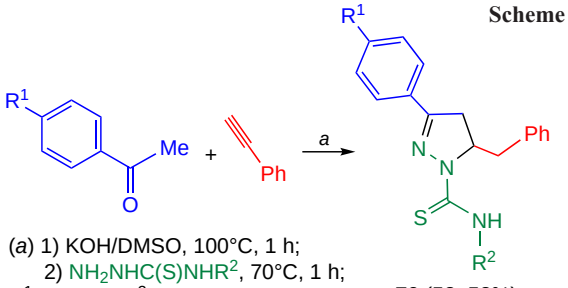


A modified sequence of similar transformations was used for the three-component one-pot synthesis of 4,5-dihydropyrazole-1-carbothioamides **76** from acetophenones, phenylacetylene and thiosemicarbazides in the presence of KOH/DMSO catalytic pair (Scheme 42).[85]

β,γ-Ethylenic ketones **1** were the key reaction partner in the assembly of 1-formyl-4,5-dihydropyrazoles **77** directly from ketones, arylacetylenes, hydrazine, and formic acid in a one-pot procedure (Scheme 43).[86]

The assembly of pyrazolines **77** comprises the formation of hydrazones **78** and their acylation with formic acid. The acylated unsaturated hydrazone intermediates **79** then undergo the ring closure to the functionalized dihydropyrazole ring (Scheme 44).[86] This mechanistic hypothesis was proved by the synthesis of intermediate β,γ-unsaturated hydrazones **78**, which

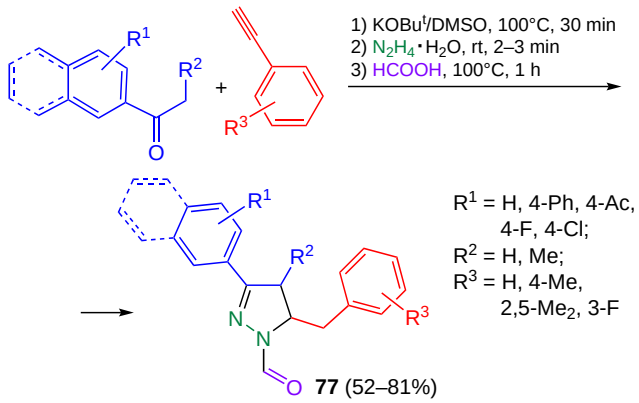
Scheme 42



(*a*) 1) KOH/DMSO, 100°C, 1 h;
2) $NH_2NHC(S)NHR^2$, 70°C, 1 h;
R^1 = H, Ph, R^2 = H, 4-EtC_6H_4

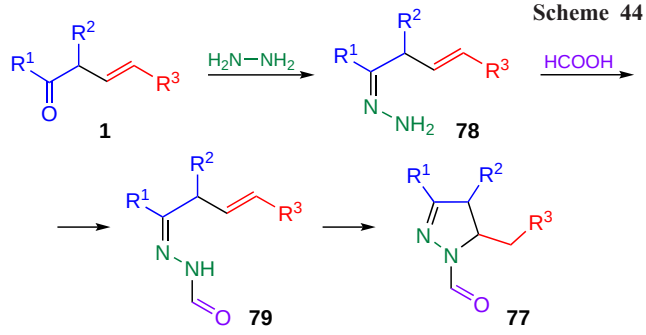
76 (52–58%)

Scheme 43



R^1 = H, 4-Ph, 4-Ac, 4-F, 4-Cl;
R^2 = H, Me;
R^3 = H, 4-Me, 2,5-Me_2, 3-F

Scheme 44



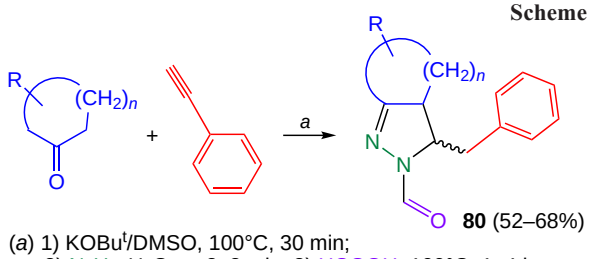
did readily cyclize to the corresponding pyrazolines **77** in the presence of formic acid under the above conditions.

As a further development of this rewarding approach to the construction of functionalized pyrazoline derivatives, a one-pot synthesis of a previously unknown family of cycloalka[*c*]-pyrazoline-2-carbaldehydes **80** *via* the sequence of the reactions between cyclic ketones, phenylacetylene, hydrazine hydrate, and formic acid was implemented (Scheme 45).[87]

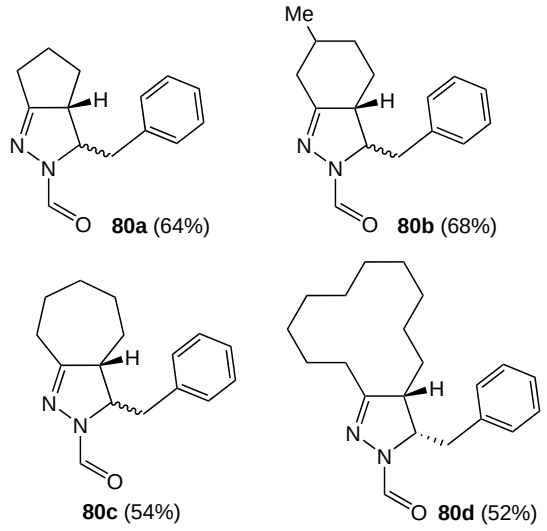
Later, hydrazones **78**, prepared from β,γ-ethylenic ketones **1**, underwent I_2/DMSO-mediated oxidative cyclization to produce either substituted 5,6-dihydropyridazines **81** or *N*-arylamino-pyrrole derivatives **82** (Scheme 46).[88] Pyridazines **81** were formed from hydrazones **78** with electron-withdrawing substituents, whereas pyrroles **82** were obtained from those with electron-donating substituents. According to the Density Functional Theory (DFT) calculations,[88] this regioselective substituent-controlled switching of the cyclization path was explained by the different stability of the two corresponding transition state structures and the different nucleophilicity of the two nitrogen atoms, which depends on the electronic effects of the substituents.

The solvent-controlled oxidative cyclization of the same unsaturated hydrazones **78** in the presence of molecular oxygen

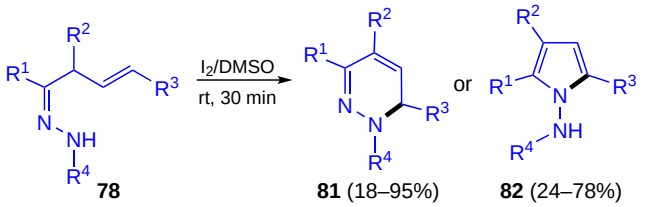
Scheme 45



(*a*) 1) KOBu^t/DMSO, 100°C, 30 min;
2) $N_2H_4 \cdot H_2O$, rt, 2–3 min; 3) HCOOH, 100°C, 1–4 h;
R = H, 4-Me; *n* = 2, 3, 4, 9

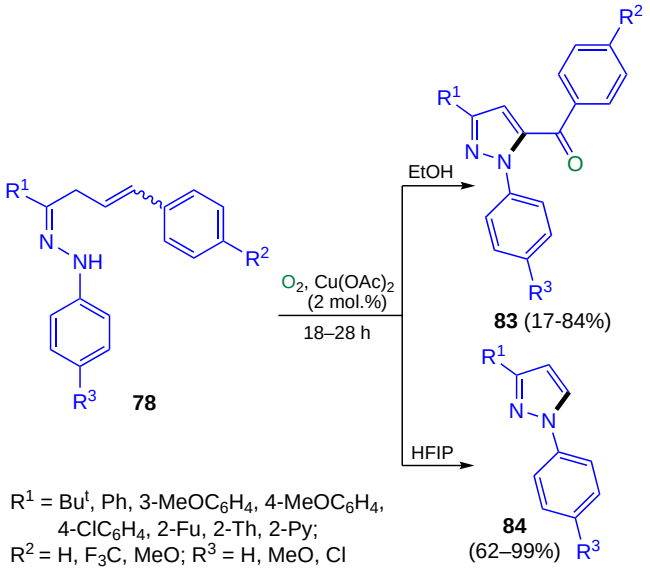


Scheme 46



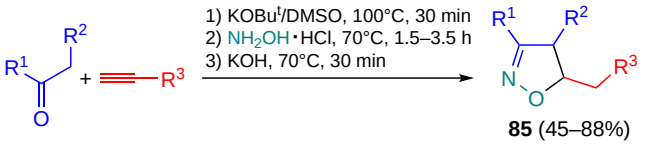
R^1 = cyclo-C_3H_5, Ph, 3-MeC_6H_4, 4-MeC_6H_4, 4-PhC_6H_4, 4-MeOC_6H_4, 4-F_3CC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, 2-Naph, 2-Fu, 2-Th, 2-Py;
R^2= Me, Et; R^1–R^2 = $(CH_2)_4$, $(CH_2)_{10}$;
R^3 = Ph, 2-MeC_6H_4, 3-MeC_6H_4, 4-MeC_6H_4, 4-MeOC_6H_4, 4-F_3CC_6H_4, 4-FC_6H_4, 3-ClC_6H_4, 4-ClC_6H_4;
R^4 = Ph, Ts, Ac

Scheme 47



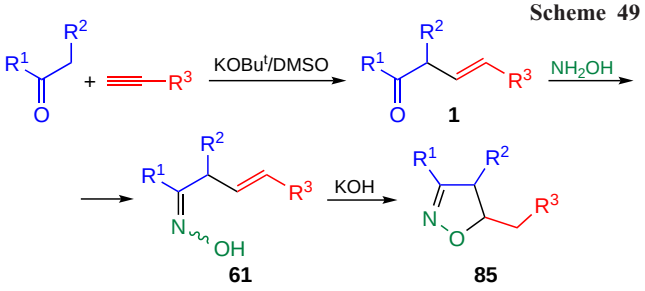
R^1 = Bu^t, Ph, 3-MeOC_6H_4, 4-MeOC_6H_4, 4-ClC_6H_4, 2-Fu, 2-Th, 2-Py;
R^2 = H, F_3C, MeO; R^3 = H, MeO, Cl

Scheme 48



R^1 = Me, Et, Pr^n, Bu^n, Ph, 4-FC_6H_4, 4-PhC_6H_4, 4-AcC_6H_4, 2-Naph;
R^2 = H, Me, Et, Pr^n, Bu^n; R^1–R^2 = $(CH_2)_5$, Me(CH)$(CH_2)_4$

Scheme 49



and $Cu(OAc)_2$ catalyst gave two different groups of pyrazoles. 1,3,5-Trisubstituted pyrazoles **83** with an acyl functionality at the C-5 position were obtained as the major products when carrying out the reaction in ethanol, whereas 1,3-disubstituted pyrazoles **84** were exclusively formed in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (Scheme 47).[89]

A new general strategy for the one-pot synthesis of substituted 4,5-dihydroisoxazoles **85** based on β,γ-ethylenic ketones **1** and their oximes **61**, generated *in situ* from ketones, aryl alkynes, and hydroxylamine hydrochloride (Scheme 48),[90] was one of the first synthetic applications of the superbase-promoted *C*-vinylation of ketones with alkynes.[28–30] This strategy has been proven to be applicable to the preparation of a wide range of 4,5-dihydroisoxazoles **85** due to a great diversity of both starting ketones (dialkyl, cycloalkyl, and alkylaryl) and aryl alkynes.[90]

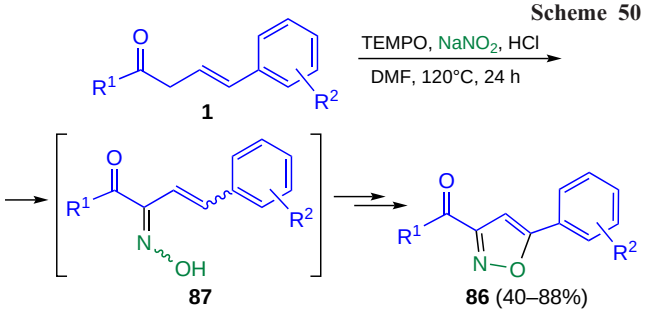
The assembly of 4,5-dihydroisoxazoles **85** involves first the KOBu^t/DMSO-mediated addition of deprotonated ketones to arylacetylenes to form β,γ-ethylenic ketones **1**, which further react with NH_2OH. Intermediate oximes **61** further undergo KOH/DMSO-catalyzed cyclization (Scheme 49).

The radical cyclization of β,γ-ethylenic ketones **1** with sodium nitrite in the presence of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) allowed a broad range of differently substituted 3-acylisoxazoles **86** to be constructed (Scheme 50).[91] The mechanistic studies revealed that the reaction proceeds *via* the nitrosation of the α-CH bond of ketones **1** followed by the radical 5-*endo-trig* cyclization of the resulting oximes **87** and aromatization, the native carbonyl group being intact.

A number of functionalized 1,2,3-triazoles **89** were synthesized by the DBU/DMSO-catalyzed formal [3+2] cycloaddition of various substituted β,γ-ethylenic ketones **1** with different substituted aryl azides **88** (including those sugar-derived) (Scheme 51).[92] All the substrates underwent the cycloaddition very smoothly (room temperature) to give the corresponding functionally rich *C*-styryl-1,2,3-triazoles **89** of the stilbenoid type in excellent yields.

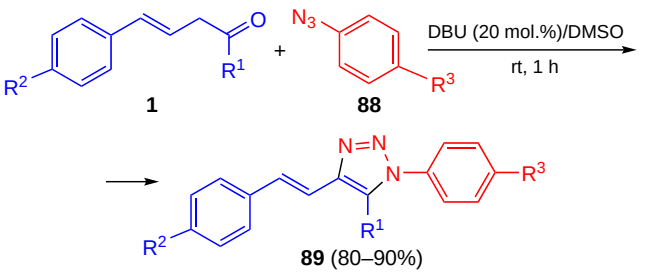
This nonconventional click reaction involves first the enolization of β,γ-ethylenic ketones **1** to dienols **90**, the addition

Scheme 50

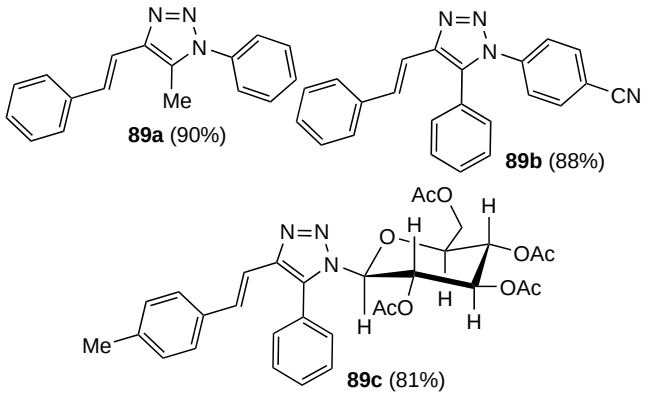


R^1 = Me, Bu^t, 1-adamantyl, Ph, 2-MeC_6H_4, 3-MeC_6H_4, 4-MeC_6H_4, 3-MeOC_6H_4, 4-MeOC_6H_4, 3,4-$(MeO)_2C_6H_3$, 4-FC_6H_4, 4-ClC_6H_4, 4-NCC_6H_4, 4-F_3CC_6H_4, 4-PhC_6H_4, 2-Naph, 2-Fu, 2-Th;
R^2 = H, 4-Me, 4-MeO, 4-F, 2-Cl, 3-Cl, 4-Cl, 3,5-Cl_2, 4-F_3C

Scheme 51



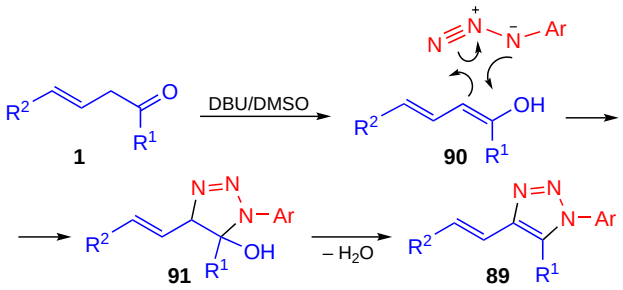
R^1 = Me, Ph, 4-F_3CC_6H_4, 4-MeOC_6H_4, 4-ClC_6H_4;
R^2 = H, Me; R^3 = H, MeO, NC, F



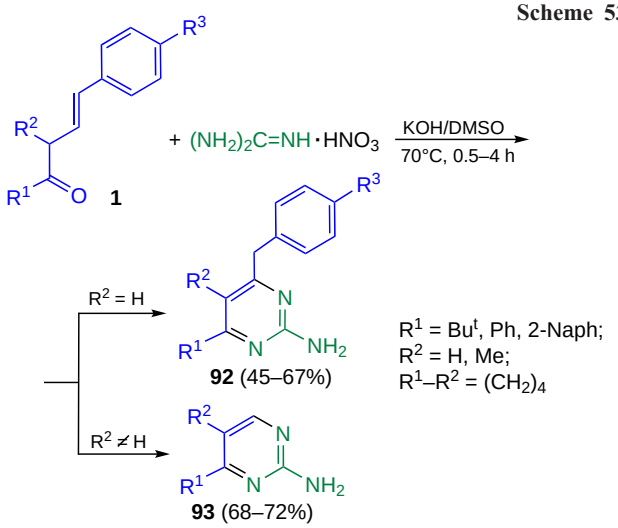
of azides **88** to the enol double bond and the elimination of a water molecule from the intermediate adducts **91** (Scheme 52).

The reaction of β,γ-ethylenic ketones **1** with guanidine nitrate was successfully employed to obtain two types of 2-aminopyrimidines (Scheme 53):[93] 4-benzyl-substituted (**92**) and 4-unsubstituted (**93**). The latter result from the elimination of methylbenzenes.

Scheme 52



Scheme 53

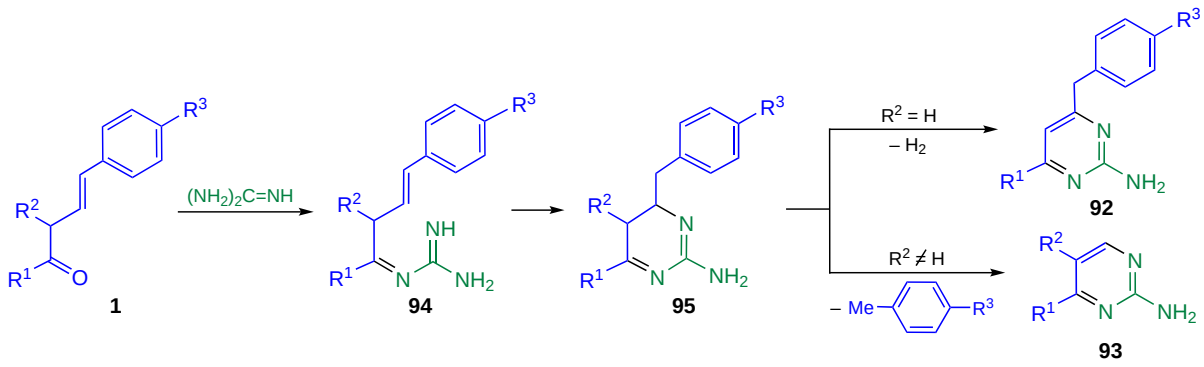


R^1 = Bu^t, Ph, 2-Naph;
R^2 = H, Me;
R^1–R^2 = $(CH_2)_4$

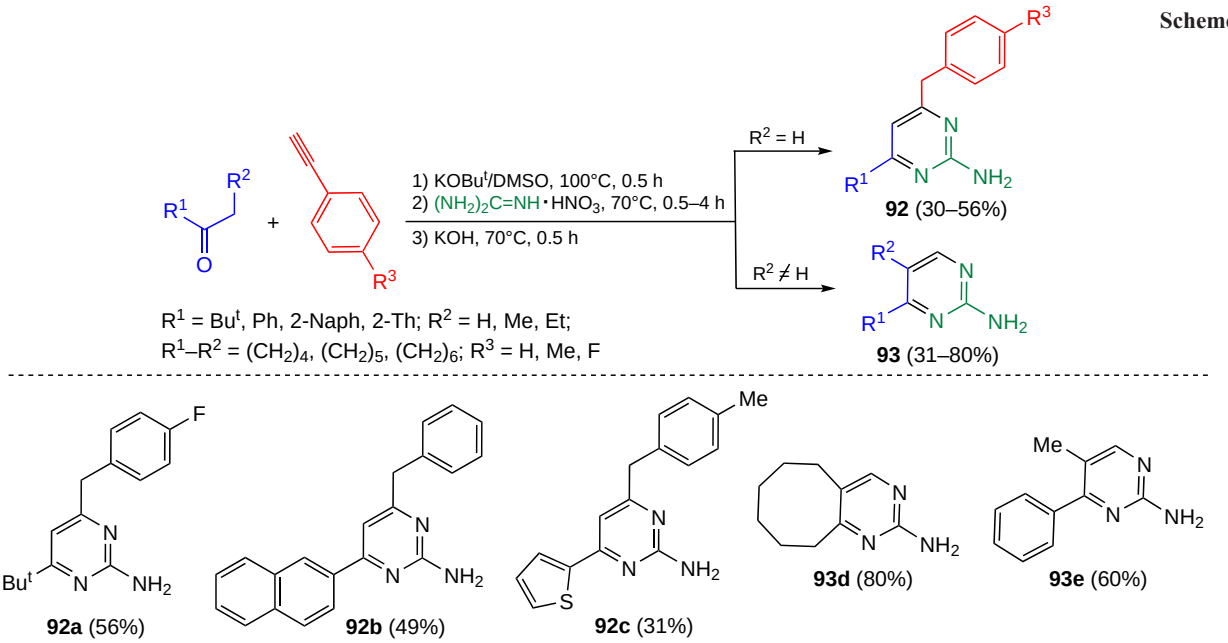
The assembly of 2-aminopyrimidines **92** and **93** (Scheme 54)[93] involves the formation of adducts of β,γ-ethylenic ketones **1** with guanidine (**94**), which then undergo the ring-closure to afford dihydropyrimidines **95**. Aromatization of the latter occurs *via* two pathways: when R^2 = H, intermediates **95** typically lose a hydrogen molecule to give 2-amino-4-benzylpyrimidines **92**. In contrast, when $R^2 \neq$ H, elimination of methylbenzenes from the dihydropyrimidine ring takes place to deliver 4-unsubstituted 2-aminopyrimidines **93**. The final step in the formation of 2-aminopyrimidines **93** (the unusual elimination of methyl aromatics) has been proved experimentally.

Based on these results (see Schemes 53, 54),[93] the one-pot synthesis of substituted 2-aminopyrimidines **92**, **93** *via* a sequential three-component reaction of ketones, aryl alkynes,

Scheme 54



Scheme 55

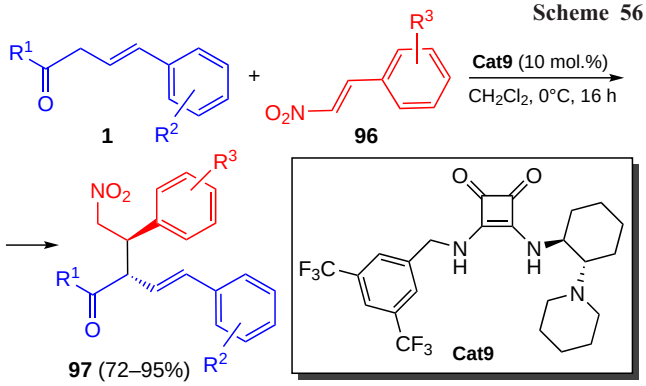


and guanidine mediated by the KOBu^t/DMSO catalytic dyad was developed (Scheme 55).[94] The strategy proved effective for a diversity of ketones such as aliphatic, cycloaliphatic, and alkylaromatic as well as for the substituted arylacetylenes.

4.3. Miscellaneous reactions

The organocatalytic enantioselective Michael reactions of β,γ-ethylenic ketones **1** as α-C-nucleophiles significantly expanded the scope of their synthetic applications. Within this approach, various ketones **1** were utilized in a chiral tertiary amine (*e.g.*, **Cat9**)-promoted Michael addition to nitro styrenes **96**. The reaction is regioselective to produce adducts **97** with two vicinal tertiary carbon stereocentres in diastereomeric ratios of up to >20 : 1 and enantioselectivities in the 90–98% *ee* range (Scheme 56).[95]

Scheme 56

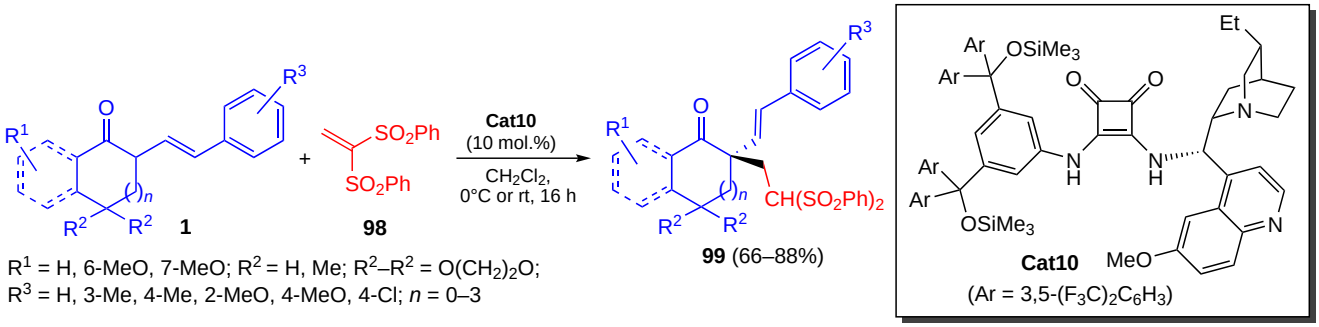


Using a chiral tertiary amine catalyst (**Cat10**), cyclic β,γ-ethylenic ketones **1**, including those fused with benzene rings, were smoothly added as α-C-nucleophiles to vinyl bis(sulfone) **98** affording the corresponding all-carbon quaternary adducts **99** in good yields, and with enantioselectivity of up to 99% *ee* (Scheme 57).[96]

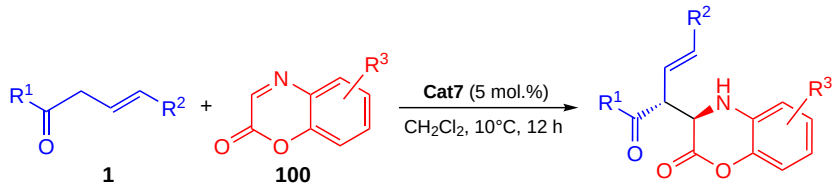
The regio-, diastereo-, and enantioselective Mannich-like reaction of ketones **1** with cyclic imines **100** under Lewis acid/Brønsted base cooperative catalysis was realized.[97] This reaction selectively involves the α-position of ketones **1** leading to the corresponding adducts **101** with two consecutive tertiary carbon stereocentres with 20 : 1 *dr* and up to 99% *ee* (Scheme 58).

Under catalyst- and solvent-free conditions, β,γ-ethylenic ketones **1** (as Michael acceptors) regioselectively add secondary phosphine chalcogenides **102** affording γ-ketophosphine chalcogenides **103** in high yields (Scheme 59).[98] The addition exclusively occurs across the double bond, leaving the carbonyl function intact and providing ample opportunity for further functionalization of the resulting compounds.

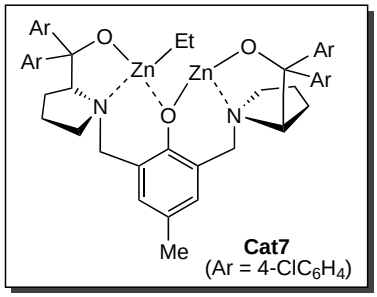
Scheme 57



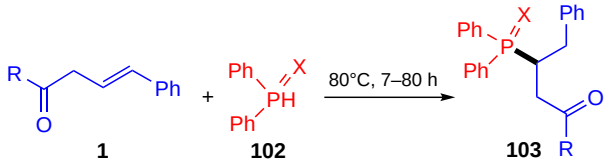
Scheme 58



R^1 = Ph, 2-MeC_6H_4, 4-MeC_6H_4, 2-MeOC_6H_4, 3-MeOC_6H_4, 4-MeOC_6H_4, 3-FC_6H_4, 4-FC_6H_4, 3-BrC_6H_4, 4-ClC_6H_4, 2-Naph, 2-Fu, 2-Th;
R^2 = Ph, 4-MeC_6H_4, 4-MeOC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4;
R^3 = H, 6-Me, 6-Bu^t, 7-Me, 6-F, 6-Cl, 6-Br, 7-F, 7-Cl, 7-Br

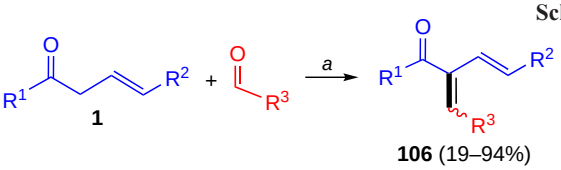


Scheme 59



R = Bu^t, Ph, 4-PhC_6H_4, 4-MeC_6H_4, 4-ClC_6H_4, 4-AcC_6H_4;
X = O, S, Se

Scheme 61



(*a*) piperidine (10 mol.%), AcOH (10 mol.%), PhMe, 110–115°C, 3–8 h;
R^1 = Ph, 4-PhC_6H_4, 4-MeOC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, 2-Naph, 2-Th;
R^2 = Ph, 4-PhC_6H_4, 3-MeOC_6H_4, 3-FC_6H_4, 3-Th;
R^3 = Ph, 4-O_2NC_6H_4, 4-ClC_6H_4, 4-Me_2NC_6H_4, pyrrol-2-yl, 2-Fu

The synthetic potential of β,γ-ethylenic ketones **1** was demonstrated through the regioselective ligand-free AgOTf-catalyzed Friedel–Crafts hydroarylation with electron-rich arenes **104** to provide the corresponding γ-diarylated ketones **105** (Scheme 60).[40]

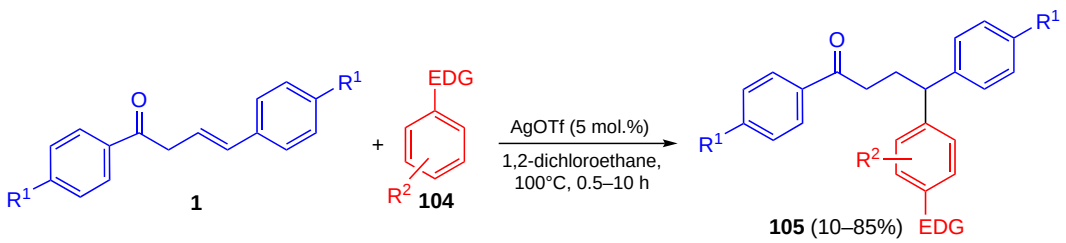
Polyconjugated electron-deficient dienes (2-acylbuta-1,3-dienes **106**), which are synthetically attractive but less accessible compounds than the well-explored 1-acylbutadienes, were obtained regioselectively from aromatic and heteroaromatic β,γ-ethylenic ketones **1** by their condensation (as active methylene compounds) with aromatic and heteroaromatic aldehydes (Scheme 61).[99] The reaction proceeds smoothly with piperidine/acetic acid catalytic pair in boiling toluene. Piperidine, acting as a base, increases the acidity of the methylene group in the α-position of ketones **1**, while the addition of acetic acid enhances the electrophilicity of the aldehyde function. 2-Acylbuta-1,3-dienes **106** (yields from good to high) are formed as a mixture of *E*- and *Z*-isomers relative to the newly formed C=C bond, while the existing C=C bond of the starting ketones **1** remained in the *E*-configuration.

Diverse (het)arylsubstituted β,γ-ethylenic ketones **1**, readily accessible from (het)aromatic ketones and (het)aryl alkynes, were used to synthesize polyarylated α-alkenyl-β-diketones **107** *via* the regio- and stereoselective acylation with acyl chlorides in the presence of magnesium bromide etherate/*N*,*N*-diisopropylethylamine (DIPEA) system (Scheme 62).[100]

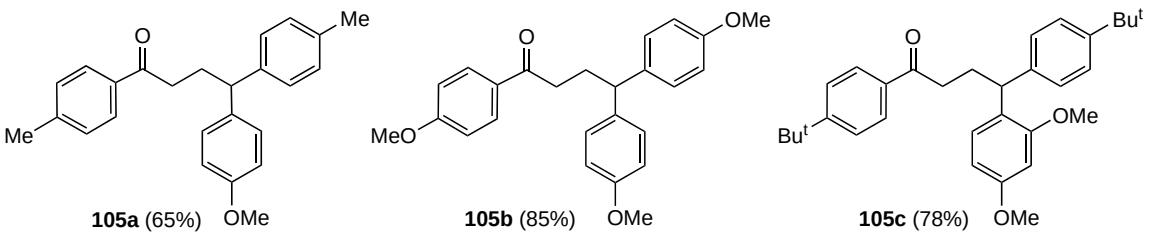
This approach (a soft enolization) involved the initial formation of a coordination complex **108** between Lewis acid (magnesium bromide) and ketone **1**, providing stronger polarization of the carbonyl function. Consequently, the acidity of the α-protons increases, ensuring enolization with mild organic bases (Scheme 63).[100] In addition, the Lewis acid blocks the oxygen nucleophilic centre, thus securing *C*-regioselective acylation of the intermediate enolates **109**.

As a versatile synthons, β,γ-ethylenic ketones **1** successfully undergo DABCO-catalyzed allylation with Morita–Baylis–Hillman carbonates **110** to give 2-alkoxycarbonylallyl β,γ-unsaturated ketones **111** in high yields and with excellent diastereoselectivities (see Scheme 63).[101] Starting ketones **1**

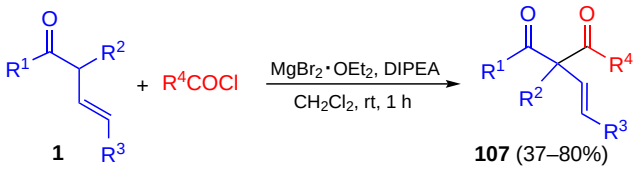
Scheme 60



R^1 = H, Me, Bu^t, F_3C, MeO, Br; R^2 = H, 3-MeO, 4-MeO; EDG (electrone donated group) = Me, MeO

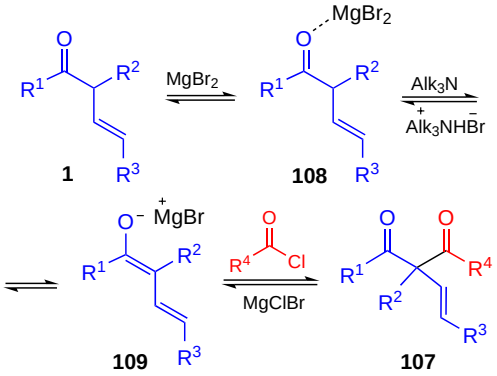


Scheme 62



R^1 = Ph, 4-PhC_6H_4, 4-MeOC_6H_4, 4-ClC_6H_4, 2-Naph, 2-Th;
R^2 = H, Me;
R^3 = Ph, 4-PhC_6H_4, 3-MeOC_6H_4, 3-FC_6H_4, 3-Th;
R^4 = Ph, 4-MeC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, 4-MeOC_6H_4, 4-O_2NC_6H_4, 2-Fu, 2-Th

Scheme 63

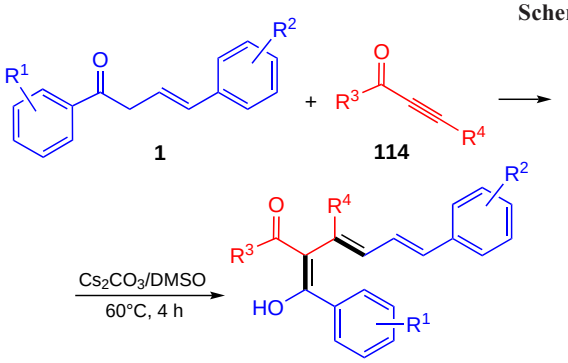


bearing aromatic substituents with diverse electronic properties were tolerant to this nucleophilic substitution reaction. The reaction features mild reaction conditions (room temperature, no strict water-free or oxygen-free conditions) and short reaction times in most cases. Depending on the reaction conditions, double allylation products, α,α-(**112**) and α,γ-di(2-alkoxycarbonyl)allyl (**113**) β,γ-ethylenic ketones, were obtained in overall yield of 33–91% (Scheme 64).

Based on the reaction of β,γ-ethylenic ketones **1** with acylacetylenes **114** in the Cs_2CO_3/DMSO system, protocol for the stereoselective synthesis of a broad range of substituted 1,3,5-trienes **115** has been developed (Scheme 65).[102]

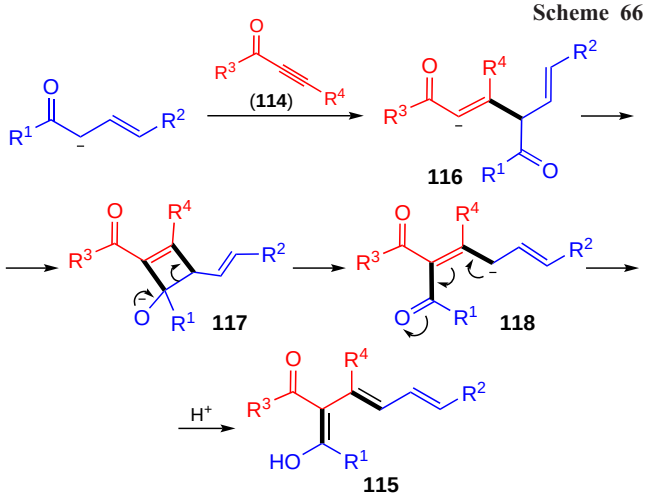
A possible reaction mechanism for the formation of 1,3,5-trienes **115** involves the initial nucleophilic attack of deprotonated β,γ-ethylenic ketones **1** on the triple bond of acetylenic ketones **114** (Scheme 66).[102] After that, vinyl carbanions **116** intramolecularly add to the carbonyl function. Then, ring opening occurs in anions **117** to give intermediates

Scheme 65



R^1 = H, 4-Me, 4-MeO, 4-F, 3-Br;
R^2 = H, 4-Me, 4-MeO, 4-NC, 3-F, 4-F, 4-Cl;
R^3 = Et, Bu^t, Ph, 4-MeC_6H_4, 4-MeOC_6H_4, 3,4-$(MeO)_2C_6H_3$, 2-Naph, 2-Fu, 1-methylindol-2-yl;
R^4 = Ph, 4-MeOC_6H_4, 3-ClC_6H_4, 4-IC_6H_4, 2-Th; R^3–R^4 = $(CH_2)_5$

Scheme 66

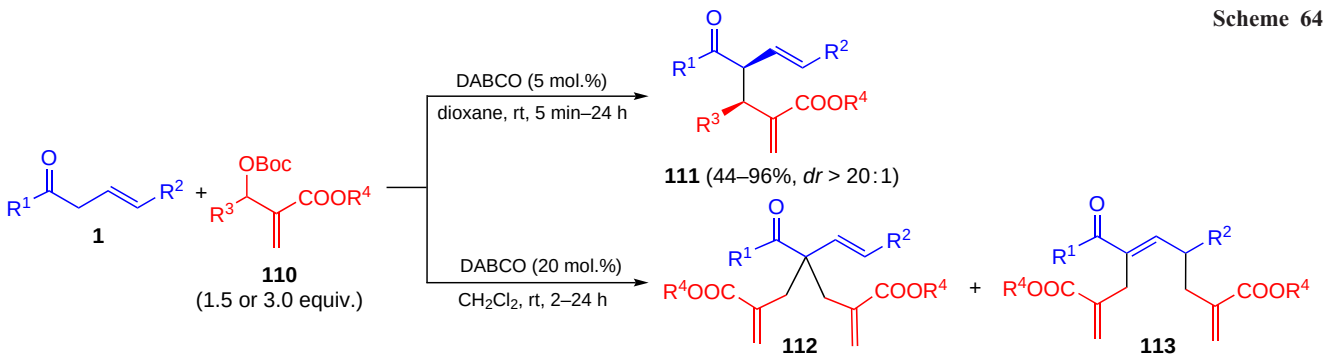


118, which undergo tautomerization and protonation to produce conjugated trienes **115**.

5. Conclusion

Since the discovery of the base-mediated *C*-vinylation reaction of ketones with alkynes in 2010, the chemistry of γ-aryl-β,γ-ethylenic ketones and their synthetic applications has become an intensively researched area. The three different reaction centres

Scheme 64



R^1 = Ph, 4-MeC_6H_4, 4-EtC_6H_4, 4-MeOC_6H_4, 4-F_3CC_6H_4, 3-FC_6H_4, 3-ClC_6H_4, 4-ClC_6H_4, 3-BrC_6H_4;
R^2 = Ph, 4-MeC_6H_4, 4-EtC_6H_4, 4-Bu^nC_6H_4, 3-MeOC_6H_4, 4-MeOC_6H_4, 3-FC_6H_4, 4-FC_6H_4, 3-ClC_6H_4, 4-ClC_6H_4, 3-BrC_6H_4, 4-BrC_6H_4;
R^3 = H, Ph, 2-MeC_6H_4, 3-MeC_6H_4, 4-MeC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4; R^4 = Me, Et, Pr^n, Bu^n, Bu^t

(carbonyl function, double bond and α-CH active group) provide a rich and intriguing chemistry of these compounds. An overview of the current state of the art in this field shows that the multifaceted reactivity of β,γ-ethylenic ketones opens up almost unlimited opportunities for the synthesis of a wide variety of new classes of complex functionalized compounds. As further possible progress in this field, there is envisioned the realization of a range of nucleophilic additions of β,γ-ethylenic ketones to various functionalized electrophiles, especially in an asymmetric manner, wherein the nucleophilic centre is the deprotonated α-CH_2-group. In turn, β,γ-ethylenic ketones may behave as electrophiles when attacked at their double bond by N-, P-, S-, and Se-centered nucleophiles that will provide numerous functionalized, so far inaccessible, nitrogen-, phosphorus-, sulfur-, and selenium-containing ketones, promising synthetic building blocks and ligands for new metal complexes.

This review provides first examples of successful application of β,γ-ethylenic ketones as dienophiles in asymmetric hetero-Diels–Alder cycloaddition that promises further spreading of this rewarding approach to the optically active functionalized compounds. As follows from few cases of arylation with electron-rich arenes, this methodology may by successfully applied to the preparation of densely functionalized aromatic and heteroaromatic systems. Almost unlimited possibilities for the design of tetra(het)aryl substituted benzenes are expected from the crotonic autodimerization of β,γ-ethylenic ketones as evidenced from the review. A lot of interesting synthetic surprises can be met upon investigation of dienol forms of β,γ-ethylenic ketones, *i.e*. hydroxy-1,3-dienes, especially those stabilized as silyl ethers. Such functionalized dienes capped by aromatic or heteroaromatic substituents can find wide applications in organic synthesis. Various families of dienes, both conjugated and skipped, can be obtained by a simple crotonic condensation of β,γ-ethylenic ketones with aldehydes or ketones. The Favorsky reaction of β,γ-ethylenic ketones with acetylene can afford vinylacetylenic alcohols, which, after dehydration, should furnish functionalized acetylenic dienes (hexa-1,3-dien-5-ynes).

Thus, the superbase-mediated *C*-vinylation of ketones (hydrocarbonylation of acetylenes) represents a kind of silent breakthrough in the acetylene chemistry, which for more than a century did not admit the inversion of the Favorsky reaction. This novel feature of the acetylene reactivity became a base for the readily scalable and technologically feasible synthesis of β,γ-ethylenic ketones, which now paves the ways to new directions of not yet explored acetylene-related fine and industrial organic synthesis. No doubt, this reaction and the fascinating chemistry of its products, β,γ-ethylenic ketones, will bring many prospective and diverse discoveries in the coming years.

6. List of abbreviations

The following abbreviations and designations are used in the review:

All — allyl,
Boc — *tert*-butoxycarbonyl,
Cp* — pentamethylcyclopentadienyl,
DABCO — 1,4-diazabicyclo[2.2.2]octane,
DBU — 1,8-diazabicyclo[5.4.0]undec-7-ene,
DFT — density functional theory,
DIPEA — *N*,*N*-diisopropylethylamine,
dr — diastereomeric ratio,
EDG — electron-donating groups,
ee — enantiomeric excess,
er — enantiomeric ratio,
Fu — furyl,
HFIP — 1,1,1,3,3,3-hexafluoro-2-propanol,
MS — molecular sieves,
Ms — methanesulfonyl (mesyl),
Naph — naphthyl,
Py — pyridyl,
TBDPS — *tert*-butyldiphenylsilyl,
TEMPO — 2,2,6,6-tetramethylpiperidine-1-oxyl,
Tf — trifluoromethanesulfonyl (triflyl),
Th — thienyl,
Ts — *p*-toluenesulfonyl (tosyl),
p-TSA — *p*-toluenesulfonic acid.

7. References

1. A.E.Favorsky. *Zh. Russ. Fiz.-Khim. O-va*, **37**, 643 (1906)
2. A.E.Favorsky. *Bull. Soc. Chim. France*, **2**, 1087 (1907)
3. M.Smith, J.March. In *March's Advanced Organic Chemistry*. (6th Edn). (New York: Wiley, 2007). P. 1360
4. R.T.Blickenstaff, A.C.Ghosh, G.C.Wolf. *Total Synthesis of Steroids*. (New York: Academic Press, 1974). P. 328
5. R.J.Tedeschi. *Acetylene-Based Chemicals from Coal and Other Natural Resources*. (New York: Marcel Dekker, 1982)
6. I.-T.Trotus, T.Zimmermann, F.Schueth. *Chem. Rev*., **114**, 1761 (2014); https://doi.org/10.1021/cr400357r
7. *The Dictionary of Drugs: Chemical Data. Chemical Data, Structures and Bibliographies*. (Eds J.Elks, C.R.Ganellin). (Berlin: Springer, 2014)
8. H.Qian, D.Huang, Y.Bi, G.Yan. *Adv. Synth. Catal*., **361**, 3240 (2019); https://doi.org/10.1002/adsc.201801719
9. R.J.Tedeschi. In *Encyclopedia of Physical Science and Technology*. Vol. 1. (Academic Press, 1992). P. 27
10. K.Endo, T.Hatakeyama, M.Nakamura, E.Nakamura. *J. Am. Chem. Soc*., **129**, 5264 (2007); https://doi.org/10.1021/ja0702014
11. P.G.M.Wuts, T.W.Greene. In *Protection for the Alkynes*. (Hoboken: Wiley, 2007). P. 932
12. E.F.Lopes, B.T.Dalberto, G.Perin, D.Alves, T.Barcellos, E.J.Lenardao. *Chem. – Eur. J*., **23**, 13760 (2017); https://doi.org/10.1002/chem.201702493
13. N.A.Danilkina, A.A.Vasileva, I.A.Balova. *Russ. Chem. Rev*., **89**, 125 (2020); https://doi.org/10.1070/RCR4902
14. A.Giovanelli, M.Carlotti. *J. Fluorine Chem*., **283**–**284**, 110405 (2025); https://doi.org/10.1016/j.jfluchem.2025.110405
15. F.G.Bordwell. *Acc. Chem. Res.*, **21**, 456 (1988); https://doi.org/10.1021/ar00156a004
16. W.S.Matthews, J.E.Bares, J.E.Bartmess, F.G.Bordwell, F.J.Cornforth, G.E.Drucker, Z.Margolin, R.J.McCallum, G.J.McCollum, N.R.Vanier. *J. Am. Chem. Soc.*, **97**, 7006 (1975); https://doi.org/10.1021/ja00857a010
17. F.G.Bordwell, G.E.Drucker, N.H.Andersen, A.D.Denniston. *J. Am. Chem. Soc*., **108**, 7310 (1986); https://doi.org/10.1021/ja00283a028
18. B.A.Trofimov. *Russ. Chem. Rev*., **50**, 138 (1981); https://doi.org/10.1070/RC1981v050n02ABEH002551
19. B.A.Trofimov. C*urr. Org. Chem*., **6**, 1121 (2002); https://doi.org/10.2174/1385272023373581
20. B.A.Trofimov, N.K.Gusarova. *Russ. Chem. Rev*., **76**, 507 (2007); https://doi.org/10.1070/RC2007v076n06ABEH003712
21. B.A.Trofimov, E.Yu.Schmidt. *Acc. Chem. Res.*, **51**, 1117 (2018); https://doi.org/10.1021/acs.accounts.7b00618
22. E.Yu.Schmidt, B.A.Trofimov. *Russ. Chem. Rev.*, **93** (10), RCR5145 (2024); https://doi.org/10.59761/RCR5145
23. W.N.Olmstead, Z.Margolin, F.G.Bordwell. *J. Org. Chem*., **45**, 3295 (1980); https://doi.org/10.1021/jo01304a032

24. Y.Yuan, I.Thomé, S.H.Kim, D.Chen, A.Beyer, J.Bonnamour, E.Zuidema, S.Chang, C.Bolm. *Adv. Synth. Catal*., **352**, 2892 (2010); https://doi.org/10.1002/adsc.201000575
25. N.M.Vitkovskaya, V.B.Orel, V.B.Kobychev, A.S.Bobkov, D.Z.Absalyamov, B.A.Trofimov. *Int. J. Quantum Chem.*, **120**, e26158 (2020); https://doi.org/10.1002/qua.26158
26. V.B.Kobychev. *J. Phys.: Conf. Ser*., **1847**, 012054 (2021); https://doi.org/10.1088/1742-6596/1847/1/012054
27. N.M.Vitkovskaya, V.B.Orel, V.B.Kobychev, A.S.Bobkov. *Russ. J. Org. Chem*., **59**, 1660 (2023); https://doi.org/10.1134/S1070428023100020
28. B.A.Trofimov, E.Yu.Schmidt, I.A.Ushakov, N.V.Zorina, E.V.Skital'tseva, N.I.Protsuk, A.I.Mikhaleva. *Chem. – Eur. J*., **16**, 8516 (2010); https://doi.org/10.1002/chem.201000227
29. B.A.Trofimov, E.Yu.Schmidt, N.V.Zorina, E.V.Ivanova, I.A.Ushakov, A.I.Mikhaleva. *Adv. Synth. Catal*., **354**, 1813 (2012); https://doi.org/10.1002/adsc.201200210
30. B.A.Trofimov, E.Yu.Schmidt, N.V.Zorina, E.V.Ivanova, I.A.Ushakov. *J. Org. Chem*., **77**, 6880 (2012); https://doi.org/10.1021/jo301005p
31. J.I.Dickstein, S.I.Miller. In *The Chemistry of the Carbon–Carbon Triple Bond*. Pt 2. (Ed. S.Patai). (Chichester: Wiley, 1978). P. 813
32. R.C.Larock, Y.-D.Lu. *J. Org. Chem*., **58**, 2846 (1993); https://doi.org/10.1021/jo00062a031
33. A.S.-Y.Lee, L.-S.Lin. *Tetrahedron Lett*., **41**, 8803 (2000); https://doi.org/10.1016/S0040-4039(00)01446-5
34. M.Yamaguchi, T.Tsukagoshi, M.Arisawa. *J. Am. Chem. Soc*., **121**, 4074 (1999); https://doi.org/10.1021/ja9840221
35. K.Takami, H.Yorimitsu, K.Oshima. *Org. Lett*., **6**, 4555 (2004); https://doi.org/10.1021/ol048070o
36. J.-X.Wang, X.Jia, T.Meng, L.Xin. *Synthesis*, 2838 (2005); https://doi.org/10.1055/s-2005-872178
37. P.R.Krishna, R.Srinivas. *Tetrahedron: Asymmetry*, **19**, 1153 (2008); https://doi.org/10.1016/j.tetasy.2008.04.016
38. F.Shibahara, J.F.Bower, M.J.Krische. *J. Am. Chem. Soc*., **130**, 14120 (2008); https://doi.org/10.1021/ja805356j
39. S.Omura, T.Fukuyama, J.Horiguchi, Y.Murakami, I.Ryu. *J. Am. Chem. Soc*., **130**, 14094 (2008); https://doi.org/10.1021/ja806929y
40. M.Zhang, H.Jiang, P.H.Dixneuf. *Adv. Synth. Catal*., **351**, 1488 (2009); https://doi.org/10.1002/adsc.200900236
41. H.M.R.Hoffmann, T.Tsushima. *J. Am. Chem. Soc*., **99**, 6003 (1977); https://doi.org/10.1021/ja00460a028
42. P.Beak, K.R.Berger. *J. Am. Chem. Soc*., **102**, 3848 (1980); https://doi.org/10.1021/ja00531a029
43. C.Earnshaw, R.S.Torr, S.Warren. *J. Chem. Soc., Perkin Trans. 1*, 2893 (1983); https://doi.org/10.1039/P19830002893
44. B.Baruah, A.Boruah, D.Prajapati, J.S.Sandhu. *Tetrahedron Lett*., **37**, 9087 (1996); https://doi.org/10.1016/S0040-4039(96)02092-8
45. J.S.Yadav, D.Srinivas, G.S.Reddy, K.H.Bindu. *Tetrahedron Lett*., **38**, 8745 (1997); https://doi.org/10.1016/S0040-4039(97)10341-0
46. B.C.Ranu, A.Majee, A.R.Das. *Tetrahedron Lett*., **37**, 1109 (1996); https://doi.org/10.1016/0040-4039(95)02317-8
47. C.Sämann, P.Knochel. *Synthesis*, **45**, 1870 (2013); https://doi.org/10.1055/s-0033-1338415
48. Y.L.N.Murthy, B.S.Diwakar, B.Govindh, K.Nagalakshmi, I.V.K.Viswanath, R.Singh. *J. Chem. Sci*., **124**, 639 (2012); https://doi.org/10.1007/s12039-012-0258-9
49. P.S.Akula, B.-C.Hong, G.-H.Lee. *Org. Lett*., **20**, 7835 (2018); https://doi.org/10.1021/acs.orglett.8b03335
50. Y.Zhang, D.Wang, X.Tong. *Chem. Commun.*, **57**, 3488 (2021); https://doi.org/10.1039/d1cc00368b
51. B.Xiang, Y.Wang, C.Xiao, F.He, Y.Huang. *Chin. Chem. Lett.*, **35**, 108777 (2024); https://doi.org/10.1016/j.cclet.2023.108777
52. X.Kong, J.Song, J.Liu, M.Meng, S.Yang, M.Zeng, X.Zhan, C.Li, X.Fang. *Chem. Commun.*, **54**, 4266 (2018); https://doi.org/10.1039/C8CC01020J
53. R.Chib, B.A.Shah, N.Anand, A.Pandey, K.Kapoor, S.Bani, V.K.Gupta, V.K.Rajnikant, Sethi, S.C.Taneja. *Bioorg. Med. Chem. Lett*., **21**, 4847 (2011); https://doi.org/10.1016/j.bmcl.2011.06.037
54. E.Yu.Schmidt, I.V.Tatarinova, I.A.Ushakov, B.A.Trofimov. *Mendeleev Commun*., **26**, 378 (2016); https://doi.org/10.1016/j.mencom.2016.09.003
55. Z.-P.Xie, M.Zeng, W.Shi, D.-M.Cui, C.Zhang. *J. Saudi Chem. Soc.*, **23**, 215 (2019); https://doi.org/10.1016/j.jscs.2018.06.009
56. *Electronic Materials: The Oligomer Approach*. (Eds K.Muellen, G.Wegner). (Weinheim: Wiley-VCH, 1998)
57. H.Sasabe, Y.-J.Pu, K.Nakayama, J.Kido. *Chem. Commun*., 6655 (2009); https://doi.org/10.1039/B908139A
58. H.A.Yemam, A.Mahl, J.S.Tinkham, J.T.Koubek, U.Greife, A.Sellinger. *Chem. – Eur. J.*, **23**, 8921 (2017); https://doi.org/10.1002/chem.201700877
59. E.Yu.Schmidt, E.V.Ivanova, I.V.Tatarinova, I.A.Ushakov, N.V.Semenova, A.V.Vashchenko, B.A.Trofimov. *Org. Lett*., **18**, 2158 (2016); https://doi.org/10.1021/acs.orglett.6b00782
60. S.Undeela, J.P.Ramchandra, R.S.Menon. *Tetrahedron Lett*., **55**, 5667 (2014); https://doi.org/10.1016/j.tetlet.2014.08.039
61. H.Zhang, J.He, Y.Chen, C.Zhuang, C.Jiang, K.Xiao, Z.Su, X.Ren, T.Wang. *Angew. Chem., Int. Ed*., **60**, 19860 (2021); https://doi.org/10.1002/anie.202106046
62. P.S.Akula, Y.-J.Wang, B.-C.Hong, G.-H.Lee, S.-Y.Chien. *Org. Lett*., **23**, 4688 (2021); https://doi.org/10.1021/acs.orglett.1c01426
63. W.Zhong, Y.Chen, Z.Mai, X.Wei, J.Wang, Q.Zeng, X.Chen, X.Tian, W.Zhang, F.Wang, S.Zhang. *J. Org. Chem*., **85**, 12754 (2020); https://doi.org/10.1021/acs.joc.0c01407
64. X.Wang, L.Zhou, H.Zhang, X.Ren, G.Gao, T.Wang. *Org. Lett*., **24**, 38 (2022); https://doi.org/10.1021/acs.orglett.1c03567
65. K.Stankovianska, V.Nemethova, T.Peňaška, J.Borko, M.Mečiarova, R.Šebesta. *Eur. J. Org. Chem.*, **27**, e202400588 (2024); https://doi.org/10.1002/ejoc.202400588
66. X.Li, X.Kong, S.Yang, M.Meng, X.Zhan, M.Zeng, X.Fang. *Org. Lett*., **21**, 1979 (2019); https://doi.org/10.1021/acs.orglett.9b00035
67. T.Peňaška, V.Modrocka, K.Stankovianska, M.Mečiarova, E.Rakovsky, R.Šebesta. *ChemSusChem*, **15**, e202200028 (2022); https://doi.org/10.1002/cssc.202200028
68. N.Bania, D.Barman, S.C.Pan. *J. Org. Chem.*, **88**, 9584 (2023); https://doi.org/10.1021/acs.joc.3c01063
69. K.X.Yang, D.-S.Ji, H.Zheng, Y.Gu, P.-F.Xu. *Chem. Commun*., **58**, 4227 (2022); https://doi.org/10.1039/D2CC00457G
70. Y.Lin, X.-Q.Hou, B.-Y.Li, D.-M.Du. *Adv. Synth. Catal*., **362**, 5728 (2020); https://doi.org/10.1002/adsc.202001242
71. Y.-H.Miao, Y.-Z.Hua, S.-K.Jia, X.Xiao, M.-C.Wang, G.-J.Mei. *Chem. Commun*., **59**, 6929 (2023); https://doi.org/10.1039/D3CC01641B
72. Q.Zhang, F.Zhang, Z.Wei, X.Shi, L.He, J.Liu, G.Du. *Asian J. Org. Chem.*, **14**, e202400619 (2025); https://doi.org/10.1002/ajoc.202400619
73. L.Ouyang, C.Qi, H.He, Y.Peng, W.Xiong, Y.Ren, H.Jiang. *J. Org. Chem.*, **81**, 912 (2016); https://doi.org/10.1021/acs.joc.5b02487
74. E.Yu.Schmidt, I.V.Tatarinova, N.V.Semenova, N.I.Protsuk, I.A.Ushakov, B.A.Trofimov. *J. Org. Chem*., **83**, 10272 (2018); https://doi.org/10.1021/acs.joc.8b01449
75. W.Zhang, R.Tong. *J. Org. Chem*., **81**, 2203 (2016); https://doi.org/10.1021/acs.joc.6b00246
76. E.Yu.Schmidt, N.V.Zorina, E.V.Ivanova, I.V.Tatarinova, I.A.Ushakov, A.I.Mikhaleva, B.A.Trofimov. *Mendeleev Commun.*, **23**, 340 (2013); https://doi.org/10.1016/j.mencom.2013.11.012
77. D.Z.Wang. *Comprehensive Organic Name Reactions and Reagents*. Pt 3. (London: Wiley, 2009). P. 2793
78. *Name Reactions in Heterocyclic Chemistry II*. (Ed. J.J.Li). (Hoboken: Wiley-VCH, 2011). P. 72

79. S.Frankowski, A.Skrzyńska, L.Sieroń, Ł.Albrecht. *Adv. Synth. Catal.*, **362**, 2658 (2020); https://doi.org/10.1002/adsc.202000197
80. F.Kröhnke. *Synthesis*, 1 (1976); https://doi.org/10.1055/s-1976-23941
81. P.Galatsis. In *Name Reactions in Heterocyclic Chemistry*. (Ed. J.J.Li). (Hoboken: Wiley, 2005). P. 311
82. T.N.Francisco, H.M.T.Albuquerge, A.M.S.Silva. *Chem. – Eur. J.*, **30**, e202401762 (2024); https://doi.org/10.1002/chem.202401672
83. D.A.Shabalin, M.Yu.Dvorko, E.Yu.Schmidt, B.A.Trofimov. *Org. Biomol. Chem.*, **19**, 2703 (2021); https://doi.org/10.1039/D1OB00193K
84. Y.-C.Wang, H.-S.Wang, G.-B.Huang, F.-P.Huang, K.Hu, Y.-M.Pan. *Tetrahedron*, **70**, 1621 (2014); https://doi.org/10.1016/j.tet.2014.01.021
85. E.Yu.Shmidt, I.V.Tatarinova, B.A.Trofimov. *Russ. J. Org. Chem*., **51**, 136 (2015); https://doi.org/10.1134/S1070428015010273
86. E.Yu.Schmidt, E.V.Ivanova, I.V.Tatarinova, N.V.Semenova, I.A.Ushakov, B.A.Trofimov. *Synthesis*, **47**, 1329 (2015); https://doi.org/10.1055/s-0034-1378687
87. E.Yu.Schmidt, E.V.Ivanova, I.V.Tatarinova, I.A.Ushakov, N.I.Protsuk, B.A.Trofimov. *Chem. Heterocycl. Compd.*, **52**, 242 (2015); https://doi.org/10.1007/s10593-015-1691-8
88. Q.Liu, J.Jiang, X.Ye, J.Sun, Y.Wu, Y.Shao, C.Deng, F.Zhang. *J. Org. Chem.*, **88**, 10632 (2023); https://doi.org/10.1021/acs.joc.3c00669
89. F.Pünner, Y.Sohtome, M.Sodeoka. *Chem. Commun.*, **52**, 14093 (2016); https://doi.org/10.1039/c6cc06935e
90. E.Yu.Schmidt, I.V.Tatarinova, E.V.Ivanova, N.V.Zorina, I.A.Ushakov, B.A.Trofimov. *Org. Lett*., **15**, 104 (2013); https://doi.org/10.1021/ol303132u
91. P.Jiang, Y.Wang, D.Chen, Y.Zheng, S.Huang. *Eur. J. Org. Chem.*, **25**, e202101411 (2022); https://doi.org/10.1002/ejoc.202101411
92. G.S.Reddy, D.B.Ramachary. *Org. Chem. Front*., **6**, 3620 (2019); https://doi.org/10.1039/C9QO00864K
93. E.Yu.Schmidt, I.V.Tatarinova, E.V.Ivanova, B.A.Trofimov. *Mendeleev Commun.*, **27**, 283 (2017); https://doi.org/10.1016/j.mencom.2017.05.022
94. E.Yu.Schmidt, I.V.Tatarinova, N.I.Protsuk, I.A.Ushakov, B.A.Trofimov. *J. Org. Chem*., **82**, 119 (2017); https://doi.org/10.1021/acs.joc.6b02233
95. I.Iriarte, O.Olaizola, S.Vera, I.Gamboa, M.Oiarbide, C.Palomo. *Angew. Chem., Int. Ed*., **56**, 8860 (2017); https://doi.org/10.1002/anie.201703764
96. I.Urruzuno, O.Mugica, G.Zanella, S.Vera, E.Gómez-Bengoa, M.Oiarbide, C.Palomo. *Chem. – Eur. J*., **25**, 9701 (2019); https://doi.org/10.1002/chem.201901694
97. Y.-H.Geng, Y.-Z.Hua, S.-K.Jia, M.-C.Wang. *Chem. – Eur. J*., **27**, 5130 (2021); https://doi.org/10.1002/chem.202100284
98. A.V.Artem'ev, S.F.Malysheva, N.A.Belogorlova, N.I.Protzuk, A.I.Albanov, I.Yu.Bagryanskaya, E.Yu.Schmidt, N.K.Gusarova, B.A.Trofimov. *Heteroat. Chem.*, **26**, 455 (2015); https://doi.org/10.1002/hc.21281
99. D.A.Shabalin, E.V.Ivanova, I.A.Ushakov, E.Yu.Schmidt, B.A.Trofimov. *Synthesis*, **51**, 3825 (2019); https://doi.org/10.1055/s-0039-1690003
100. D.A.Shabalin, E.V.Ivanova, I.A.Ushakov, E.Yu.Schmidt, B.A.Trofimov. *J. Org. Chem*., **85**, 8429 (2020); https://doi.org/10.1021/acs.joc.0c00768
101. G.Yue, B.Du, Q.Wang, S.Cheng, L.Ma, C.Lu, J.Feng, H.Hu, S.Li, Q.He. *New J. Chem.*, **48**, 15446 (2024); https://doi.org/10.1039/D4NJ02086C
102. L.Cheng, M.Wang, Y.Yang, Z.Wang, Y.Zhu, L.Kong, Y.Li. *Org. Chem. Front*., **9**, 3354 (2022); https://doi.org/10.1039/D2QO00617K