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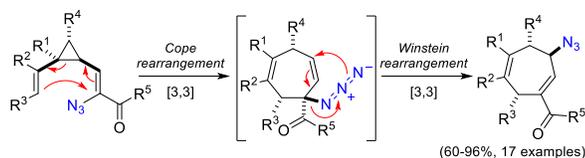
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Cascade Cope/Winstein Rearrangements: Synthesis of Azido-Cycloheptadienes from Dialkenylcyclopropanes Possessing a Vinyl Azide

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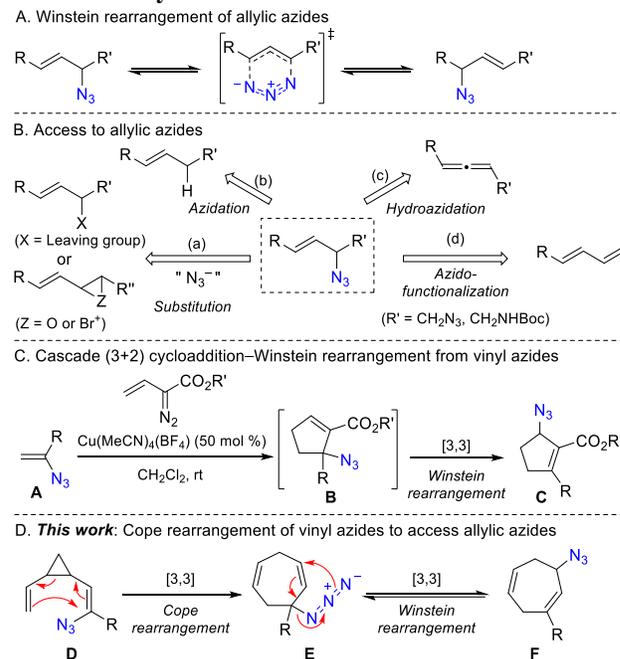


ABSTRACT: *cis*-1,2-Dialkenylcyclopropanes incorporating a vinyl azide, generated by Knoevenagel condensations between the corresponding cyclopropanecarbaldehydes and α -azido ketones, undergo cascade Cope and Winstein [3,3]-sigmatropic rearrangements, under mild conditions. The sequence allows access to diversely substituted 1,4-cycloheptadienes armed with a secondary allylic azide with up to three stereocenters.

Azides have found countless applications in organic chemistry encompassing their use as amines precursors to the development of bioorthogonal ligation reactions.^{1,2} Recent years have seen a renewed interest in the chemistry of aliphatic azides with a particular focus on allylic and vinylic azides.³⁻⁵ The reactivity of allylic azides is dominated by their ability to undergo a facile allylic transposition, known as the Winstein rearrangement (Scheme 1A).³ Steric and electronic factors influencing the position of the equilibrium between interconverting allylic azides have been investigated^{3,6} and the Winstein rearrangement has been coupled with other transformations that can exclusively or preferentially (kinetic dynamic transformations) occur on one regio- or stereoisomer.^{3,7,8} The synthesis of allyl azides is usually accomplished by substitution reactions involving allylic halides or alcohol derivatives, or by ring-opening of vinyl oxiranes or bromonium ions, with a nucleophilic azide source,³ sometimes in the presence of a transition metal catalyst (Scheme 1B, path a).^{3,9} Allylic C–H bond azidation (Scheme 1B, path b),¹⁰ allene hydroazidation (Scheme 1B, path c)¹¹ or 1,3-dienes azido-functionalizations (Scheme 1B, path d)¹² have also emerged as alternative strategies. Because of their versatile reactivity, vinyl azides have been identified as an “emerging class” of hetero-substituted alkenes.⁴ Whilst denitrogenative transformations are the most documented, these latter substrates can serve as precursors of functionalized aliphatic azides.⁵ However, to our knowledge, the synthesis of allyl azides from vinyl azides **A** seems to be restricted to a copper-catalyzed formal (3+2) cycloaddition with vinyl diazoacetates which is followed by a Winstein rearrangement of the initially formed allylic azides **B**, the driving force of which is the formation of the more stable tetrasubstituted cyclopentenoates **C** (Scheme 1C).¹³ Interestingly, sigmatropic rearrangements constitute a class of reactions in which vinyl azides have not been involved so far, despite their potential interest to access other classes of unsaturated aliphatic azides. Perhaps the required conditions and reagents may have deterred chemists from considering these latter

hazardous, reactive and thermally labile substrates, which can generate 2*H*-azirines and/or vinyl nitrenes upon heating.¹⁴

Scheme 1. Allylic azides: Synthesis, Winstein Rearrangement and Vinyl Azides as Potential Precursors.

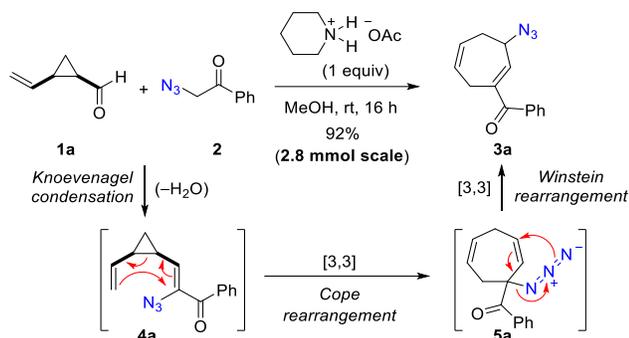


Herein, we report the Cope rearrangement of *cis*-dialkenyl cyclopropanes **D** incorporating a vinyl azide,¹⁵ as a route to cycloheptadienes **E** possessing a tertiary allylic azide and their subsequent isomerization into azido-cycloheptadienes **F** by a Winstein rearrangement (Scheme 1D).

The preparation of *cis*-(2-alkenylcyclopropyl)alkenyl azides **D** required for this study was envisioned by a Knoevenagel condensation between the corresponding cyclopropanecarbaldehydes and α -azido carbonyl compounds.^{16,17} Aldehyde **1a** was

involved in a Knoevenagel condensation with α -azido acetophenone **2** in the presence of piperidinium acetate (MeOH, rt, 16 h).¹⁶ Under these conditions, the 1,4-cycloheptadiene **3a**, possessing a secondary azide, was identified as the new product and was isolated in high yield (92%). Hence, the *cis*-1,2-dialkenylcyclopropane **4a**, arising from the Knoevenagel condensation underwent an efficient Cope rearrangement and the resulting 1,4-cycloheptadiene **5a**, incorporating a tertiary allylic azide, further evolved by a Winstein rearrangement which is completely shifted toward the more stable secondary allylic azide **3a**, possessing an α,β -unsaturated ketone (Scheme 2).

Scheme 2. Cascade Knoevenagel condensation–Cope and Winstein sigmatropic rearrangements from aldehyde **1a**.



The scope of the cascade Knoevenagel condensation–Cope and Winstein sigmatropic rearrangements was then explored with diversely substituted *cis*-(2-alkenylcyclopropane)-carbaldehydes **1b–1l** and α -azido acetophenone **2** (Table 1). The reaction accommodates a substituent at the α position of the alkene on the cyclopropyl aldehyde **1b**, as illustrated with the formation of cycloheptadiene **3b** (76%) (Table 1, entry 1). Aldehyde **1c** possessing an α,α -disubstituted olefin was a viable partner in the Knoevenagel condensation with **2** but the Cope/Winstein cascade rearrangements leading to cycloheptadiene **3c** (66%) incorporating an enol phosphate only occurred after heating the crude vinyl azide intermediate (EtOH, reflux, 16 h) (Table 1, entry 2). The reactivity of aldehydes **1d–1g** possessing an α,β -disubstituted olefin was next explored. Aldehydes **1d** and **1e**, substituted by a phenyl or a (*tert*-butyldiphenylsilyloxy)methyl group on the alkene ($E/Z > 96:4$), respectively led to the azido-cycloheptadienes **3d** (73%) and **3e** (78%) as single detectable diastereomers ($dr > 96:4$, by ¹H NMR spectroscopy) (Table 1, entries 3 and 4). Interestingly, in the case of aldehydes **1f** and **1g** in which the α,β -disubstituted alkene was not fully controlled ($E/Z = 92:8$), cycloheptadienes **3f** (72%) and **3g** (87%) were respectively obtained as single diastereomers (Table 1, entries 5 and 6). As confirmed later in the case of substrate **1i** (*vide infra*), both geometric isomers of **1f** and **1g** probably underwent the Knoevenagel condensation with **2** but only the (*E*) isomers subsequently evolve by a Cope rearrangement. 2-Vinylcyclopropanecarbaldehydes possessing a 1,2,3-trisubstituted three-membered ring could also be considered as substrates but the Cope rearrangement proceeds only when the additional substituent (R^4) is *trans* to the alkenyl chains.¹⁸

Table 1. Cascade Knoevenagel condensation–Cope and Winstein sigmatropic rearrangements from cyclopropane-carbaldehydes **1b–1l and α -azido ketone **2**.**

entry	substrate	product	yield
1	1b	3b	76%
2 ^a	1c	3c	66%
3 ^b	1d , $R^3 = \text{Ph}$ ($E/Z = 96:4$)	3d , $R^3 = \text{Ph}$	73%
4	1e , $R^3 = \text{CH}_2\text{OTBDPS}$ ($E/Z = 96:4$)	3e , $R^3 = \text{CH}_2\text{OTBDPS}$	78%
5	1f , $R^3 = n\text{-Pent}$ ($E/Z = 92:8$)	3f , $R^3 = n\text{-Pent}$	72%
6	1g , $R^3 = (\text{CH}_2)_2\text{CO}_2\text{Et}$ ($E/Z = 92:8$)	3g , $R^3 = (\text{CH}_2)_2\text{CO}_2\text{Et}$	87%
7 ^c	1h	3h ($dr > 96:4$)	66%
8 ^d	1i , $R^3 = \text{Ph}$ ($E/Z = 65:35$)	3i ($dr > 96:4$)	68%
9 ^e	1j	3j (0%) and 6 (54%)	
10	1k , $R^3 = \text{H}$	3k , $R^3 = \text{H}$	90%
11	1l , $R^3 = \text{Ph}$ ($E/Z > 96:4$)	3l , $R^3 = \text{Ph}$	90%

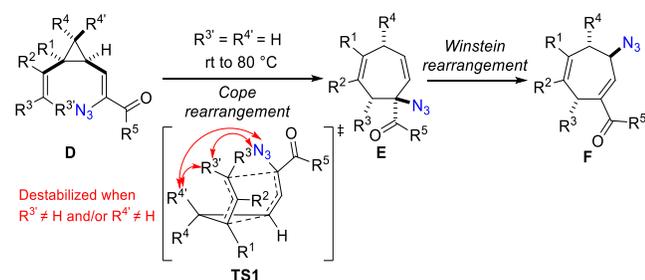
^a The crude product was further heated in refluxing EtOH for 16 h. ^b Experiments conducted at a scale ≥ 1 mmol. ^c The crude product was further heated in CDCl_3 at 40 °C for 24 h. ^d The crude product was further heated in refluxing CH_2Cl_2 for 24 h. ^e Reaction run in EtOH (rt, 16 h then 70 °C, 24 h).

In the case of aldehyde **1h** substituted by a phenyl group, the Knoevenagel condensation with **2** leading to azide **4h** was complete after the usual reaction time (16 h) but cycloheptadiene **3h** was only a minor product (20%) at this stage. Heating was required to trigger the Cope rearrangement, which was immediately followed by the Winstein transposition leading to cycloheptadiene **3h** as a single diastereomer (66%), as evidenced by monitoring using ¹H NMR spectroscopy (CDCl_3 , 40 °C, 24 h)

(Table 1, entry 7). The reactivity of aldehyde **1i** (*E/Z* = 65:35) paralleled that of **1f**, **1g** and **1h** since both geometric isomers underwent the Knoevenagel condensation with **2** but subsequent heating (CH₂Cl₂, reflux, 24 h) triggered the cascade Cope-Winstein rearrangements of the (*E*) geometric isomer exclusively which afforded cycloheptadiene **3i** (68%, based on (*E*)-**1i**) (Table 1, entry 8), whereas the vinyl azide generated from (*Z*)-**1i** did not react further. The presence of an ester in substrate **1j** retarded the Cope rearrangement so the crude product arising from the Knoevenagel condensation was heated in refluxing EtOH. However, under these conditions, the azido-cycloheptadiene **3j** generated by the cascade sigmatropic rearrangements underwent elimination of HN₃ to produce the conjugated cycloheptatriene **6** (Table 1, entry 9). By contrast with **1h** and **1j**, a silyloxymethyl substituent on the cyclopropane ring in substrates **1k** and **1l** did not have any adverse effect on the rate of the Cope rearrangement which proceeded at rt and after Winstein rearrangement, the desired tri- and tetrasubstituted cycloheptadienes, **3k** and **3l** respectively, were isolated in 90% yield (Table 1, entries 10 and 11).

The relative stereochemistry of the azido-cycloheptadiene **3i** was established by X-ray diffraction analysis¹⁹ and that of the other products **3d–3k** was assigned by analogy. The stereochemical outcome can be understood considering that the Knoevenagel condensation between aldehydes and α -azido ketones is known to afford α -azido trisubstituted enones **D** of (*Z*) configuration¹⁶ and that the Cope rearrangement of divinylcyclopropanes occurs through a boat transition state **TS1**.¹⁵ Additionally, the subsequent rapid Winstein rearrangement of the initially formed tertiary allylic cycloheptadienyl azides **E**, which have never been detected as intermediate products, would proceed in a suprafacial manner and with complete chirality conversion.³ It is worth noting that despite the presence of a trisubstituted alkene, the low steric demand of the azido group enables dialkenylcyclopropanes **D** to undergo the Cope rearrangement under mild conditions (at rt, in most cases, or 40–80 °C) which do not jeopardize the thermally labile vinyl azide moiety. Limitation of the scope to substrates **D** devoid of substituent on the three-membered ring *cis* to the alkenyl groups ($R^4 = H$) or to (*E*)- α,β -disubstituted alkenes ($R^3 = H$) can also be understood from the transition state model **TS1**. Indeed, for substrates **D** in which R^3 or R^4 would differ from hydrogen atoms, the transition state of the Cope rearrangement would be significantly destabilized by steric interactions (A^{1,3} strain or eclipsing interaction between the R^3 and N₃ substituents)^{15,20} and hence the reaction would require higher temperatures, incompatible with the vinyl azide (Scheme 3).¹⁸

Scheme 3. Transition state of the Cope rearrangement of *cis*-dialkenyl cyclopropanes **D**.



The scope of the Knoevenagel condensation–Cope/Winstein rearrangements cascade was further explored with different α -azido ketones (Table 2).

Table 2. Cascade Knoevenagel condensation–Cope and Winstein sigmatropic rearrangements from cyclopropane-carbaldehydes **1d–1l and α -azido ketones **7–11**.**

entry	aldehyde	α -azido ketone	product	yield
1	1d , $R^4 = H$	7 , $R = OMe$	12 , $R = OMe$	72%
2	1d , $R^4 = H$	8 , $R = Cl$	13 , $R = Cl$	87%
3	1d , $R^4 = H$	9 , $R = F$	14 , $R = F$	96%
4	1d , $R^4 = H$	10 , $R = Ph$	15 , $R = Ph$	89%
5	1d , $R^4 = H$	11 , $R = OBz$	16 , $R = OBz$	60%
			17 , $R = OBz$	59%
6	1l , $R^4 = CH_2OTBS$	8 , $R = Cl$	18 , $R = Cl$	96%

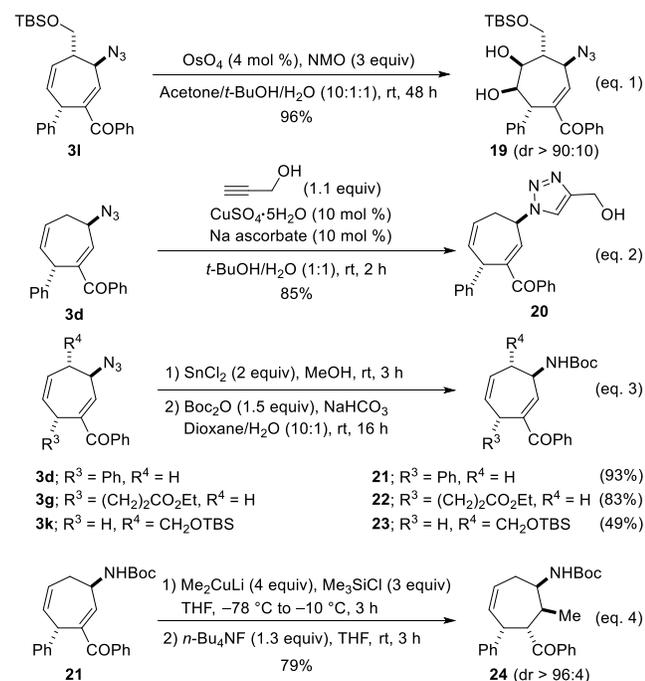
1) DIBAL-H (3 equiv), CH₂Cl₂, -78 °C to -40 °C
 2) NaIO₄, THF/H₂O, rt

The reaction of aldehyde **1d** with α -azido *p*-methoxy- and *p*-chloroacetophenone, **7** and **8**, as well as with *o*-fluoroacetophenone **9**, under usual conditions (piperidinium acetate, MeOH, rt, 16 h) delivered the azido-cycloheptadienes **12** (72%), **13** (87%) and **14** (96%), respectively (Table 2, entries 1–3). Besides acetophenones, α -azido chalcone **10** and α -azido α' -(benzoyloxy)acetone **11** could be successfully used as partners with aldehyde **1d** and delivered the corresponding cycloheptadienes **15** (89%) and **16** (60%) (Table 2, entries 4 and 5). It is worth pointing out that α -azido ketone **11** can act as a surrogate for α -azido acetaldehyde in the Knoevenagel condensation since chemoselective reduction of the ketone and the ester in compound **16** with DIBAL-H, followed by oxidative cleavage of the resulting 1,2-diol with NaIO₄, delivered the α,β -unsaturated aldehyde **17** (59%) (Table 2, entry 5). The reaction between **1l** and α -azido ketone **8** also afforded the tetrasubstituted azido-cycloheptadiene **18** in excellent yield (96%) (Table 2, entry 6).

Seven-membered carbocycles are less represented than cyclic systems of smaller size in bioactive compounds but are currently eliciting a growing interest in medicinal chemistry.²¹ Hence, with several azido-cycloheptadienes of type **F** in hands,

some post-functionalization reactions were carried out to highlight the synthetic interest of these latter functionalized seven-membered carbocycles (Scheme 4).

Scheme 4. Post-functionalization reactions.



The electron-rich olefin in compound **3l** could be chemoselectively dihydroxylated under standard conditions to afford the corresponding 1,2-diol **19** (96%) with high diastereoselectivity (dr > 90:10), presumably arising from a steric control (dihydroxylation occurring *trans* to both adjacent allylic substituents) (Scheme 4, eq. 1). Transformations involving the azido group were next investigated. The azido-cycloheptadiene **3d** was involved in a copper-catalyzed (3+2)-cycloaddition with propargyl alcohol to deliver the corresponding 1,4-triazole **20** (85%) (Scheme 4, eq. 2). Reduction of the azido group in compounds **3d**, **3g** and **3k** was efficiently accomplished using SnCl₂ (MeOH, rt)²² and the crude amine hydrochlorides were converted to *N*-Boc carbamates **21** (93%), **22** (83%) and **23** (49%), respectively (Scheme 4, eq. 3). The presence of an enone moiety in these latter products led us to explore the feasibility of the conjugate addition of organocuprates. The *N*-Boc carbamate **21** underwent 1,4-addition of Me₂CuLi in the presence of Me₃SiCl.²³ After subsequent protodesilylation of the silyl enol ether with *n*-Bu₄NF, the tetrasubstituted cycloheptene **24** was obtained as a single diastereomer (79%) and the relative stereochemistry of this latter crystalline compound was unambiguously established by X-ray diffraction analysis. Since the *N*Hoc group did not exert a directing effect in previously reported examples of cuprates addition to γ -amino α,β -unsaturated compounds,²³ the stereochemical outcome may be due to a faster silylation of the d- π^* cuprate-enone complex when the copper is *trans* to the bulky phenyl group of **21**.²⁴ This could explain the *trans* relationship between the phenyl and the methyl groups after reductive elimination of the copper(III) β -adduct, whilst protodesilylation of the silyl enol ether would result in proton transfer on the face opposite to the phenyl group (Scheme 4, eq. 4).

In conclusion, we have shown that 1,2-dialkenyl cyclopropanes, generated by a Knoevenagel condensation between *cis*-(2-alkenyl)cyclopropanecarbaldehydes and α -azido ketones, readily undergo cascade Cope and Winstein rearrangements leading to azido-cycloheptadienes incorporating up to three stereocenters. Hence, an access to allylic azides, complementary to the existing strategies, has been devised and the products are seven-membered carbocycles with new substitution patterns, armed with an azido group potentially useful for further derivatization. These results highlight the synthetic interest of vinyl azides in sigmatropic rearrangement as a route to different classes of aliphatic azides.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures, ¹H, ¹³C and ¹⁹F NMR spectra, and characterization data of new compounds (PDF)

Crystallographic data for compounds **3l** and **24** (cif)

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Author Contributions

All authors have given approval to the final version of the manuscript.

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REFERENCES

- (a) Bräse, S.; Gil, C.; Knepper, K.; Zimmermann, V. Organic Azides: an Exploding Diversity of a Unique Class of Compounds. *Angew. Chem., Int. Ed.* **2005**, *44*, 5188–5240. (b) Bräse, S.; Banert, K. *Organic Azides: Syntheses and Applications*; John Wiley & Sons, Ltd: Chichester, **2010**.
- (a) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. A Stepwise Huisgen Cycloaddition Process: Copper(I)-Catalyzed Regioselective “Ligation” of Azides and Terminal Alkynes. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596–2599. (b) Wang, Q.; Chan, T. R.; Hilgraf, R.; Fokin, V. V.; Sharpless, K. B.; Finn, M. G. Bioconjugation by Copper(I)-Catalyzed Azide-Alkyne [3 + 2] Cycloaddition. *J. Am. Chem. Soc.* **2003**, *125*, 3192–3193. (c) Agard, N. J.; Prescher, J. A.; Bertozzi, C. R. A Strain-Promoted [3 + 2] Azide-Alkyne Cycloaddition for Covalent Modification of Biomolecules in Living Systems. *J. Am. Chem. Soc.* **2004**, *126*, 15046–15047. (d) Schilling, C. I.; Jung, N.; Biskup, M.; Schepers, U.; Bräse, S. Bioconjugation via azide-Staudinger ligation: an overview. *Chem. Soc. Rev.* **2011**, *40*, 4840–4871.
- Carlson, A. S.; Topczewski, J. J. Allylic Azides: Synthesis, Reactivity, and the Winstein Rearrangement. *Org. Biomol. Chem.* **2019**, *17*, 4406–4429.
- (a) Chiba, S. Application of Organic Azides for the Synthesis of Nitrogen-Containing Molecules. *Synlett* **2012**, 21–44. (b) Hu, B.; DiMagno, S. G. Reactivities of vinyl azides and their recent applications in nitrogen heterocycle synthesis. *Org. Biomol. Chem.* **2015**, *13*, 3844–3855. (c) Fu, J.; Zanoni, G.; Anderson, E. A.; Bi, X. α -Substituted vinyl azides: an emerging functionalized alkene. *Chem. Soc. Rev.* **2017**, *46*, 7208–7228. (d) Hayashi, H.; Kaga, A.; Chiba, S. Application

- of Vinyl Azides in Chemical Synthesis: A Recent Update. *J. Org. Chem.* **2017**, *82*, 11981–11989.
- (5) Sivaguru, P.; Ning, Y.; Bi, X. New Strategies for the Synthesis of Aliphatic Azides. *Chem. Rev.* **2021**, *121*, 4253–4307.
- (6) (a) Gagneux, A.; Winstein, S.; Young, W. G. Rearrangement of Allylic Azides. *J. Am. Chem. Soc.* **1960**, *82*, 5956–5957. (b) Ott, A. A.; Packard, M. H.; Ortuño, M. A.; Johnson, A.; Suding, V. P.; Cramer, C. J.; Topczewski, J. J. Evidence for a Sigmatropic and an Ionic Pathway in the Winstein Rearrangement. *J. Org. Chem.* **2018**, *83*, 8214–8224. (c) Vallejos, M. M.; Labadie, G. R. Insight into the factors controlling the equilibrium of allylic azides. *RSC Adv.* **2020**, *10*, 4404–4413.
- (7) For selected examples, see: (a) Craig, D.; Harvey, J. W.; O'Brien, A. G.; White, A. J. P. Claisen rearrangements of equilibrating allylic azides. *Org. Biomol. Chem.* **2011**, *9*, 7057–7061. (b) Tjeng, A. A.; Handore, K. L.; Batey, R. A. Stereocontrolled Microwave-Assisted Domino [3,3]-Sigmatropic Reactions: A Winstein–Overman rearrangement for the Formation of Differentiated Contiguous C–N Bonds. *Org. Lett.* **2020**, *22*, 3050–3055.
- (8) For selected examples, see: (a) Ott, A. A.; Goshey, C. S.; Topczewski, J. J. Dynamic Kinetic Resolution of Allylic Azides via Asymmetric Dihydroxylation. *J. Am. Chem. Soc.* **2017**, *139*, 7737–7740. (b) Porter, M. R.; Shaker, R. M.; Calcanas, C.; Topczewski, J. J. Stereoselective Dynamic Cyclization of Allylic Azides: Synthesis of Tetralins, Chromanes and Tetrahydroquinolines. *J. Am. Chem. Soc.* **2018**, *140*, 1211–1214. (c) Liu, R.; Zhang, Y.; Xu, J. Selective hydroboration of equilibrating allylic azides. *Chem. Commun.* **2021**, *57*, 8913–8916. (d) Liu, E.-C.; Topczewski, J. J. Enantioselective Nickel-Catalyzed Alkyne–Azide Cycloaddition by Dynamic Kinetic Resolution. *J. Am. Chem. Soc.* **2021**, *143*, 5308–5313.
- (9) (a) Goswami, M.; de Bruin, B. Metal-Catalysed Azidation of Organic Molecules. *Eur. J. Org. Chem.* **2017**, 1152–1176. (b) Sala, R.; Loro, C.; Foschi, F.; Brogini, G. Transition Metal Catalyzed Azidation Reactions. *Catalysts* **2020**, *10*, 1173.
- (10) (a) Chen, H.; Yang, W.; Wu, W.; Jiang, H. Palladium-catalyzed regioselective azidation of allylic C–H bonds under atmospheric pressure of dioxygen. *Org. Biomol. Chem.* **2014**, *12*, 3340–3343. (b) Karimov, R. R.; Sharma, A.; Hartwig, J. F. Late Stage Azidation of Complex Molecules. *ACS Cent. Sci.* **2016**, *2*, 715–724.
- (11) (a) Hurtado-Rodrigo, C.; Hoehne, S.; Muñoz, M. P. A new gold-catalysed azidation of allenes. *Chem. Commun.* **2014**, *50*, 1494–1496. (b) Khrakovsky, D. A.; Tao, C.; Johnson, M. W.; Thornbury, R. T.; Shevick, S. L.; Toste, F. D. Enantioselective, Stereodivergent Hydroazidation and Hydroamination of Allenes Catalyzed by Acyclic Diaminocarbene (ADC) Gold(I) Complexes. *Angew. Chem., Int. Ed.* **2016**, *55*, 6079–6083.
- (12) (a) Zhou, H.; Jian, W.; Qian, B.; Ye, C.; Li, D.; Zhou, J.; Bao, H. Copper-Catalyzed Ligand-Free Diazidation of Olefins with TMSN₃ in CH₃CN or in H₂O. *Org. Lett.* **2017**, *19*, 6120–6123. (b) Forster, D.; Guo, W.; Wang, Q.; Zhu, J. Photoredox Catalytic Three-Component Aminoazidation of 1,3-Dienes. *ACS Catal.* **2021**, *11*, 10871–10877.
- (13) López, E.; López, L. A. Synthesis of Functionalized Cyclopentene Derivatives from Vinyl diazo Compounds and Vinyl Azides through Sequential Copper-Promoted [3+2] Cycloaddition/Azide Rearrangement. *Angew. Chem., Int. Ed.* **2017**, *56*, 5121–5124.
- (14) (a) L'abbé, G. Reactions of Vinyl Azides. *Angew. Chem., Int. Ed.* **1975**, *14*, 775–830. (b) Khlebnikov, A. F.; Novikov, M. S. Recent advances in 2*H*-azirine chemistry. *Tetrahedron* **2013**, *69*, 3363–3401. (c) Khlebnikov, A. F.; Novikov, M. S.; Rostovskii, N. V. Advances in 2*H*-azirine chemistry: A seven-year update. *Tetrahedron* **2019**, *75*, 2555–2624.
- (15) (a) Hudlicky, T.; Fan, R.; Reed, J. W.; Gadamasetti, K. G. Divinylcyclopropane-Cycloheptadiene Rearrangement. *Org. React.* **1992**, *41*, 1–133. (b) Krüger, S.; Gaich, T. Recent applications of the divinylcyclopropane-cycloheptadiene rearrangement in organic synthesis. *Beilstein J. Org. Chem.* **2014**, *10*, 163–193. For selected recent applications, see: (c) Apel C.; Hartmann, S. S.; Lentz, D.; Christmann, M. Dienamine-Induced Divinylcyclopropane-Cycloheptadiene Rearrangements. *Angew. Chem., Int. Ed.* **2019**, *58*, 5075–5079. (d) Sommer, H.; Weissbrod, T.; Marek, I. A Tandem Iridium-Catalyzed "Chain Walking"/Cope Rearrangement Sequence. *ACS Catal.* **2019**, *9*, 2400–2406.
- (16) Knittel, D.; Hemetsberger, H.; Weidmann, H. Enazide, 2. Mitt.: Synthese von 1,3-Diaryl-3-azido-propenenen (α -Azido-chalkonen). *Monatsh. Chem.* **1970**, *101*, 157–160.
- (17) Attempts to use ethyl azidoacetate as partner in the Knoevenagel condensation (EtONa/EtOH) with cyclopropyl aldehydes led to very low yields of adducts, despite two previously reported examples (without indication of the yields), see: (a) Isomura, K.; Kawasaki, H.; Takehara, K.; Taniguchi, H. Thermal reactions of 2-Cyclopropyl-2*H*-Azirines. *Heterocycles* **1995**, *40*, 511–514. Modified conditions were tested without any improvement, see: (b) Heaner, W. L. IV; Gelbaum, C. S.; Gelbaum, L.; Pollet, P.; Richman, K. W.; DuBay, W.; Butler, J. D.; Wells, G.; Liotta, C. L. Indoles via Knoevenagel-Hemetsberger reaction sequence. *RSC Adv.* **2013**, *3*, 13232–13242.
- (18) For additional experiments dealing with attempted Cope rearrangement of substrates of type **D** incorporating a 1,2,3-*cis*-trisubstituted or a 1,2-*trans*-disubstituted cyclopropane, see the Supporting Information.
- (19) CCDC2158744 (**31**) and CCDC2170704 (**24**) contain the crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
- (20) Osler, J. D.; Unsworth, W. P.; Taylor, R. J. K. The Cope Rearrangement of *gem*-dimethyl substituted divinylcyclopropanes. *Org. Biomol. Chem.* **2013**, *11*, 7587–7594.
- (21) Ouvry, G. Recent applications of seven-membered rings in drug design. *Bioorg. Med. Chem.* **2022**, *57*, 116650.
- (22) Maiti, S. N.; Singh, M. P.; Micetich, R. G. Facile Conversion of Azides into Amines. *Tetrahedron Lett.* **1986**, *27*, 1423–1424.
- (23) (a) Yoda, H.; Naito, S.; Takabe, K.; Tanaka, N.; Hosoya, K. Conjugate addition to chiral γ -heterosubstituted δ -lactones as pivotal synthons from L-glutamic acid. Synthesis of an optically active lignan lactone; (–)-hinokinin. *Tetrahedron Lett.* **1990**, *31*, 7623–7626. (b) Evans, D. A.; Britton, T. C.; Ellman, J. A.; Dorow, R. L. The Asymmetric Synthesis of α -Amino Acids. Electrophilic Azidation of Chiral Imide Enolates, a Practical Approach to the Synthesis of (*R*)- and (*S*)- α -Azido Carboxylic Acids. *J. Am. Chem. Soc.* **1990**, *112*, 4011–4030.
- (24) Frantz, D. E.; Singleton, D. A. Isotope Effects and the Mechanism of Chlorotrimethylsilane-Mediated Addition of Cuprates to Enones. *J. Am. Chem. Soc.* **2000**, *122*, 3288–3295.