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Aromatization-driven deconstruction/refunctionalization of unstrained rings

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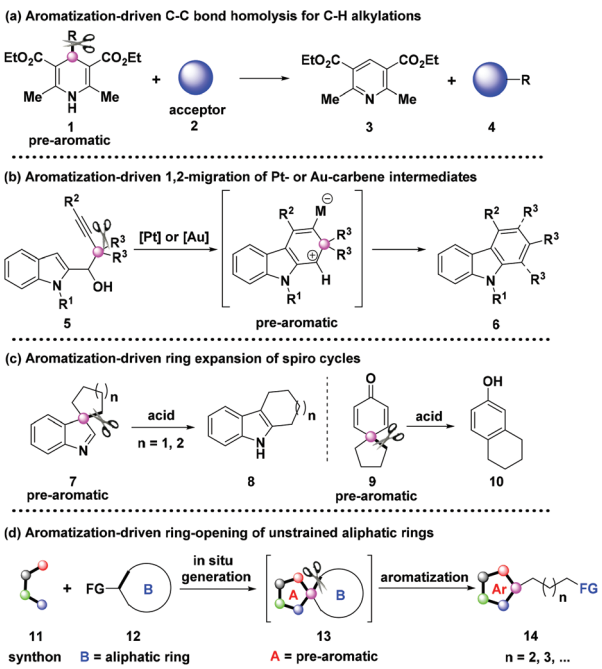
Aromatization-driven ring-opening/functionalization of common unstrained rings has been developed with the *in situ* generation of pre-aromatic fused spiro heterocycles as the key step, featuring (1) simple operation *via* a convenient one-pot reaction and (2) broad scope of various ring systems which do not require pre-activation.

As is well known, aromatization is an important thermodynamic driving force for the formation of stable aromatic rings in organic synthesis.[1] And the C–C bond activation as a significant route for molecular modification is a hot research field.[2] Remarkably, the exploitation of aromatization-driven C–C bond cleavage can be traced back to 1972 with the assistance of transition metals.[3] However, since then, the utilization of aromatization as a driving force for C–C bond cleavage has been unappreciated for a long time, and only a few relevant studies have been reported.[3,4] Recently, this strategy has been revived gradually for elaborate transformations and has drawn increasing attention from chemists.[5–8] For example, Melchiorre,[6a] Molander,[6b] and Chen[6c] developed C–H alkylation reactions independently by employing the aromatization-driven C–C bond homolysis strategy of 4-alkyl-1,4-dihydropyridines **1** (Scheme 1a). The Ma group performed the pioneering work on the aromatization-driven 1,2-migration of Pt- or Au-carbene intermediates for the synthesis of carbazoles (Scheme 1b).[7] Besides, You[8a–e] and other groups[8f–g] reported the aromatization-driven ring-expanding rearomatization of spiroindolenines **7** for the construction of polycyclic indoles **8** *via* acid-mediated migration, respectively. In addition, the spirocyclization-dienone-phenol rearrangement cascade reactions have been reported as well with the promotion of aromatization (Scheme 1c).[9] Yet the major reason that restricts the wide application of aromatization as a driving force for synthetic transformations is the difficulty in the *in situ* generation of pre-aromatic substrates, which usually need to be prefabricated through tedious steps.

Aliphatic rings are ubiquitous in various kinds of organic compounds including pharmaceutical drugs, natural products, and functional materials.[10] Thus, employing the widely-sourced aliphatic rings as starting materials for deconstruction and re-functionalization would be significantly important for the development of organic synthesis and industrial production. However, for a long time, chemists have been limited in the cleavage of strained rings, which were equipped with an inherent thermodynamic driving force for releasing the ring strain (Fig. 1).[11] The C–C bond cleavage/editing of unstrained aliphatic rings is a compelling challenge owing to the high C–C bond dissociation energy.

This highlight article aims to provide a concise overview of the aromatization-driven ring deconstruction strategy of



Scheme 1 Representative types of aromatization-driven C–C bond cleavage.

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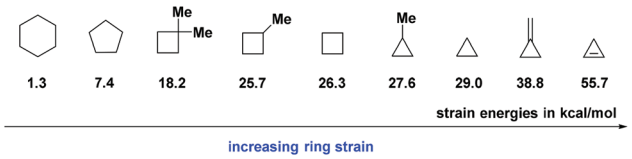


Fig. 1 Strain energies of different sizes of aliphatic rings.

readily available unstrained cycloalkanones and cycloalkanamines *via* radical-mediated C–C bond fragmentation. The protocol features the *in situ* generation of pre-aromatic fused spiro cycles **13**, as shown in Scheme 1d, which might bring a distinct research direction for the development of organic chemistry.

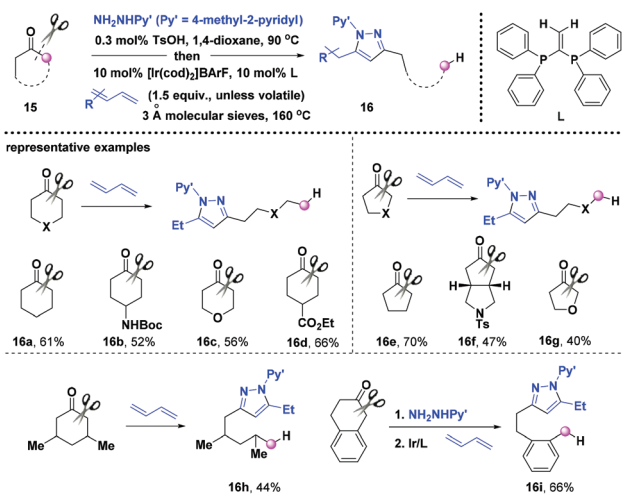
Aromatization-driven C–C bond cleavage of unstrained cycloalkanones

C–C bond activation/functionalization of cycloalkanones emerged as a useful method for synthesizing complex scaffolds. Seminal work by Jun developed the rhodium(I)-catalyzed ring-opening of medium to large cycloalkanone imines to provide various aliphatic chain decorated ketones in 2001.[12] Afterwards, the pursuit for the C–C bond activation/functionalization of cycloalkanones went on uninterrupted, but only sporadic works were reported for unstrained ring activation.[13] Among them, the Dong group has made outstanding contributions to the transition-metal catalyzed unstrained C–C bond activation with the assistance of *in situ* formed directing groups.[13b–e]

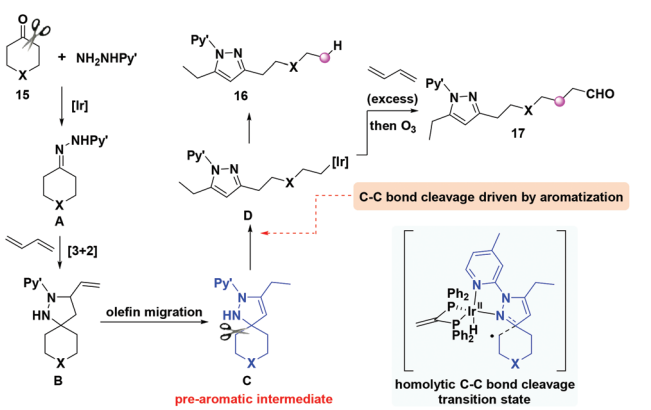
Very recently, Dong and co-workers reported the efficient ring-opening reactions of unstrained cycloalkanones based on radical fragmentation involved aromatization-driven C–C bond activation (Scheme 2).[14] These deacylative transformations provided various skeleton-functionalized aliphatic chains linking pyrazole *via* a three-component coupling in the presence of an iridium/phosphine combination. Considering the less-accessible carbocyclic pre-aromatics, the authors designed the three component involved 1,3-dipolar addition to prepare the precursor of the pre-aromatized heterocycle which serves as the key intermediate for the subsequent conversion. Various cycloalkanones **15** with different substitutions and ring sizes are available for the aromatization-driven deconstructive transformations. In addition, good regioselectivity has been observed when unsymmetrical ketones and heterocyclic ketones were used, and the bond scission preferentially occurred at more substituted carbons or the α-position of heteroatoms. Besides, various natural products were well tolerated for the C–C bond transformation.

Based on mechanistic studies and DFT calculations, an aromatization-promoted homolytic C–C cleavage/radical recombination mechanism was proposed (Scheme 3). The initial [3 + 2] cycloaddition occurs between 1,3-butadiene and the hydrazone intermediate **A**, generating cyclic adduct **B** which could be isolated. Then olefin migration takes place to afford the dihydropyrazole intermediate **C** which serves as the pre-aromatic substrate to drive the following homolytic C–C bond cleavage with the promotion of an iridium catalyst. The control experiments indicate that no C–C cleavage occurs without the endocyclic double bond or the five-membered ring structure, which demonstrates the significant role of the intermediate **C**. Subsequently, the aromatization-driven deconstruction of the unstrained ring occurs, providing the iridium complex **D** bearing aromatized pyrazole. Then the C–H reductive elimination or coupling with 1,3-butadiene of iridium complex **D** takes place to afford the corresponding products **16** and **17**, respectively. In addition to cycloalkanones, the deacylative transformations are suitable for a variety of linear ketones as well, which offer strategic bond disconnections for editing of the molecular skeleton.

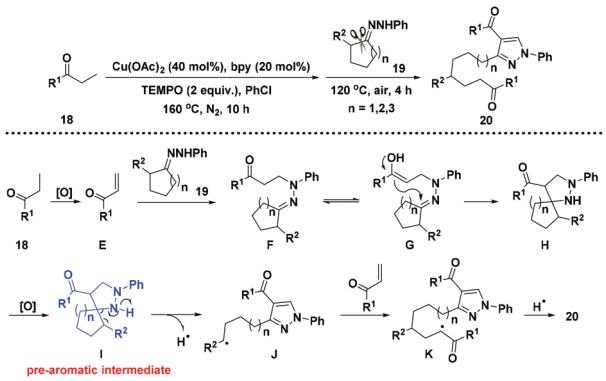
In addition, Fan and co-workers described the ring-opening reactions through [3 + 2] cycloaddition of enone with unstrained cyclic ketone hydrazone followed by an aromatization-driven



Scheme 2 Deconstructive pyrazole synthesis from unstrained cycloalkanones.



Scheme 3 Plausible mechanism for deconstructive pyrazole synthesis from unstrained cycloalkanones.



Scheme 4 Ring-opening reactions for the synthesis of 4-acylpyrazole from unstrained cyclic ketone hydrazine.

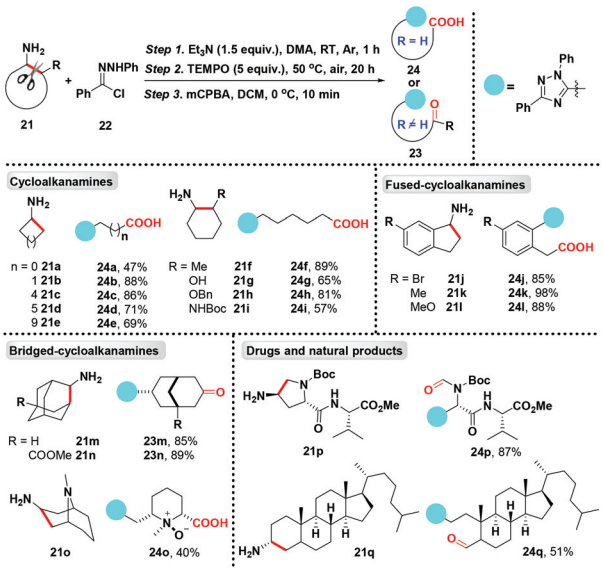
homolytic C–C bond cleavage/radical reorganization (Scheme 4).[15] In this reaction, the *in situ* generated pre-aromatic **I** is considered as the key intermediate likewise to drive the subsequent C–C bond disconnection for aromatization.

Aromatization-driven C–C bond cleavage of unstrained cycloalkanamines

Cycloalkanamines as essential structural units are widely found in natural products, pharmaceuticals, and agrochemicals. The development of convenient methods to make use of the widespread cycloalkanamines is extremely meaningful for modern chemical production. At present, the utilization of cycloalkanamines *via* ring-opening reconstruction is underdeveloped, and the scarce cases that are reported are almost limited to strained rings.[16]

For example, Zheng and co-workers conducted the pioneering work on the photogenerated amine radical cation-involved ring-extension reactions of cyclopropyl- and cyclobutyl-anilines with alkenes and alkynes.[16a–d] Recently, Waser and co-workers described an oxidative ring-opening strategy to transform aminocyclopropanes into 1,3-dielectrophilic carbon intermediates bearing a halide atom (Br, I) and a *N*,*O*-acetal which could be converted into a wide range of α,γ-difunctionalized amines in a one-pot or two-step operation.[16e]

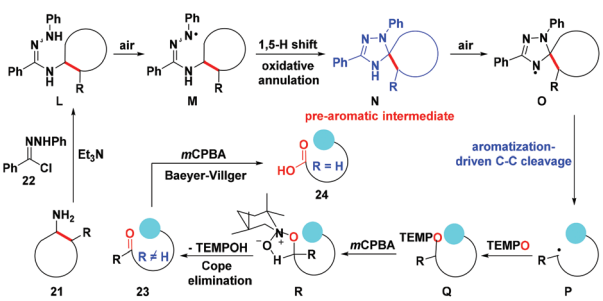
Despite the developments mentioned above on the application of cycloalkanamines as building blocks through ring-reconstruction and functionalization, ring-opening of unstrained cycloalkanamines still remains a compelling challenge. This situation can be attributed to ring-strain release as a thermodynamic driving force for strained cycloalkanamines, and the high reverse *exo*-cyclization rate constant of nitrile and imine for unstrained cycloalkanamines, especially for 5- or 6-membered cycloalkanamines.[11,17] In this context, Han and co-workers achieved the introduction of aromatization as both dynamic and thermodynamic driving forces for driving ring-opening of unstrained primary cycloalkanamines.[18] In this



Scheme 5 Deconstruction/functionalization of unstrained primary cycloalkanamines.

metal-free reaction, the deconstruction/functionalization of unstrained primary cycloalkanamines has been developed unprecedentedly, producing carbonyl compound tethered aliphatic chains and 1,2,4-triazole directly through the autooxidative aromatization-driven $C(sp^3)$–$C(sp^3)$ bond cleavage (Scheme 5). Similarly, the C–C bond cleavage of cycloalkanamines preferentially at more substituted carbons or the α-position of heteroatoms was achieved. The wide substrate scope tolerance of this protocol has been revealed by meticulous evaluations, including monocyclic, bicyclic, bridged, and complex natural product derivatives containing primary cycloalkanamine moieties, which indicated its potential application in the pharmaceutical and chemical industries. In addition, the *in situ* generation of the pre-aromatic heterocycle remains the core of this transformation, which is consistent with Dong and Fan's work.

In the proposed catalytic cycle (Scheme 6), the initial nucleophilic substitution occurs between cycloalkanamine **21** and hydrazonyl chloride **22** to produce hydrazonamide **L** which is auto-oxidized by air to generate aminyl radical **M**.



Scheme 6 Proposed mechanism for the deconstruction/functionalization of unstrained primary cycloalkanamines.

Then radical **M** undergoes the tandem 1,5-hydrogen atom shift/further oxidation/annulation process to form the key pre-aromatic heterocycle **N**, which could be isolated. The spiro heterocycle **N** tends to be oxidized by air to afford the cyclic amino radical intermediate **O** which appears in many N-containing heteroaryl migration reactions.[19] Then aromatization serves as a driving force to promote the radical C–C bond cleavage to furnish the aromatic 1,2,4-triazole. The generated distal alkyl radical **P** linking aromatic 1,2,4-triazole is immediately intercepted by TEMPO to give the ring-opening product **Q**. The final acyclic carbonyl compounds **23** and **24** carrying 1,2,4-triazole could be obtained by the treatment of *m*CPBA *via* the oxidation/Cope-elimination sequence.

Conclusions

The C–C bond disconnection is of significant importance for editing the molecular skeleton in organic synthesis, especially for the cleavage of ubiquitous unstrained aliphatic rings. Aromatization as both dynamic and thermodynamic driving forces for promoting C–C bond cleavage could compensate for the chemical inertness of unstrained aliphatic rings. We have highlighted the aromatization-driven homolytic C–C bond cleavage of common unstrained rings promoted by the *in situ* generated pre-aromatic fused spiro cycles, which featured (1) simple operation *via* a convenient one-pot reaction and (2) broad scope of various ring systems which do not require pre-activation. From our viewpoint, the aromatization-driven deconstruction/refunctionalization of organic molecules would be a powerful toolbox for modifying molecular skeletons and enriching the diversity of molecules.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

1 (*a*) P. V. R. Schleyer and F. Pühlhofer, Recommendations for the evaluation of aromatic stabilization energies, *Org. Lett.*, 2002, **4**, 2873–2876; (*b*) M. A. Halcrow, F. Urbanos and B. Chaudret, Aromatization of the B-ring of 5,7-dienyl steroids by the electrophilic ruthenium fragment "[Cp*Ru]+", *Organometallics*, 1993, **12**, 955–957.

2 (*a*) M. Murakami and Y. Ito, Cleavage of carbon–carbon single bonds by transition metals, *Top. Organomet. Chem.*, 1999, **3**, 97–129; (*b*) F. Chen, T. Wang and N. Jiao, Recent advances in transition-metal-catalyzed functionalization of unstrained carbon-carbon bonds, *Chem. Rev.*, 2014, **114**, 8613–8661; (*c*) D.-S. Kim, W.-J. Park and C.-H. Jun, Metal–organic cooperative catalysis in C–H and C–C bond activation, *Chem. Rev.*, 2017, **117**, 8977–9015; (*d*) F. Song, T. Gou, B.-Q. Wang and Z.-J. Shi, Catalytic activations of unstrained C–C bond involving organometallic intermediates, *Chem. Soc. Rev.*, 2018, **47**, 7078–7115; (*e*) X. Wu and C. Zhu, Recent advances in radical-mediated C-C bond fragmentation of non-strained molecules, *Chin. J. Chem.*, 2019, **37**, 171–182; (*f*) *C–C bond activation*, Top. Curr. Chem., ed. G. Dong, Springer, Berlin, 2014, vol. 346, pp. 1–262; (*g*) P.-h. Chen, B. A. Billett, T. Tsukamoto and G. Dong, "Cut and Sew" Transformations via transition-metal-catalyzed carbon–carbon bond activation, *ACS Catal.*, 2017, **7**, 1340–1360; (*h*) L. Deng and G. Dong, Carbon-Carbon bond activation of ketones, *Trends Chem.*, 2020, **2**, 183–198.

3 R. B. King and A. Efraty, Pentamethylcyclopentadienyl derivatives of transition metals. II. Synthesis of pentamethylcyclopentadienyl metal carbonyls from 5-acetyl-1,2,3,4,5-pentamethylcyclopentadiene, *J. Am. Chem. Soc.*, 1972, **94**, 3773–3779.

4 (*a*) R. H. Crabtree, R. P. Dion, D. J. Gibboni, D. V. Mcgrath and E. M. Holt, Carbon-carbon bond cleavage in hydrocarbons by iridium complexes, *J. Am. Chem. Soc.*, 1986, **108**, 7222–7227; (*b*) G. Smits, B. Audic, M. D. Wodrich, C. Corminboeuf and N. Cramer, A β-Carbon elimination strategy for convenient in situ access to cyclopentadienyl metal complexes, *Chem. Sci.*, 2017, **8**, 7174–7179.

5 (*a*) J. Guin, C. Muck-Lichtenfeld, S. Grimme and A. Studer, Radical transfer hydroamination with aminated cyclohexadienes using polarity reversal catalysis: scope and limitations, *J. Am. Chem. Soc.*, 2007, **129**, 4498–4503; (*b*) S. W. Youn, B. S. Kim and A. R. Jagdale, Pd-Catalyzed sequential C–C bond formation and cleavage: evidence for an unexpected generation of arylpalladium(II) species, *J. Am. Chem. Soc.*, 2012, **134**, 11308–11311.

6 (*a*) L. Buzzetti, A. Prieto, S. R. Roy and P. Melchiorre, Radical-based C-C bond-forming processes enabled by the photoexcitation of 4-alkyl-1,4-dihydropyridines, *Angew. Chem.*, 2017, **129**, 15235–15239; (*b*) á. Gutierrez-Bonet, C. Remeur, J. K. Matsui and G. A. Molander, Late-stage C–H alkylation of heterocycles and 1,4-quinones via oxidative homolysis of 1,4-dihydropyridines, *J. Am. Chem. Soc.*, 2017, **139**, 12251–12258; (*c*) X. Chen, F. Ye, X. Luo, X. Liu, J. Zhao, S. Wang, Q. Zhou, G. Chen and P. Wang, Histidine-specific peptide modification via visible-light-promoted C–H alkylation, *J. Am. Chem. Soc.*, 2019, **141**, 18230–18237.

7 (*a*) Y. Qiu, D. Ma, W. Kong, C. Fu and S. Ma, Regiocontrolled 1,2-migration in cyclization of 1-(indol-2-yl)-3-alkyn-1-ols: (Ph3P)Au+vs. PtCl4, *Org. Chem. Front.*, 2014, **1**, 62–67; (*b*) W. Kong, Y. Qiu, X. Zhang, C. Fu and S. Ma, Exclusive 1,2-aryl shift in platinum(II) chloride-catalyzed cyclization of 1-(Indol-2-yl)-2,3-allenols, *Adv. Synth. Catal.*, 2012, **354**, 2339–2347; (*c*) W. Kong, C. Fu and S. Ma, Efficient synthesis of carbazoles via PtCl2-catalyzed RT cyclization of 1-(indol-2-yl)-2,3-allenols: scope and mechanism, *Org. Biomol. Chem.*, 2012, **10**, 2164–2173; (*d*) W. Kong, C. Fu and S. Ma, General Au-catalyzed benzannulation towards naturally occurring carbazole alkaloids from methoxypropadiene, *Chem. – Eur. J.*, 2011, **17**, 13134–13137; (*e*) W. Kong, C. Fu and S. Ma, An efficient synthesis of carbazoles from PtCl2-catalyzed cyclization of 1-(indol-2-yl)-2,3-allenols, *Chem. Commun.*, 2009, 4572–4574; (*f*) X. Zhang and S. Ma, Transition metal-catalyzed benzannulation towards naturally occurring carbazole alkaloids, *Isr. J. Chem.*, 2018, **58**, 608–621.

8 (*a*) Y. Wang, C. Zheng and S.-L. You, Iridium-catalyzed asymmetric allylic dearomatization by a desymmetrization strategy, *Angew. Chem., Int. Ed.*, 2017, **56**, 15093–15097; (*b*) Q.-F. Wu, C. Zheng and S.-L. You, Enantioselective synthesis of spiro cyclopentane-1,3′-indoles and 2,3,4,9-tetrahydro-1H-carbazoles by Iridium-catalyzed allylic dearomatization and stereospecific migration, *Angew. Chem., Int. Ed.*, 2012, **51**, 1680–1683; (*c*) C.-X. Zhuo, Q. Cheng, W.-B. Liu, Q. Zhao and S.-L. You, Enantioselective synthesis of pyrrole-based spiro- and polycyclic derivatives by Iridium-catalyzed asymmetric allylic dearomatization and controllable migration reactions, *Angew. Chem., Int. Ed.*, 2015, **54**, 8475–8479; (*d*) C.-X. Zhuo, Y. Zhou, Q. Cheng, L. Huang and S.-L. You, Enantioselective construction of spiroindolines with three contiguous stereogenic centers and chiral tryptamine derivatives via reactive spiroindolenine intermediates, *Angew. Chem., Int. Ed.*, 2015, **54**, 14146–14149; (*e*) C. Zheng, Z.-L. Xia and S.-L. You, Unified mechanistic understandings of Pictet-Spengler reactions, *Chem*, 2018, **4**, 1952–1966; (*f*) V. Gobé, V. Gandon and X. Guinchard, Reactions involving tryptamines and δ-allenyl aldehydes: competition between Pictet-Spengler reaction and cyclization to 1-aminotetralins, *Adv. Synth. Catal.*, 2018, **360**, 1280–1288; (*g*) G. Bai, F. Dong, L. Xu, Y. Liu, L. Wang and S.-S. Li, Controllable syntheses of spiroindolenines and senzazepinoindoles via hexafluoroisopropanol-mediated Redox-Neutral cascade process, *Org. Lett.*, 2019, **21**, 6225–6230.

9 (*a*) M. Yoshida, T. Nozaki, T. Nemoto and Y. Hamada, Formal meta-specific intramolecular Friedel–Crafts allylic alkylation of phenols through a spirocyclization–dienone–phenol rearrangement cascade, *Tetrahedron*, 2013, **69**, 9609–9615; (*b*) R. A. Bauer, T. A. Wenderski and D. S. Tan, Biomimetic diversity-oriented synthesis of benzannulated medium rings via ring expansion, *Nat. Chem. Biol.*, 2013, **9**, 21–29.

10 (*a*) *Biologically Active Natural Products: Pharmaceuticals*, ed. J. C. Stephen and H. G. Cutler, CRC Press, Boca Raton, FL, 2000; (*b*) *Comprehensive natural products II: Chemistry and Biology*, ed. L. Mander and H.-W. Liu, Elsevier, Amsterdam, 2010.

11 For reviews on ring-opening of strained rings, see: (*a*) G. Fumagalli, S. Stanton and J. F. Bower, Recent methodologies that exploit C–C single-bond cleavage of strained ring systems by transition metal complexes, *Chem. Rev.*, 2017, **117**, 9404–9432; (*b*) M. Murakami and N. Ishida, Potential of metal-catalyzed C–C single bond cleavage for organic synthesis, *J. Am. Chem. Soc.*, 2016, **138**, 13759–13769; (*c*) L. Souillart and N. Cramer, Catalytic C–C bond activations via oxidative addition to transition metals, *Chem. Rev.*, 2015, **115**, 9410–9464; (*d*) F. Wang, S. Yu and X. Li, Transition metal-catalysed couplings between arenes and strained or reactive rings: combination of C–H activation and ring scission, *Chem. Soc. Rev.*, 2016, **45**, 6462–6477.

12 C.-H. Jun, H. Lee and S.-G. Lim, The C–C bond activation and skeletal rearrangement of cycloalkanone imine by Rh (I) catalysts, *J. Am. Chem. Soc.*, 2001, **123**, 751–752.

13 (*a*) M. Wang, M. Li, S. Yang, X.-S. Xue, X. Wu and C. Zhu, Radical-mediated C-C cleavage of unstrained cycloketones and DFT study for unusual regioselectivity, *Nat. Commun.*, 2020, **11**, 672–678; (*b*) H. M. Ko and G. Dong, Cooperative activation of cyclobutanones and olefins leads to bridged ring systems by a catalytic [4+2] coupling, *Nat. Chem.*, 2014, **6**, 739–744; (*c*) Y. Xia, G. Lu, P. Liu and G. Dong, Catalytic activation of carbon–carbon bonds in cyclopentanones, *Nature*, 2016, **539**, 546–550; (*d*) Y. Xia, J. B. Wang and G. Dong, Distal-Bond-Selective C–C activation of ring-fused cyclopentanones: an efficient access to spiroindanones, *Angew. Chem., Int. Ed.*, 2017, **56**, 2376–2380; (*e*) Y. Xia, J. B. Wang and G. Dong, Suzuki–Miyaura coupling of simple ketones via activation of unstrained carbon–carbon bonds, *J. Am. Chem. Soc.*, 2018, **140**, 5347–5351.

14 Y. Xu, X. Qi, P. Zheng, C. C. Berti, P. Liu and G. Dong, Deacylative transformations of ketones via aromatization-promoted C–C bond activation, *Nature*, 2019, **567**, 373–378.

15 M. Tian, X. Shi, X. Zhang and X. Fan, Synthesis of 4-acylpyrazoles from saturated ketones and hydrazones featured with multiple C(sp3)–H bond functionalization and C–C bond cleavage and reorganization, *J. Org. Chem.*, 2017, **82**, 7363–7372.

16 For representative works on ring-opening of strained cycloalkanamines, see: (*a*) S. Maity, M. Zhu, R. S. Shinabery and N. Zheng, Intermolecular [3+2] cycloaddition of cyclopropylamines with olefins by visible-light photocatalysis, *Angew. Chem., Int. Ed.*, 2012, **51**, 222–226; (*b*) Y. Cai, J. Wang, Y. Zhang, Z. Li, D. Hu, N. Zheng and H. Chen, Detection of fleeting amine radical cations and elucidation of chain processes in visible-light-mediated [3+2] annulation by online mass spectrometric techniques, *J. Am. Chem. Soc.*, 2017, **139**, 12259–12266; (*c*) J. Wang and N. Zheng, The Cleavage of a C-C bond in cyclobutylanilines by visible-light photoredox catalysis: development of a [4+2] annulation method, *Angew. Chem., Int. Ed.*, 2015, **54**, 11424–

11427; (*d*) S. A. Morris, J. Wang and N. Zheng, The prowess of photogenerated amine radical cations in cascade reactions: from carbocycles to heterocycles, *Acc. Chem. Res.*, 2016, **49**, 1957–1968; (*e*) M.-M. Wang and J. Waser, 1,3-difunctionalization of aminocyclopropanes via dielectrophilic intermediates, *Angew. Chem., Int. Ed.*, 2019, **58**, 13880–13884.

17 (*a*) J. H. Horner, F. N. Martinez, O. M. Musa, M. Newcomb and H. E. Shahin, Kinetics of dialkylaminium cation radical reactions: radical clocks, solvent effects, acidity constants, and rate constants for reactions with hydrogen atom donors, *J. Am. Chem. Soc.*, 1995, **117**, 11124–11133; (*b*) O. M. Musa, J. H. Horner, H. Shahin and M. Newcomb, A kinetic scale for dialkylaminyl radical reactions, *J. Am. Chem. Soc.*, 1996, **118**, 3862–3868; (*c*) W. R. Bowman, C. F. Bridge and P. Brookes, Radical cyclisation onto nitriles, *Tetrahedron Lett.*, 2000, **41**, 8989–8994; (*d*) J. Jin and M. Newcomb, Rate constants and arrhenius functions for ring opening of a cyclobutylcarbinyl radical clock and for hydrogen atom transfer from the Et3B–t3Bical cloc, *J. Org. Chem.*, 2008, **73**, 4740–4742.

18 J.-W. Zhang, Y.-R. Wang, J.-H. Pan, Y.-H. He, W. Yu and B. Han, Deconstructive oxygenation of unstrained cycloalkanamines, *Angew. Chem.*, 2020, **59**, 3900–3904.

19 For the representative works on N-containing heteroaryl migration via a cyclic amino radical intermediate, see: (*a*) X. Wu, M. Wang, L. Huan, D. Wang, J. Wang and C. Zhu, Tertiary-alcohol-directed functionalization of remote C(sp3)-H bonds by sequential hydrogen atom and heteroaryl migrations, *Angew. Chem., Int. Ed.*, 2018, **57**, 1640–1644; (*b*) J. Yu, Z. Wu and C. Zhu, Efficient docking–migration strategy for selective radical difluoromethylation of alkenes, *Angew. Chem., Int. Ed.*, 2018, **57**, 17156–17160; (*c*) M. Wang, Z. Wu, B. Zhang and C. Zhu, Azidoheteroarylation of unactivated olefins through distal heteroaryl migration, *Org. Chem. Front.*, 2018, **5**, 1896–1899; (*d*) D. Chen, Z. Wu, Y. Yao and C. Zhu, Phosphinoyl-functionalization of unactivated alkenes through phosphinoyl radical-triggered distal functional group migration, *Org. Chem. Front.*, 2018, **5**, 2370–2374; (*e*) H. Zhang, X. Wu, Q. Zhao and C. Zhu, Copper-catalyzed heteroarylsilylation of unactivated olefins through distal heteroaryl migration, *Chem. - Asian J.*, 2018, **13**, 2453–2457.