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PAPER

Palladium(II) acetate mediated oxidative cyclization of ω-unsaturated α-cyano ketones for facile construction of methylenecyclohexane ring system†

Min-Tsang Hsieh,*[a] Kak-Shan Shia,[b] Hsing-Jang Liu[c] and Sheng-Chu Kuo*[d]

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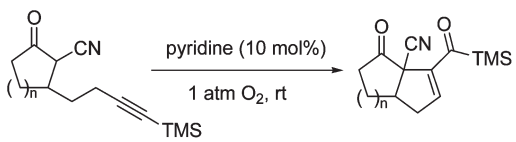
A highly efficient annulative approach towards the construction of the structurally attractive methylenecyclohexane ring was developed through a convenient 1,4-addition of 4-pentenylmagnesium bromide to 2-cyano-2-cycloalkenones followed by a Pd(II)-mediated oxidative cyclization of the resulting ω-unsaturated α-cyano ketones. Based on this newly developed protocol, polycyclic adducts bearing various ring sizes and substitutions can be prepared in moderate to high yields.

Cyclic motifs containing a methylene appendage, such as methylenecyclohexane and methylenecyclopentane systems, are found in high abundance in naturally occurring products,[1] the construction of which is typically a rather complex process.[2] During the past decade, our long-term efforts to discover a facile annulation process have developed several convenient synthetic protocols,[3] part of which has been employed as a key operation for the synthesis of natural products.[4] Our previous research not only showed that the α-cyano moiety could serve as a versatile directing group in facilitating the methylenecyclopentane annulative process,[3a] but also disclosed the unique nature of the α-cyano group in a hitherto unknown autoxidative annulation as shown in Scheme 1.[3c]

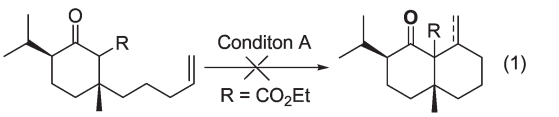
Regarding transition metal catalyzed methylenecyclohexane annulation,[5] it has been well documented that a quaternary center adjacent to the ester functional group (Scheme 2, eqn (1)) and the vinyl center β to the silyl enol ether moiety (Scheme 2, eqn (2)) would completely hamper the occurrence of a methylenecyclohexane annulative process, presumably due to the steric congestion encountered during the carbon–carbon bond formation.

As demonstrated previously,[3] the cyano group represented a vital functionality in our previous intramolecular annulative cases. We thus speculated that the cyano group might serve a more powerful directing group than the ester functionality to facilitate the methylenecyclohexane annulative process. As such, being an extension of our previous work, the objective of the following investigation is to develop a facile methylenecyclohexane annulative approach of the title system containing an α-cyano moiety as an activating group instead.

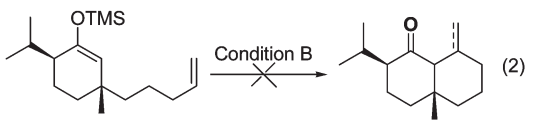
Our investigation began with the preparation of structurally diverse 2-cyano-2-cycloalkenones as substrates, *via* a two-step sequence, involving Thorpe–Ziegler condensation[6] of the corresponding alkanedinitriles followed by phenylselenenylation-oxidative elimination or a four-step synthetic sequence, involving formylation, isoxazole formation and its subsequent rearrangement,[7] and phenylselenenylation-oxidative elimination.[8] 2-Cyano-2-cycloalkenones thus formed, except **7** and **9**, are



Scheme 1



Condition A: $Pd(CH_3CN)_2Cl_2$, TMSCl; $Pd(CH_3CN)_2Cl_2$, $Yb(OTf)_3$



Condition B: $Pd(OAc)_2$; $Cu(OAc)_2$; $Mn(OAc)_3$; $Pd(CH_3CN)Cl_2$, benzoquinone

Scheme 2

[a]*Chinese Medicinal Research and Development Center, China Medical University Hospital, 2 Yude Road, Taichung 40447, Taiwan, R.O.C. E-mail: d917410@alumni.nthu.edu.tw; Tel: +886-4-22053366 ext: 5605*
[b]*Institute of Biotechnology and Pharmaceutical Research, National Health Research Institutes, Miaoli County 35053, Taiwan, R.O.C.*
[c]*Department of Chemistry, National Tsing Hua University, Hsinchu, Taiwan 30013, R.O.C.*
[d]*Graduate Institute of Pharmaceutical Chemistry, China Medical University, Taiwan, R.O.C.*

†Electronic supplementary information (ESI) available: ^1H and ^{13}C spectra for all new compounds and X-ray crystallographic analysis of **24a**[13] and **28**[14]. CCDC 851795 and 851796. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2ob25161b

unstable under air atmosphere and must be freshly prepared and used for subsequent 1,4-addition. Sterically uncongested 2-cyano-2-cycloalkenones **1–9** are highly reactive Michael acceptors and able to undergo 1,4-addition with Grignard reagents without any assistance with metal catalysts (*e.g.*, Mn(II) and Cu(I)).[9–11] For the present studies, an array of structurally diverse ω-unsaturated α-cyano ketones **12–22**, as compiled in Table 1, were readily provided in moderate to good yields by treating substrates **1–11** with excess freshly prepared 4-pentenylmagnesium bromide (1.5 equiv.) at −78 °C. In most cases, the catalyst-free conjugate addition took place effectively within 2 h, with the exception that compounds **10** and **11** required an addition of a catalytic amount of CuI–Me_2S[12] complex (0.5 equiv.) to promote the 1,4-addition.

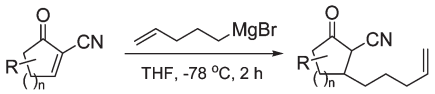
With these ω-unsaturated α-cyano ketones in hand, the methylenecyclohexane annulation of the title system was then examined under catalysis with $Pd(OAc)_2$. As expected, the annulation reaction was found to be remarkably facile under mild reaction conditions. Results are listed in Table 2. As a typical example, upon treatment with 1 equiv. of $Pd(OAc)_2$ in THF at ambient temperature for 20 min, cyano ketone **13** underwent intramolecular annulation smoothly in a regio- and stereocontrol manner to afford bicyclic adduct **24** as a sole product in 82% yield. Similarly, substrates **14–22**, irrespective of the parent ring size, could readily undergo cyclization to afford products **25–33** in fair to good yields (59–86%). It is noteworthy that α-cyano ketone **22** (Table 2; entry 11), in sharp contrast to its α-ester counterpart (Scheme 2, eqn (1)), could undergo annulation smoothly to give bicyclic product **33** in 68% yield. This distinct difference in reaction activity again demonstrates that the α-cyano group appears superior to the α-ester in serving as an auxiliary functionality for above annulation.

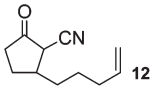
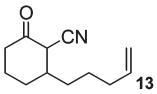
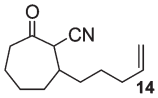
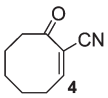
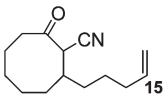
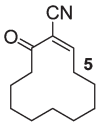
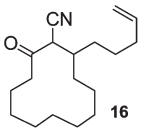
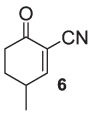
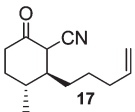
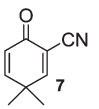
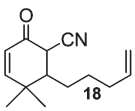
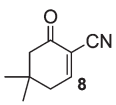
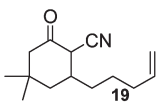
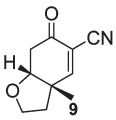
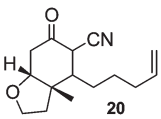
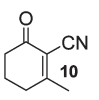
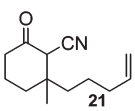
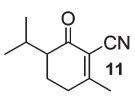
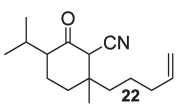
The spectral data of **24** are in full agreement with the assigned structure and its relative configuration was confirmed by a single crystal X-ray analysis of its corresponding hydrazone derivative **24a**,[13] readily produced by treating **24** with 2,4-dinitrophenyl hydrazine and a catalytic amount of *p*-TSA in refluxing toluene (Scheme 3). In addition, the structure of product **28** was determined unambiguously by an X-ray analysis,[14] further implying that other 6/6 fused bicyclic ketones **29a** and **30–33** are very likely to possess a *cis* ring junction as well. On the other hand, the stereochemistry of macrobicyclic adducts **25–27** remains to be determined in that all efforts to grow desirable crystals for X-ray analyses turned out to be fruitless. Intriguingly, as α-cyano ketone **12** was employed as a substrate (Table 2; entry 1), enone product **23** was isolated as a major component instead of the anticipated 5/6 fused adduct, indicating that the oxidative elimination might occur rapidly on the cyclopentanone core.

Similar results are also observed with substrate **18**, in which an equal amount of bicyclic product **29a** and enone **29b** were obtained. A possible explanation for these could be that for substrates **12** and **18**, the carbon center β to both carbonyl and cyano groups is somehow activated, rendering the initial oxo-π-allyl palladium(II) complex to undergo oxidative elimination more easily than the regular cyclization process for expected products.

In light of the high price of palladium reagents, a more economic alternative for the annulation reaction of the title system was then explored. Accordingly, the inexpensive $Cu(OAc)_2$ was chosen as a co-oxidant to regenerate the active Pd(II) species so that the loading of $Pd(OAc)_2$ could be dramatically reduced to 0.25 equiv.[15] The cyclization did occur to afford the expected products, but yields were lower than those of stoichiometric conditions by 10–15% as indicated in Table 3.

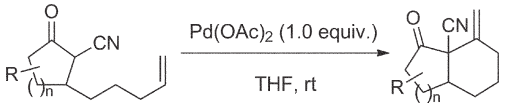
Table 1 1,4-Addition of 4-pentenylmagnesium bromide to 2-cyano-2-cycloalkenones

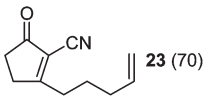
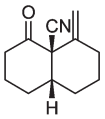
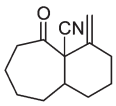
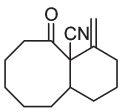
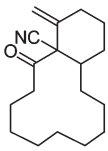
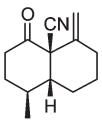
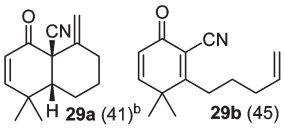
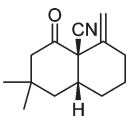
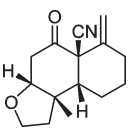
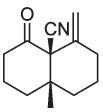
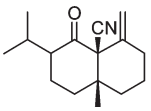


Substrate	Product	Yield[a] (%)
		71 (*cis* : *trans* = 1 : 5.2)[b]
		76 (*cis* : *trans* = 1 : 1.8)[b]
		73 (*cis* : *trans* = 1 : 2.8)[b]
		75 (*cis* : *trans* = 1 : 4)[b]
		75 (*cis* : *trans* = 1 : 3)[b]
		73 (*cis* : *trans* = 1 : 1.3)[b]
		76 (*cis* : *trans* = 1 : 1.2)[b]
		79 (*cis* : *trans* = 1 : 1.1)[b]
		69 (*cis* : *trans* = 1 : 1.5)[b,c]
		82 (*cis* : *trans* = 1 : 1.5)[b,d]
		71 (*cis* : *trans* = 1 : 1.7)[b,d]

[a] Yields refer to isolated, chromatographically pure products. [b] The ratio of the keto : keto diastereomeric forms. [c] The stereochemistry was confirmed by NOE experiments. [d] The reactions were performed at −40 °C in the presence of CuI–Me_2S (0.5 equiv.) for 3 h.

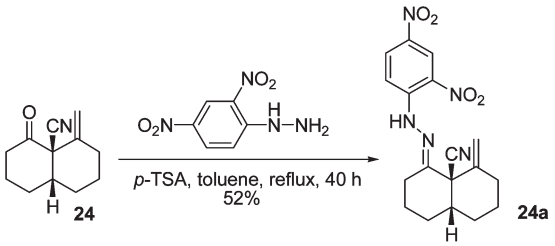
Table 2 Palladium(II) acetate mediated methylenecyclohexane annulation process



Entry	Substrate	Product[a] (% Yield)	Time
1	**12**	 **23** (70)	10 min
2	**13**	 **24** (82)	20 min
3	**14**	 **25** (86)	18 min
4	**15**	 **26** (82)	25 min
5	**16**	 **27** (81)	20 min
6	**17**	 **28** (79)	45 min
7	**18**	 **29a** (41)[b] **29b** (45)	2 h
8	**19**	 **30** (76)[b]	25 min
9	**20**	 **31** (59)[b]	3 h
10	**21**	 **32** (62)[b]	5 h
11	**22**	 **33** (68)[b]	6.5 h

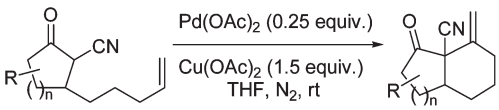
[a] Yields refer to isolated, chromatographically pure products. [b] The *cis* configuration is tentatively assigned based on other structurally related products **24** and **28**.

Nevertheless, when the above catalytic systems were carried out under one atmosphere of oxygen,[16a–c] the amount of Pd metal could be further reduced to 0.1 equiv., but yields remained inferior to those subject to the stoichiometric amount (Scheme 4). Other catalytic systems combining milder oxidizing agents, including benzoquinone and copper chloride, were also explored, but all resulted in lower yields relative to the current reaction system.[16d–f]



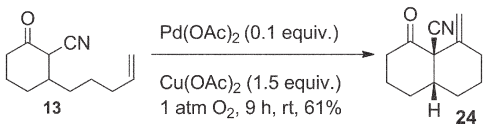
Scheme 3

Table 3 Palladium(II) acetate mediated methylenecyclohexane annulation process with a co-oxidant copper(II) acetate



Substrate	Time (h)	Product	Yield[a] (%)
12	3.5	**23**	65
13	7	**24**	67
14	7.5	**25**	73
15	8.5	**26**	69
16	10	**27**	72
19	8	**30**	63

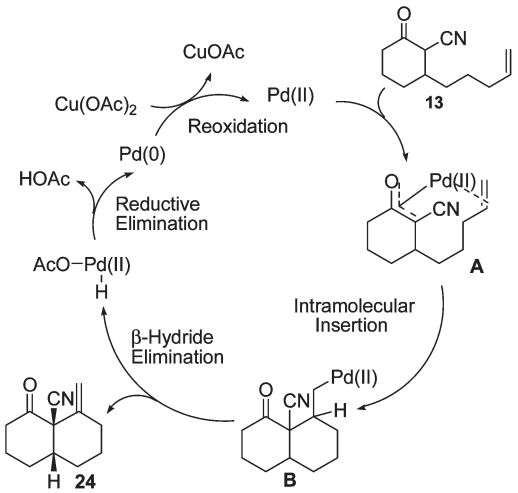
[a] Yields refer to isolated, chromatographically pure products.



Scheme 4

As illustrated in Scheme 5, the annulative process is proposed to proceed in a 6-exo-trig fashion, wherein the olefinic terminus first coordinates with Pd(II) to form oxo-π-allyl palladium(II) complex A followed by intramolecular insertion to generate complex B and finally, β-elimination takes place to provide cyclic products and Pd(0), which can be re-oxidized by $Cu(OAc)_2$ to Pd(II) species to initiate the catalytic cycle again.

Adducts thus obtained in Table 2 were further applied to reductive decyanation process according to established protocols.[17,18] Treatment with lithium naphthalenide (LN) followed by capturing the enolates with appropriate electrophiles resulted in the formation of the corresponding decyanated products in moderate to good yields. As shown in Table 4, the angular cyano group in **24**, **25** and **27** was protonated to give rise to products **34–36** with concomitant transposition of the exocyclic olefin to the fully conjugated position. Alternatively, the reductive decyanation alkylation could take place in a stereoselective manner to



Scheme 5

give a single *trans* adduct with the exo double bond intact as demonstrated by treating substrate **24** with LN and benzyl bromide.

In conclusion, an efficient methylenecyclohexane annulative process has been developed, which involves a highly facile 1,4-addition of 4-pentenylmagnesium bromide to 2-cyano-2-cycloalkenones followed by a Pd(II)-mediated cyclization of the resulting ω-unsaturated α-cyano ketones to give various bicyclic products with an exocyclic double bond in a stereo- and regio-selective manner.

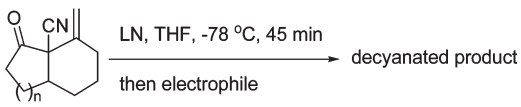
Experimental

General

All reactions were performed under an atmosphere of argon or nitrogen unless otherwise stated. All solvents were dried prior to use and reagents were employed as revived. Analytical thin layer chromatography was performed on SiO_2 60 F-254 plates and flash column chromatography was carried out using SiO_2 60 (particle size 0.040–0.055 mm, 230–400 mesh), both of which are available from E. Merck. Visualization was performed under UV irradiation at 254 nm followed by staining with vanillin (60 g of vanillin in 1 L of 95% ethanol containing 10 mL of conc. H_2SO_4) and charring by heat gun. Fourier transform infrared spectra (IR) were recorded on Bomen MR-100 and expressed in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded on Bruker Avance EX 400 FT NMR or Bruker DMX-600. Chloroform-d was used as the solvent and TMS (δ = 0.00 ppm) as an internal standard. Chemical shifts are reported as δ values in ppm as referenced to TMS. Multiplicities are recorded as s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), sept (septet), dd (doublet of doublet), dt (doublet of triplet), br (broadened), m (multiplet). Coupling constants (J) are expressed in Hz. HRMS were measured by JEOL JMS-HX110 spectrometer and spectral data were recorded as m/z values.

General procedure for 1,4-addition in the synthesis of compounds 12–22. The general procedure is illustrated immediately below with compound **12** as a specific example.

Table 4 LN induced reductive decyanation of **24**, **25** and **27**



Substrate	Electrophile	Time	Product/Yield[a] (%)
24	H_2O	15 min	**34** (85)
25	H_2O	15 min	**35** (81)
27	H_2O	15 min	**36** (86)
24	BnBr	6 h	**37**[b] (71)

[a] Yields refer to isolated, chromatographically pure products. [b] The *trans* configuration is proposed on the basis of NOE experiment.

2-Oxo-5-pent-4-enylcyclopentanecarbonitrile (12). Freshly prepared 4-pentenylmagnesium bromide solution (8.0 mL, 0.65 M in THF, 5.16 mmol) was added dropwise to a stirred solution of compound **1** (0.368 g, 3.44 mmol) in THF (10 mL) at −78 °C. The resulting mixture was stirred for another 2 h at the same temperature. Saturated NH_4Cl solution (8 mL) was added to quench the reaction. The aqueous layer was separated and extracted with EA (2 × 15 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated to give the crude residue, which was purified by flash chromatography on silical gel with EtOAc–*n*-hexane (1 : 5) to afford compound **12** [432 mg, 71% yield, a mixture of keto isomers in a ratio of 1 : 5.2 (*cis* : *trans*)] as a yellow oil.

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2925, 2854, 2236, 1749; ^1H NMR ($CDCl_3$, 600 MHz) major isomer: δ 5.81–5.74 (m, 1H), 5.03–4.96 (m, 2H), 2.81 (d, J = 12.1 Hz, 1H), 2.49 (dd, J = 18.8, 8.2 Hz, 1H), 2.45–2.25 (m, 3H), 2.12–2.08 (m, 2H), 1.79–1.75 (m, 1H), 1.58–1.48 (m, 4H); minor isomer: δ 3.32 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) major isomer: δ 206.5 (C), 137.8 (CH), 116.4 (C), 115.3 (CH_2), 46.3 (CH), 42.6 (CH), 37.2 (CH_2), 33.8 (CH_2), 33.4 (CH_2), 27.6 (CH_2), 26.0 (CH_2); HRMS (EI) calcd for $C_{11}H_{15}NO$: 177.1154; found: 177.1159.

2-Oxo-6-pent-4-enylcyclohexanecarbonitrile (13). A mixture of keto isomers in a ratio of 1 : 1.8 (*cis* : *trans*) was obtained as a yellow oil (76% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2954, 2825, 2238, 1710, 1460; ^1H NMR ($CDCl_3$, 600 MHz) major isomer: δ 5.79–5.70 (m, 1H), 5.00–4.93 (m, 2H), 3.23 (d, J = 11.6 Hz, 1H), 2.57–2.54

(m, 1H), 2.27 (dt, J = 14.4, 5.9 Hz, 1H), 2.12–1.92 (m, 4H), 1.81 (m, 2H), 1.53 (m, 5H), minor isomer: δ 3.45 (d, J = 3.4 Hz, 1H), 2.71–2.68 (m, 1H), 2.39–2.34 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) major isomer: δ 200.3 (C), 137.9 (CH), 115.9 (C), 115.1 (CH_2), 49.9 (CH), 43.2 (CH), 40.4 (CH_2), 34.2 (CH_2), 33.4 (CH_2), 29.4 (CH_2), 25.3 (CH_2), 24.9 (CH_2), minor isomer: δ 201.3 (C), 137.8 (CH), 115.6 (C), 115.1 (CH_2), 47.9 (CH), 42.0 (CH), 38.9 (CH_2), 33.3 (CH_2), 31.6 (CH_2), 27.4 (CH_2), 25.7 (CH_2), 24.7 (CH_2); HRMS (EI) calcd for $C_{12}H_{17}NO$: 191.1310; found: 191.1307.

2-Oxo-7-pent-4-enylcycloheptanecarbonitrile (14). A mixture of keto isomers in a ratio of 1 : 2.8 (*cis* : *trans*) was obtained as a yellow oil (73% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2935, 2863, 2236, 1709, 1451; ^{1}H NMR ($CDCl_3$, 600 MHz) major isomer: δ 5.79–5.72 (m, 1H), 5.01–4.94 (m, 2H), 3.61 (d, J = 3.1 Hz, 1H), 2.74–2.69 (m, 1H), 2.58–2.52 (m, 1H), 2.06 (m, 2H), 1.97–1.84 (m, 4H), 1.65–1.59 (m, 2H), 1.49–1.39 (m, 5H), minor isomer: 3.45 (d, J = 8.4 Hz, 1H), 2.81–2.77 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) major isomer: δ 203.3 (C), 137.9 (CH), 116.3 (C), 115.1 (CH_2), 50.1 (CH), 42.3 (CH_2), 39.9 (CH), 33.6 (CH_2), 33.3 (CH_2 × 2), 26.3 (CH_2), 22.7 (CH_2), 26.0 (CH_2), minor isomer: 137.9 (CH), 49.8 (CH), 42.0 (CH_2), 39.3 (CH), 32.4 (CH_2), 25.9 (CH_2), 25.6 (CH_2), 23.9 (CH_2); HRMS (EI) calcd for $C_{13}H_{19}NO$: 205.1467; found: 205.1468.

2-Oxo-8-pent-4-enylcyclooctanecarbonitrile (15). A mixture of keto isomers in a ratio of 1 : 4 (*cis* : *trans*) was obtained as a yellow oil (75% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2933, 2860, 2239, 1708, 1448; ^{1}H NMR ($CDCl_3$, 600 MHz) major isomer: δ 5.79–5.75 (m, 1H), 5.02–4.95 (m, 2H), 3.53 (d, J = 3.5 Hz, 1H), 2.58–2.51 (m, 2H), 2.41–2.38 (m, 1H), 2.09 (m, 2H), 1.97–1.87 (m, 2H), 1.80–1.74 (m, 2H), 1.62–1.43 (m, 6H), 1.35–1.31 (m, 1H), 1.22–1.18 (m, 1H), minor isomer: 3.51 (d, J = 10.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 206.2 (C), 137.9 (CH), 115.5 (C), 115.2 (CH_2), 50.5 (CH), 40.0 (CH_2), 38.0 (CH), 34.4 (CH_2), 33.4 (CH_2), 31.2 (CH_2), 27.7 (CH_2), 26.4 (CH_2), 26.2 (CH_2), 23.9 (CH_2); HRMS (EI) calcd for $C_{14}H_{21}NO$: 219.1623; found: 219.1618.

2-Oxo-12-pent-4-enylcyclododecanecarbonitrile (16). A mixture of keto isomers in a ratio of 1 : 3 (*cis* : *trans*) was obtained as a yellow oil (75% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2963, 2236, 1709, 1641, 1457; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 5.83–5.72 (m, 1H), 5.04–4.97 (m, 2H), 3.68–3.66 (m, 1H), 2.89–2.80 (m, 1H), 2.47–2.40 (m, 1H), 2.13 (m, 4H), 2.03–1.98 (m, 2H), 1.71–1.65 (m, 2H), 1.57–1.51 (m, 3H), 1.39–1.19 (m, 12H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 201.6 (C), 137.9 (CH), 115.7 (C), 115.2 (CH_2), 49.6 (CH), 37.6 (CH_2), 37.5 (CH), 33.5 (CH_2), 31.7 (CH_2), 27.9 (CH_2), 26.5 (CH_2), 26.0 (CH_2), 24.3 (CH_2), 23.5 (CH_2), 23.4 (CH_2), 22.9 (CH_2), 22.5 (CH_2), 21.1 (CH_2); HRMS (EI) calcd for $C_{18}H_{29}NO$: 275.2249; found: 275.2252.

3-Methyl-6-oxo-2-pent-4-enylcyclohexanecarbonitrile (17). A mixture of keto isomers in a ratio of 1 : 1.3 (*cis* : *trans*) was obtained as a yellow oil (73% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2953, 2248, 1718, 1640; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 5.77–5.73 (m, 1H), 5.02–4.92 (m, 2H), 3.50–3.34 (m, 1H), 2.53–2.48 (m, 1H), 2.41–2.30 (m, 1H), 2.10 (m, 3H), 1.74–1.60 (m, 3H), 1.50–1.34 (m, 4H), 1.07–0.99 (m, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) major isomer: δ 200.7 (C), 137.8 (CH), 115.7 (C), 115.2 (CH_2), 47.6 (CH), 45.4 (CH), 40.3 (CH_2), 33.4 (CH_2), 33.2 (CH), 29.9 (CH_2), 25.5 (CH_2), 22.2 (CH_2), 18.5 (CH_3), minor isomer: δ 201.5 (C), 137.7 (CH), 116.4 (C), 115.2 (CH_2), 47.3 (CH), 38.0 (CH_2), 32.1 (CH), 18.3 (CH_3); HRMS (EI) calcd for $C_{13}H_{19}NO$: 205.1467; found: 205.1468.

5,5-Dimethyl-2-oxo-6-pent-4-enylcyclohex-3-enecarbonitrile (18). A mixture of keto isomers in a ratio of 1 : 1.2 (*cis* : *trans*) was obtained as a yellow oil (76% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2943, 2862, 2246, 1694, 1468; ^{1}H NMR ($CDCl_3$, 600 MHz) major isomer: δ 6.69 (d, J = 10.2 Hz, 1H), 5.92 (d, J = 10.2 Hz, 1H), 5.80–5.74 (m, 1H), 5.03–4.96 (m, 2H), 3.45 (d, J = 13.2 Hz, 1H), 2.11–2.07 (m, 2H), 2.05–1.97 (m, 1H), 1.90–1.83 (m, 1H), 1.68–1.41 (m, 3H), 1.25 (s, 3H), 1.18 (s, 3H), minor isomer: δ 6.72 (d, J = 10.2 Hz, 1H), 5.96 (d, J = 10.8 Hz, 1H), 3.60 (d, J = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) major isomer: δ 189.3 (C), 161.3 (CH), 137.9 (CH), 124.3 (CH), 116.6 (C), 115.2 (CH_2), 46.2 (CH), 43.9 (CH), 37.2 (C), 33.8 (CH_2), 29.8 (CH_2), 27.6 (CH_3), 27.1 (CH_2), 19.8 (CH_3), minor isomer: δ 188.6 (C), 162.2 (CH), 137.7 (CH), 124.2 (CH), 116.2 (C), 115.4 (CH_2), 44.6 (CH), 36.6 (C), 33.4 (CH_2), 28.5 (CH_2), 26.5 (CH_2); HRMS (EI) calcd for $C_{14}H_{19}NO$: 217.1467; found: 217.1467.

4,4-Dimethyl-2-oxo-6-pent-4-enylcyclohexanecarbonitrile (19). A mixture of keto isomers in a ratio of 1 : 1.1 (*cis* : *trans*) was obtained as a yellow oil (79% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2241, 1715, 1642; ^{1}H NMR ($CDCl_3$, 600 MHz) major isomer: δ 5.79–5.75 (m, 1H), 5.03–4.96 (m, 2H), 3.14 (d, J = 12.2, 1H), 2.28–2.26 (m, 1H), 2.2–2.18 (m, 1H), 2.16–2.02 (m, 2H), 1.82–1.76 (m, 2H), 1.68 (m, 1H), 1.58–1.49 (m, 3H), 1.43–1.37 (m, 1H), 1.11–1.06 (m, 3H), 0.93–0.88 (m, 3H); minor isomer: δ 2.76–0.272 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) major isomer: δ 200.0 (C), 137.8 (CH), 115.9 (C), 115.1 (CH_2), 53.3 (CH_2), 49.5 (CH), 43.2 (CH_2), 38.7 (CH), 35.3 (C), 34.5 (CH_2), 33.4 (CH_2), 31.7 (CH_3), 25.6 (CH_2), 25.3 (CH_3) minor isomer: δ 137.9 (CH), 115.0 (CH_2), 48.5 (CH_2), 37.8 (CH_2), 31.2 (CH_3), 29.2 (CH_2), 26.7 (CH_2), 26.6 (CH_3), 25.3 (CH_2); HRMS (EI) calcd for $C_{14}H_{21}NO$: 219.1623; found: 219.1615.

(3a*S,7a*R**)-Octahydro-3a-methyl-6-oxo-4-(pent-4-enyl) benzofuran-5-carbonitrile (20).** A mixture of keto isomers in a ratio of 1 : 1.5 (*cis* : *trans*) was obtained as a yellow oil (69% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2938, 2241, 1712, 1638, 1458; ^{1}H NMR ($CDCl_3$, 600 MHz) major isomer: δ 5.78–5.74 (m, 1H), 5.01–4.96 (m, 2H), 3.85–3.80 (m, 2H), 3.75–3.73 (m, 1H), 3.41 (d, J = 12.7 Hz, 1H), 2.76 (dd, J = 15.5, 4.3 Hz, 1H), 2.55 (dd, J = 15.5, 4.3 Hz, 1H), 2.09–1.99 (m, 6H), 1.87–1.84 (m, 1H), 1.78–1.68 (m, 2H), 1.63–1.46 (m, 4H), 1.12 (s, 3H), minor isomer: δ 3.43 (d, J = 4.2 Hz, 1H), 1.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) major isomer: δ 198.3 (C), 137.8 (CH), 115.9 (C), 115.3 (CH_2), 84.8 (CH), 64.7 (CH_2), 53.6 (C), 45.7 (CH), 42.3 (CH), 40.4 (CH_2), 37.4 (CH_2), 33.7 (CH_2), 30.8

(CH_2), 28.5 (CH_2), 16.0 (CH_3), minor isomer: δ 199.2 (C), 137.6 (CH), 115.9 (C), 115.4 (CH_2), 85.5 (CH), 65.0 (CH_2), 42.0 (CH), 39.3 (CH_2), 27.8 (CH_2), 26.2 (CH_2), 17.9 (CH_3); HRMS (EI) calcd for $C_{15}H_{21}NO_2$: 247.1572; found: 247.1573.

General procedure for 1,4-addition in the synthesis of compounds 21 and 22. The general procedure is illustrated immediately below with compound **21** as a specific example.

2-Methyl-6-oxo-2-pent-4-enylcyclohexanecarbonitrile (21). Freshly prepared 4-pentenylmagnesium bromide solution (4.2 mL, 0.65 M in THF, 2.73 mmol) was added to a solution of copper(I) iodide dimethyl sulfide complex (0.229 g, 0.91 mmol) in anhydrous THF (5 mL) dropwise at −78 °C. The resulting mixture was stirred at the same temperature for 30 min, after which time a solution of compound **21** (0.25 g, 1.82 mmol) in anhydrous THF (5 mL) was introduced dropwise. Then the resulting mixture was warmed and stirred at −40 °C for 3 h. H_2O (5 mL) and saturated NH_4Cl solution (5 mL) was added to quench the reaction. The aqueous layer was separated and extracted with EA (3 × 15 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated to give the crude residue, which was purified by flash chromatography on silica gel with EtOAc–*n*-hexane (1 : 9) to afford compound **21** [0.331 g, 79% yield, a mixture of keto isomers in a ratio of 1 : 1.5 (*cis* : *trans*)] as a colorless oil.

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2938, 2241, 1712, 1643, 1458; ^1H NMR ($CDCl_3$, 600 MHz) major isomer: δ 5.78–5.72 (m, 1H), 5.01–4.93 (m, 2H), 3.30 (s, 1H), 2.58–2.51 (m, 1H), 2.30–2.23 (m, 1H), 2.06–1.62 (m, 6H), 1.53–1.24 (m, 4H), 1.02 (s, 3H), minor isomer: δ 3.36 (s, 1H), 1.12 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) major isomer: δ 201.1 (C), 137.9 (CH), 115.3 (CH_2), 115.2 (C), 53.9 (CH), 42.6 (C), 40.9 (CH_2), 39.8 (CH_2), 34.5 (CH_2), 33.8 (CH_2), 22.7 (CH_2), 21.7 (CH_2), 21.0 (CH_3), minor isomer: δ 55.5 (CH), 39.5 (CH_2), 33.6 (CH_2), 25.0 (CH_3), 22.3 (CH_2), 21.5 (CH_2); HRMS (EI) calcd for $C_{13}H_{19}NO$: 205.1467; found: 205.1469.

5-Isopropyl-2-methyl-6-oxo-2-(pent-4-enyl) cyclohexanecarbonitrile (22). A mixture of keto isomers in a ratio of 1 : 1.2 (*cis* : *trans*) was obtained as a yellow oil (76% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2963, 2875, 2241, 1704; ^1H NMR ($CDCl_3$, 600 MHz) major isomer: δ 5.76–5.69 (m, 1H), 5.00–4.92 (m, 2H), 3.37 (s, 1H), 2.34–2.31 (m, 1H), 2.07–2.00 (m, 1H), 1.98–1.89 (m, 3H), 1.72–1.66 (m, 1H), 1.53–1.31 (m, 5H), 1.19 (s, 3H), 0.91 (d, J = 6.8 Hz, 3H), 0.87 (d, J = 6.8 Hz, 3H), minor isomer: δ 3.26 (s, 1H), 2.16–2.11 (m, 1H), 0.85 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) major isomer + minor isomer: δ 203.4 (C), 201.1 (C), 137.9 (CH), 137.8 (CH), 116.1 (C), 115.2 (CH_2 × 2), 57.1 (CH), 55.4 (CH), 54.3 (CH), 52.4 (CH), 43.1 (C), 38.6 (CH_2), 33.9 (CH_2), 33.8 (CH_2), 32.0 (CH_2), 31.1 (CH_2), 26.7 (CH_2), 26.5 (CH_3), 26.2 (CH_2), 23.9 (CH_2), 22.7 (CH_2), 22.9 (CH_3), 22.5 (CH_2), 22.3 (CH_2), 20.8 (CH_3), 20.8 (CH_3), 19.4 (CH_3), 18.4 (CH_3); HRMS (EI) calcd for $C_{16}H_{25}NO$: 247.1936; found: 247.1935.

The general procedure for Pd(II) mediated annulation in the synthesis of compounds 23–33. The general procedure is illustrated immediately below with compound **24** as a specific example.

(4a*S,8a*R**)-4-Methylene-5-oxooctahydronaphthalene-4a-carbonitrile (24).** $Pd(OAc)_2$ (105 mg, 0.47 mmol) was added to a solution of compound **13** (89 mg, 0.47 mmol) in THF (5 mL) at room temperature. The resulting mixture was stirred at the same temperature for 20 min. Silica gel (2g) was added and the mixture was concentrated to give crude residue which was purified by flash chromatography on silica gel with EtOAc–*n*-hexane (1 : 5) to afford compound **24** (63 mg, 82% yield) as a colorless oil.

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2967, 2866, 2233, 1730, 1645; ^1H NMR ($CDCl_3$, 600 MHz): δ 5.06 (s, 1H), 5.04 (s, 1H), 2.75 (ddd, J = 14.4, 10.4, 6.7 Hz, 1H), 2.38–2.43 (m, 1H), 2.28–2.34 (m, 2H), 2.18–2.14 (m, 2H), 1.92–1.85 (m, 2H), 1.72–1.67 (m, 2H), 1.64–1.59 (m, 1H), 1.43–1.27 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 201.9 (C), 140.7 (C), 118.6 (C), 114.9 (CH_2), 58.7 (C), 46.2 (CH), 39.2 (CH_2), 31.9 (CH_2), 27.4 (CH_2), 27.2 (CH_2), 24.6 (CH_2), 23.1 (CH_2); HRMS (EI) calcd for $C_{12}H_{15}NO$: 189.1154; found: 189.1155.

5-Oxo-2-pent-4-enylcyclopent-1-enecarbonitrile (23). Compound **23** was obtained as a yellow oil (70% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 3028, 2947, 2233, 1685, 1637; ^1H NMR ($CDCl_3$, 600 MHz): δ 5.79–5.72 (m, 1H), 5.06–5.01 (m, 2H), 2.78–2.74 (m, 2H), 2.71–2.68 (m, 2H), 2.54–2.52 (m, 2H), 2.13 (dd, J = 14.1, 7.0 Hz, 2H), 1.77–1.72 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 201.3 (C), 193.3 (C), 136.7 (CH_2), 117.3 (C), 116.2 (CH_2), 111.9 (C), 34.6 (CH_2), 33.2 (CH_2), 32.9 (CH_2), 31.1 (CH_2), 26.3 (CH_2); HRMS (EI) calcd for $C_{11}H_{13}NO$: 175.0997; found: 175.0993.

(4a*S,9a*R**)-4-Methylene-5-oxodecahydrobenzocycloheptene-4a-carbonitrile (25).** Compound **25** was obtained as a yellow oil (86% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2935, 2860, 2235, 1712, 1645, 1450; ^1H NMR ($CDCl_3$, 600 MHz): δ 4.94 (d, J = 1.8 Hz, 1H), 4.47 (d, J = 1.2 Hz, 1H), 2.80 (dt, J = 11.6, 3.9 Hz, 1H), 2.58–2.54 (m, 1H), 2.43–2.35 (m, 2H), 2.02–1.98 (m, 2H), 1.91–1.88 (m, 1H), 1.85–1.82 (m, 1H), 1.79–1.75 (m, 2H), 1.71–1.67 (m, 1H), 1.62–1.43 (m, 4H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 206.5 (C), 143.6 (C), 117.4 (C), 111.1 (CH_2), 63.9 (C), 45.1 (CH), 40.6 (CH_2), 33.5 (CH_2), 32.4 (CH_2), 30.7 (CH_2), 28.1 (CH_2), 26.7 (CH_2), 20.2 (CH_2); HRMS (EI) calcd for $C_{13}H_{17}NO$: 203.1310; found: 203.1308.

4-Methylene-5-oxodecahydrobenzocyclooctene-4a-carbonitrile (26). Compound **26** was obtained as a colorless oil (82% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2942, 2846, 2239, 1710, 1641; ^1H NMR ($CDCl_3$, 600 MHz): δ 5.02 (d, J = 1.9 Hz, 1H), 4.49 (d, J = 1.1 Hz, 1H), 2.74 (dt, J = 12.9, 3.3 Hz, 1H), 2.42–2.31 (m, 4H), 1.92–1.83 (m, 3H), 1.78–1.72 (m, 4H), 1.55–1.42 (m, 3H), 1.22–1.18 (m, 1H), 1.05–1.01 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 208.5 (C), 142.1 (C), 116.2 (C), 113.5 (CH_2), 63.4 (C), 39.2 (CH), 38.9 (CH_2), 34.2 (CH_2), 33.9 (CH_2), 30.9 (CH_2), 29.8 (CH_2), 25.9 (CH_2), 25.8 (CH_2), 23.3 (CH_2); HRMS (EI) calcd for $C_{14}H_{19}NO$: 217.1467; found: 217.1466.

4-Methylene-5-oxotetradecahydrobenzocyclododecene-4a-carbonitrile (27). Compound **27** was obtained as a colorless oil (81% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2974, 2937, 2875, 2229, 1712, 1649 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 5.00 (dd, J = 1.5 Hz, 1H), 4.60 (d, J = 0.9 Hz, 1H), 2.74–2.72 (m, 2H), 2.38–2.34 (m, 2H), 2.09–2.03 (m, 1H), 1.96–1.92 (m, 2H), 1.85–1.82 (m, 1H), 1.42–1.40 (m, 16H), 1.55–1.62 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 204.1 (C), 142.8 (C), 117.9 (C), 113.8 (CH_2), 63.9 (C), 43.2 (CH), 37.1 (CH_2), 32.5 (CH_2), 30.6 (CH_2), 27.9 (CH_2), 26.1 (CH_2), 25.6 (CH_2), 25.3 (CH_2), 25.2 (CH_2), 24.4 (CH_2), 23.9 (CH_2), 22.7 (CH_2), 21.8 (CH_2); HRMS (EI) calcd for $C_{18}H_{27}NO$: 273.2093; found: 273.2090.

(1*S,4a*S**,8a*R**)-Decahydro-1-methyl-5-methylene-4-oxonaphthalene-4a-carbonitrile (28).** Compound **28** was obtained as white solid (79% yield), which was further recrystallized from ethyl acetate and *n*-hexane to afford a crystalline compound in white color.

Mp 133–136 °C; IR (CH_2Cl_2 cast, cm^{-1}) ν max 2236, 1728, 1640; ^1H NMR ($CDCl_3$, 600 MHz): δ 5.15 (d, J = 2.0 Hz, 1H), 4.63 (d, J = 1.7 Hz, 1H), 2.67 (dt, J = 13.7, 6.1 Hz, 1H), 2.59–2.55 (m, 1H), 2.50–2.41 (m, 2H), 2.00–1.89 (m, 2H), 1.69–1.63 (m, 2H), 1.62–1.54 (m, 2H), 1.49–1.37 (m, 2H), 0.98 (d, J = 5.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 202.9 (C), 140.5 (C), 118.3 (C), 115.8 (CH_2), 59.5 (C), 49.2 (CH), 39.1 (CH_2), 34.0 (CH_2), 32.7 (CH_2), 28.3 (CH), 24.6 (CH_2), 20.9 (CH_2), 18.5 (CH_3); HRMS (EI) calcd for $C_{13}H_{17}NO$: 203.1310; found: 203.1309.

8,8-Dimethyl-4-methylene-5-oxo-1,3,4,5,8,8a-hexahydro-2*H*-naphthalene-4a-carbonitrile (29a) and 3,3-dimethyl-6-oxo-2-pent-4-enylcyclohexa-1,4-dienecarbonitrile (29b). Compound **29a** was obtained as a colorless oil (41% yield) and Compound **29b** was obtained as a colorless oil (45% yield).

Compound **29a** IR (CH_2Cl_2 cast, cm^{-1}) ν max 2237, 1697, 1638; ^1H NMR ($CDCl_3$, 600 MHz): δ 6.59 (d, J = 8.7 Hz, 1H), 6.02 (d, J = 8.1 Hz, 1H), 5.34 (d, J = 0.9 Hz, 1H), 5.21 (d, J = 1.4 Hz, 1H), 2.42 (m, 1H), 2.28–2.25 (m, 1H), 2.04–1.82 (m, 3H), 1.33–1.23 (m, 2H), 1.16 (s, 3H), 1.15 (m, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 189.3 (C), 158.3 (CH), 141.4 (C), 124.2 (CH), 118.2 (C), 115.4 (CH_2), 54.5 (C), 50.7 (CH), 37.3 (C), 32.0 (CH_2), 29.0 (CH_3), 28.5 (CH_3), 26.0 (CH_2), 25.5 (CH_2); HRMS (EI) calcd for $C_{14}H_{17}NO$: 215.1310; found: 215.1309.

Compound **29b** IR (CH_2Cl_2 cast, cm^{-1}) ν max 2238, 1691, 1640 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 6.79 (d, J = 7.9 Hz, 1H), 6.23 (d, J = 6.8 Hz, 1H), 5.56 (m, 1H), 5.08–5.02 (m, 2H), 2.62 (m, 1H), 2.55 (m, 1H), 2.23–2.20 (m, 2H), 1.78–1.73 (m, 2H), 1.65–1.63 (m, 2H), 1.33 (s, 3H), 1.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 181.2 (C), 179.9 (C), 156.9 (CH), 136.9 (CH), 127.2 (C), 125.2 (CH), 116.2 (C), 113.9 (CH_2), 41.7 (C), 41.2 (CH_2), 32.2 (CH_2), 28.5 (CH_2), 25.6 (CH_3 × 2); HRMS (EI) calcd for $C_{14}H_{17}NO$: 215.1310; found: 215.1308.

(4a*S,8a*R**)-Decahydro-2,2-dimethyl-5-methylene-4-oxonaphthalene-4a-carbonitrile (30).** Compound **30** was obtained as a colorless oil (76% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2236, 1728, 1643 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 5.16 (s, 1H), 4.63 (s, 1H), 2.59 (m, 1H), 2.51 (d, J = 13.8 Hz, 1H), 2.43–2.41 (m, 2H), 2.23 (dd, J = 13.8, 2.6 Hz, 1H), 2.10–2.04 (m, 1H), 1.85 (t, J = 13.6 Hz, 1H), 1.71–1.65 (m, 3H), 1.31–1.27 (m, 1H), 1.04 (s, 3H), 0.92 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 203.2 (C), 139.9 (C), 118.4 (C), 116.4 (CH_2), 58.3 (C), 51.4 (CH_2), 38.9 (CH), 38.8 (CH_2), 34.9 (C), 32.6 (CH_2), 31.9 (CH_3), 27.7 (CH_2), 25.6 (CH_3), 20.5 (CH_2); HRMS (EI) calcd for $C_{14}H_{19}NO$: 217.1467; found: 217.1464.

(3a*R,5a*S**,9a*R**,9b*S**)-Dodecahydro-9b-methyl-6-methylene-5-oxonaphtho[2,1-*b*]furan-5a-carbonitrile (31).** Compound **31** was obtained as a colorless oil (59% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2236, 1723, 1640 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 4.95 (d, J = 1.9 Hz, 1H), 4.66 (d, J = 1.9 Hz, 1H), 3.95 (ddd, J = 9.1, 6.6, 3.0 Hz, 1H), 3.69–3.65 (m, 2H), 2.59 (m, 1H), 2.51 (d, J = 13.8 Hz, 1H), 2.43–2.41 (m, 2H), 2.23 (dd, J = 13.8, 2.6 Hz, 1H), 2.10–2.04 (m, 1H), 1.85 (t, J = 13.6 Hz, 1H), 1.71–1.65 (m, 3H), 1.31–1.27 (m, 1H), 1.04 (s, 3H), 0.92 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 203.2 (C), 139.9 (C), 118.4 (C), 116.4 (CH_2), 58.3 (C), 51.4 (CH_2), 38.9 (CH), 38.8 (CH_2), 34.9 (C), 32.6 (CH_2), 31.9 (CH_3), 27.7 (CH_2), 25.6 (CH_3), 20.5 (CH_2); HRMS (EI) calcd for $C_{14}H_{19}NO$: 245.1416; found: 245.1416.

(4a*R,8a*R**)-Decahydro-8a-methyl-4-methylene-5-oxonaphthalene-4a-carbonitrile (32).** Compound **32** was obtained as a colorless oil (62% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2934, 2234, 1711, 1640, 1457 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 5.19 (s, 1H), 5.14 (s, 1H), 2.83 (m, 1H), 2.52–2.49 (m, 1H), 2.36–2.33 (m, 1H), 2.29–2.27 (m, 1H), 1.98–1.94 (m, 3H), 1.74–1.71 (m, 1H), 1.64 (m, 3H), 1.38–1.35 (m, 1H), 1.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 202.5 (C), 140.3 (C), 117.5 (C), 115.9 (CH_2), 63.3 (C), 43.4 (C), 38.2 (CH_2), 33.6 (CH_2), 33.0 (CH_2), 31.2 (CH_2), 24.3 (CH_3), 21.1 (CH_2 × 2); HRMS (EI) calcd for $C_{13}H_{17}NO$: 203.1310; found: 203.1314.

(4a*R,8a*R**)-Decahydro-3-isopropyl-8a-methyl-5-methylene-4-oxonaphthalene-4a-carbonitrile (33).** Compound **33** was obtained as a colorless oil (68% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2954, 2232, 1727, 1645 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 5.26 (s, 1H), 5.17 (t, J = 7.2 Hz, 1H), 2.77–2.73 (m, 1H), 2.32–2.29 (m, 2H), 2.21–2.16 (m, 1H), 2.12–2.08 (m, 1H), 2.00–1.95 (m, 1H), 1.77–1.63 (m, 2H), 1.60–1.46 (m, 1H), 1.16 (s, 3H), 0.92 (d, J = 6.8 Hz, 3H), 0.87 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 202.9 (C), 139.8 (C), 118.4 (C), 115.2 (CH_2), 63.9 (C), 52.7 (CH), 44.1 (CH_2), 36.7 (CH_2), 31.6 (CH_2), 31.1 (CH_2), 26.3 (CH), 24.2 (CH_3), 23.4 (CH_2), 21.2 (CH_2), 20.7 (CH_3), 18.4 (CH_3); HRMS (EI) calcd for $C_{16}H_{23}NO$: 245.1780; found: 245.1782.

(4a*R,8a*R**)-4-[(2,4-Dinitro-phenyl)-hydrazono]-5-methylene-octahydro-naphthalene-4a-carbonitrile (24a).** A two-neck round bottom flask equipped with a Dean-Stark and a condenser was charged with compound **24** (48 mg, 0.40 mmol), *p*-TSA (2 mg, 0.01 mmol), 2,4-dinitrophenylhydrazine (0.104 g, 0.80 mmol) and toluene (10 mL). The reaction mixture was heated to reflux for 40 hours with azeotropic removal of water and then cooled to room temperature. Saturated $NaHCO_3$ solution (5 mL) was added. The resulting aqueous solution was extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated to give the crude product, which was purified by flash chromatography on

silical gel with EtOAc–*n*-hexane (1 : 9) to afford compound **24a** (48 mg, 52% yield) as an orange solid, which was further recrystallized from ethyl acetate and *n*-hexane to afford a crystalline compound in bright-orange color.

Mp 233–236 °C; IR (CH_2Cl_2 cast, cm^{-1}) ν max 2938, 2829, 2342, 1702, 1636, 1592; ^1H NMR ($CDCl_3$, 600 MHz): δ 11.18 (s, 1H), 9.11 (d, J = 2.6 Hz, 1H), 8.33 (dd, J = 9.6, 2.5 Hz, 1H), 8.01 (d, J = 9.5 Hz, 1H), 5.19 (s, 1H), 4.95 (s, 1H), 2.73–2.69 (m, 1H), 2.54–2.50 (m, 2H), 2.45–2.41 (m, 1H), 2.35–2.32 (m, 1H), 1.97–1.89 (m, 3H), 1.80–1.70 (m, 3H), 1.66–1.59 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 152.6 (C), 145.2 (C), 142.1 (C), 138.7 (C), 130.4 (CH), 129.8 (C), 123.2 (CH), 119.5 (C), 116.8 (CH), 115.3 (CH_2), 53.4 (C), 44.0 (CH), 32.5 (CH_2), 27.8 (CH_2), 26.7 (CH_2), 24.2 (CH_2), 23.1 (CH_2), 22.5 (CH_2); HRMS (EI) calcd for $C_{18}H_{19}N_5O_4$: 369.1437; found: 369.1441.

The general procedure for LN induced reductive decyanation in the synthesis of compounds 34–36. The general procedure is illustrated immediately below with compound **34** as a specific example.

8-Methyl-3,4,4a,5,6,7-hexahydro-2*H*-naphthalen-1-one (34). Freshly prepared LN[18] reagent was slowly added to a stirred solution of compound **24** (52 mg, 0.26 mmol) in THF (8 mL) at −78 °C until the resulting solution become deep green color. The reaction was stirred at same temperature for another 15 min, at which time H_2O (10 mL) was introduced to quench the reaction. The aqueous layer was separated and extracted with EA (2 × 10 mL). The combined organic extracts were washed brine, dried over $MgSO_4$, filtered and concentrated to give the crude residue, which was purified by flash chromatography on silical gel with EtOAc–*n*-hexane (1 : 4) to afford compound **34** (36 mg, 85%) as a colorless oil.

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2962, 2933, 1675; ^1H NMR ($CDCl_3$, 600 MHz): δ 2.50–2.45 (m, 1H), 2.49 (dq, J = 13.7, 6.5 Hz, 2H), 2.09–2.06 (m, 2H), 1.97–1.93 (m, 1H), 1.90–1.84 (m, 2H), 1.83 (t, J = 1.1 Hz, 1H), 2.07–2.02 (m, 1H), 1.75–1.66 (m, 3H), 1.48–1.32 (m, 2H), 1.24–1.18 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 204.6 (C), 143.4 (C), 134.8 (C), 43.0 (CH_2), 39.1 (CH), 33.8 (CH_2), 33.0 (CH_2), 30.8 (CH_2), 23.7 (CH_2), 21.8 (CH_3), 21.3 (CH_2); HRMS (EI) calcd for $C_{11}H_{16}O$: 164.1201; found: 164.1200.

4-Methyl-1,2,3,6,7,8,9,9a-octahydrobenzocyclohepten-5-one (35). Compound **35** was obtained as a colorless oil (81% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2951, 2943, 1677; ^1H NMR ($CDCl_3$, 600 MHz): 2.57 (td, J = 12.4, 2.8 Hz, 1H), 2.43–2.40 (m, 1H), 2.35–2.31 (m, 1H), 2.10–2.05 (m, 2H), 1.90–1.85 (m, 1H), 1.84 (t, J = 0.8 Hz, 3H), 1.72–1.66 (m, 4H), 1.53–1.46 (m, 3H), 1.40–1.33 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 208.5 (C), 141.1 (C), 137.8 (C), 44.0 (CH_2), 36.9 (CH_2), 36.6 (CH), 33.0 (CH_2), 31.6 (CH_2), 30.2 (CH_2), 26.1 (CH_2), 21.5 (CH_3), 20.3 (CH_2); HRMS (EI) calcd for $C_{12}H_{18}O$: 178.1358; found: 178.1356.

4-Methyl-1,2,3,6,7,8,9,10,11,12,13,13a-dodecahydrobenzocycloundecen-5-one (36). Compound **36** was obtained as a colorless oil (86% yield).

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2971, 2953, 1682; ^1H NMR ($CDCl_3$, 600 MHz): 3.06–3.02 (m, 1H), 2.54–2.52 (m, 1H), 2.11–2.04 (m, 2H), 1.97–1.93 (m, 2H), 1.63–1.50 (m, 7H), 1.36–1.23 (m, 15H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 210.3 (C), 140.2 (C), 133.8 (C), 37.9 (CH_2), 32.9 (CH), 31.7 (CH_2), 30.2 (CH_2), 26.5 (CH_2), 26.2 (CH_2), 24.7 (CH_2), 23.9 (CH_2), 23.6 (CH_2), 23.3 (CH_2), 22.4 (CH_2), 21.7 (CH_2), 20.8 (CH_3), 19.1 (CH_2); HRMS (EI) calcd for $C_{17}H_{28}O$: 248.2140; found: 248.2146.

(4a*S,9a*R**)-4a-Benzyl-4-methylenedecahydrobenzo-cyclohepten-5-one (37).** Freshly prepared LN reagent was slowly added to a stirred solution of compound **24** (55 mg, 0.27 mmol) in THF (8 mL) at −78 °C until the resulting solution become deep green color. The reaction was stirred at the same temperature for another 45 min, at which time benzyl bromide (70 mg, 0.40 mmol) was introduced dropwise. Then the resulting mixture was warmed and kept stirring at 0 °C for 6 h. H_2O (10 mL) was added to quench the reaction. The aqueous layer was separated and extracted with EA (2 × 10 mL). The combined organic extracts were washed brine, dried over $MgSO_4$, filtered and concentrated to give the crude residue, which was purified by flash chromatography on silical gel with EtOAc–*n*-hexane (1 : 4) to afford compound **37** (49 mg, 71%) as colorless oil.

IR (CH_2Cl_2 cast, cm^{-1}) ν max 2971, 2953, 1714, 1638, 1595; ^1H NMR ($CDCl_3$, 600 MHz): 7.21–7.18 (m, 2H), 7.16–7.13 (m, 1H), 7.09–7.07 (m, 2H), 5.00 (s, 1H), 4.82 (s, 1H), 3.35 (d, J = 13.3 Hz, 1H), 2.87 (d, J = 13.3 Hz, 1H), 2.41–2.36 (m, 1H), 2.19–2.14 (m, 3H), 2.11–2.07 (m, 1H), 1.74 (td, J = 11.5, 2.4 Hz, 1H), 1.69–1.64 (m, 2H), 1.56–1.52 (m, 4H), 1.41–1.26 (m 3H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 215.3 (C), 146.8 (C), 137.3 (C), 130.5 (C × 2), 128.0 (C × 2), 126.4 (C), 113.2 (CH_2), 62.4 (C), 44.5 (CH_2), 42.6 (CH_2), 37.6 (CH), 33.2 (CH_2), 32.5 (CH_2), 29.9 (CH_2), 28.5 (CH_2), 25.2 (CH_2), 22.7 (CH_2); HRMS (EI) calcd for $C_{19}H_{24}O$: 268.1827; found: 268.1830.

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14 Crystal data for **28**: $C_{13}H_{17}NO$, M = 203.28; Triclinic, space group $P2(1)/n$; a = 9.7923(14), b = 8.0377(11), c = 14.520(2) Å, V= 93.817(2)°, V = 1140.3(3) Å^3, T = 273(2) K; Z = 4; μ = 0.074 mm^{-1}; reflections: total = 8265, unique = 2874 (R_{int} = 0.0270); R indices (all data): R_1 = 0.0699, wR_2 = 0.1905. CCDC 851795.
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