Advanced Synthesis & Catalysis

Accepted Article

Title: Cycloisomerization of Oxindole-derived 1,5-enynes: A Calcium(II) catalyzed one-pot, solvent-free synthesis of Phenanthridinones, 3-(cyclopentenylidene)indolin-2-ones and 3-spirocyclic indolin-2-ones

Authors: SRINIVASARAO YARAGORLA, Abhishek pareek, and Ravikrishna Dada

To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.201700569

Link to VoR: http://dx.doi.org/10.1002/adsc.201700569

10.1002/adsc.201700569

COMMUNICATION

DOI: 10.1002/adsc.2017((will be filled in by the editorial staff))

Cycloisomerization of Oxindole-Derived 1,5-Enynes: A Calcium(II)-Catalyzed One-Pot, Solvent-free Synthesis of Phenanthridinones, 3-(Cyclopentenylidene)indolin-2-ones and 3-Spirocyclic Indolin-2-ones

Srinivasarao Yaragorla,[a,b]*Abhishek Pareek[a,b] and Ravikrishna Dada[a,b]

[a]School of Chemistry, University of Hyderabad, Prof. C. R. Rao Road, Gachibowli, Hyderabad, 500046, India.
Email:srinivas.yaragorla@uohyd.ac.in
[b]Department of Chemistry, Central University of Rajasthan, NH8, Bandersindri, 305817, Rajasthan, India

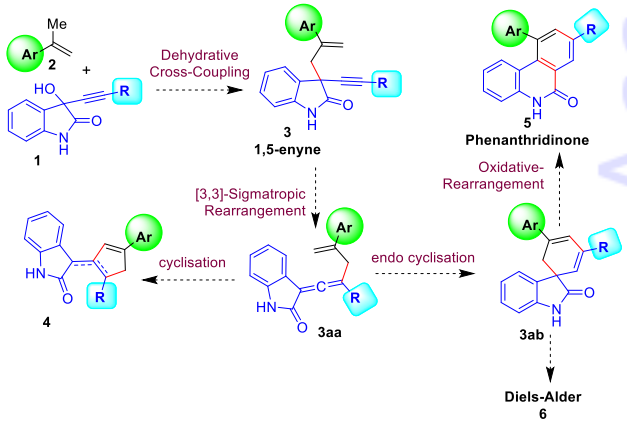
Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######. (Please delete if not appropriate)

Abstract. Calcium-catalyzed regioselective synthesis of oxindole-derived 1,5-enynes, followed by cycloisomerization, from readily accessible 3-hydroxy-3-(alkynyl)indolin-2-ones and styrenes in one-pot, under solvent-free conditions is described. This method offers the synthesis of diverse molecules: phenanthridinones, 3-(cyclopentenylidene)indolin-2-ones, and 3-spirocyclic indolin-2-ones are obtained through cascade reactions including cross-dehydrative-coupling, [3,3]-sigmatropic rearrangement, carbocyclization, isomerization, oxidative-ring rearrangement, and Diels-Alder cycloaddition. In addition, this method features atom- and step-economy, broad substrate scope, and high yields.

Keywords: 1,5-enynes; cycloisomerization; Diels-Alder reaction; phenanthridinones; regioselective; calcium catalysis

Enynes are highly potential feedstock materials for the synthesis of complex carbocyclic molecules, natural products and pharmaceutically active molecules through varieties of cycloisomerization reactions.[1] The substantial increase in the molecular/structural complexity arises from the simple acyclic starting materials made this method more significant.[1,2] In most of the cases transition metals were employed for cycloisomerization and rearrangement of enynes for developing useful organic transformations and hence considerably great research has been devoted towards the cycloisomerization/rearrangement of 1,n-enynes using Pd, Ru, Rh, Ir, Pt, Au, Hg, Ti, Cr, Fe, Co, Ni, Cu, Ag, In and Ga metal catalysts.[2] Amongst the array of available enynes, 1,5-enynes are one of the most studied and they have been efficiently converted into carbocyclic compounds such as bicycloalkenes,[3] tricyclic compounds,[4] cyclohexadienes[5] and methylenecyclopentenes.[6] Most of these metal catalyzed transformations are inherently atom economical,[7] however some of these catalysts are expensive and need special conditions (mostly inert) to handle the reaction. Furthermore, all these methods utilize the 1,5-enynes as precursor. To the best of our knowledge, no report has been available for the in situ generation of 1,5-enynes followed by cycloisomerization and also no non-transition metal has been used for the enyne isomerization yet. Owing to these reasons, it is certainly desirable to explore highly abundant, environmentally benign and less expensive catalysts for the facile synthesis and transformation of 1,5-enynes in a one-pot cascade strategy which can contribute to the sustainable goals of organic synthesis.[8] In the past few years we have been working with $Ca(OTf)_2$ as one of the alternatives and sustainable catalyst for varieties of tandem organic transformation with high regioselectivity.[9] In continuation of our research interest towards the alkyne triggered regioselective annulation reactions,[10] we disclose here a calcium catalyzed one-pot tandem process of 1,5-enyne formation and their cycloisomerizations from the readily available α-methylstyrenes/benzylic-*tert*-alcohols and 3-hydroxy-3-(alkynyl)indolin-2-ones.

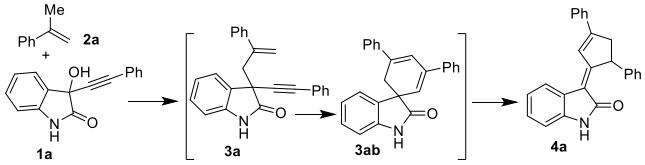


Scheme 1. Our conceptualization of one-pot 1,5-enyne formation and cycloisomerization cascade.

10.1002/adsc.201700569

As depicted in the Scheme 1, we proposed that the 1,5-enyne **3** can be synthesized through a dehydrative cross coupling of alcohol **1** and olefin **2**. 1,5-enyne **3** thus obtained further would undergo a thermal [3,3]-sigmatropic rearrangement to furnish the allene intermediate **3aa** which has two possible modes of intramolecular cyclization i.e. (i) a 5-exo/endo cyclization to yield the cyclopentenylidene **4**; (ii) 6-endo cyclization to furnish the cyclohexadiene **3ab**. Diene **3ab** could be trapped into a Diels-Alder cycloaddition (**6**) or it can undergo oxidative rearrangement to provide the phenanthridinones (**5**)

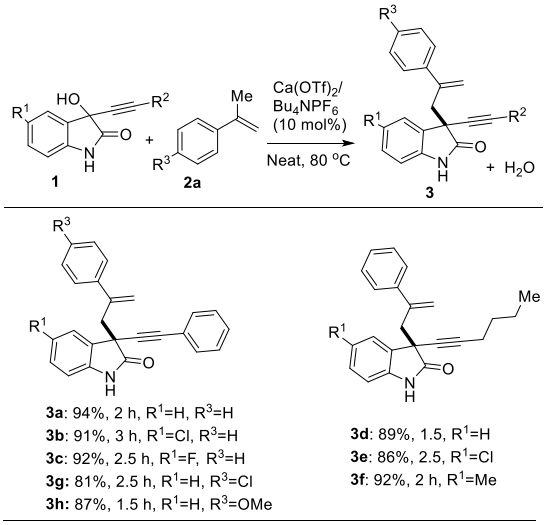
Table 1. Optimization of reaction conditions for one-pot regioselective synthesis of 3-(cyclopent-2-en-1-ylidene)indolin-2-ones [a]



Entry	Catalyst (mol%)	Reaction Conditions.[b]	Yields (%) of **3a**, **3ab**[c], **4a**
1[d]	$Ca(OTf)_2/Bu_4NPF_6$, (10/10)	neat, 80 °C, 1.5 h	94, 0, 0
2	$Ca(OTf)_2/Bu_4NPF_6$, (10/10)	neat, 110 °C, 3 h	10, 75, 0
3[e]	$Ca(OTf)_2/Bu_4NPF_6$, (10/10)	neat, 130 °C, 7 h	0, 12, 73
4	--	neat, 130 °C, 24 h	----
5	$Ca(OTf)_2$, (10)	neat, 130 °C, 12 h	12, 0, 0
6	Bu_4NPF_6, (10)	neat, 130 °C, 12 h	10, 0, 0
7	$Ca(OTf)_2/Bu_4NPF_6$, (5/5)	neat, 130 °C, 8 h	0, 5, 60
8	$Ca(OTf)_2/Bu_4NPF_6$, (5/10)	neat, 130 °C, 8 h	0, 15, 60
9	$Ca(OTf)_2/Bu_4NPF_6$, (10/5)	neat, 130 °C, 8 h	0, 10, 65
10	$Ca(OTf)_2/KPF_6$, (10/10)	neat, 130 °C, 10 h	0, 25, 0
11	$Ca(OTf)_2/Bu_4NF$, (10/10)	neat, 130 °C, 10 h	0, 10, 0
12	$CaCl_2/Bu_4NPF_6$, (10/10)	neat, 130 °C, 10 h	0, 15, 0
13	$Ca(ClO_4)_2/Bu_4NPF_6$, (10/10)	neat, 130 °C, 10 h	0, 10, 0
14	$Ca(OTf)_2/Bu_4NPF_6$, (10/10)	toluene, 120 °C, 10 h	0, 40, 30
15	$Ca(OTf)_2/Bu_4NPF_6$, (10/10)	water, 110 °C, 10 h	-
16	$Ca(OTf)_2/Bu_4NPF_6$, (10/10)	DCM, 50 °C, 10 h	45, 0, 0
17	$Mg(OTf)_2/Bu_4NPF_6$, (10/10)	neat, 130 °C, 8 h	0, 20, 30
18	p-TSA (10)	neat, 130 °C, 8 h	0, 10, 40
19	$FeCl_3$ (10)	neat, 130 °C, 8 h	0, 25, 40

[a]Conditions: 1 equiv. of **1a** and 2.2 equiv. of **2a** were used. [b]Oil bath temperature. [c]Regioisomeric hexadiene (1:0.35). [d]Optimum condition for the 1,5-enynes. [e]Optimum condition for the cyclopentenylidene; DCM = dichloromethane; Tf= trifluormethanesulfonyl; p-TSA = para toluene sulfonic acid.

Based on our preliminary results from the synthesis of internal olefins through a calcium catalyzed dehydrative cross coupling of alcohols with olefins,[9a] we chose 3-hydroxy-3-(phenylethynyl)indolin-2-one (**1a**) and α-methylstyrene (**2a**) as the substrates for the synthesis of 1,5-enyne **3a** and hence heated them at 80 °C with 10 mol% of $Ca(OTf)_2/Bu_4NPF_6$. Gratifyingly, this reaction proceeded with high efficiency to furnish the 1,5-enyne **3a** (3-(2-phenylallyl)-3-(phenylethynyl)indolin-2-one) as the sole product with 94% yield in 1.5 h (Table 1, entry 1). When the reaction temperature raised to 110 °C we found that most of the 1,5-enyne underwent cycloisomerization to form spirohexadiene (regioisomeric mixture) **3ab** in 75% after 3 h. Further increase in temperature to 130 °C, spirocyclic hexadiene **3ab** was rearranged to a stable cyclopentene derivative **4a** in 73% after 7 h (entry 3). The absence of $Ca(OTf)_2/Bu_4NPF_6$ (entry 4) or presence of catalyst alone (entry 5) or additive (Bu_4NPF_6) alone (entry 6) was found to be inefficient. Neither the decrease of catalyst loading nor the change in catalyst/additive combinations could give the satisfactory results (Entries 7-11). Other calcium salts such as $CaCl_2$ and $Ca(ClO_4)_2$ were ineffective (entries 12, 13). Solvents such as toluene, water and dichloromethane were not found to be suitable solvents (entries 14-16). Other catalysts such as $Mg(OTf)_2$, *p*-TSA and $FeCl_3$ could not give the satisfactory results (entries 17-19).



Scheme 2. Synthesis of quaternary-oxindolyl 1,5-enynes through calcium triflate mediated a dehydrative cross coupling. General conditions:1 equiv. of **1a,** 2.2 equiv. of **2a,** 10 mol% of $Ca(OTf)_2$, 10 mol% of Bu_4NPF_6. Isolated yields.

Considering the entry 1 (Table 1) as the standard condition for the synthesis of quaternary-oxindolyl 1,5-enynes, we extended this protocol to check its substrate scope. As depicted in the Scheme 2, we synthesized the 1,5-enynes with the substitution on isatin-aryl ring **3b, 3c** in 91% and 92% respective yields. Not only aryl alkynes but also aliphatic alkynes gave 1,5-enynes **3d**, **3e** and **3f** in excellent yields as depicted in the Scheme 2. Substituted α-methylstyrenes such as 1-chloro-4-(prop-1-en-2-yl)benzene and 1-methoxy-4-(prop-1-en-2-yl)benzene also showed good reactivity towards the enyne formation, however owing to the +M-effect of _-OMe

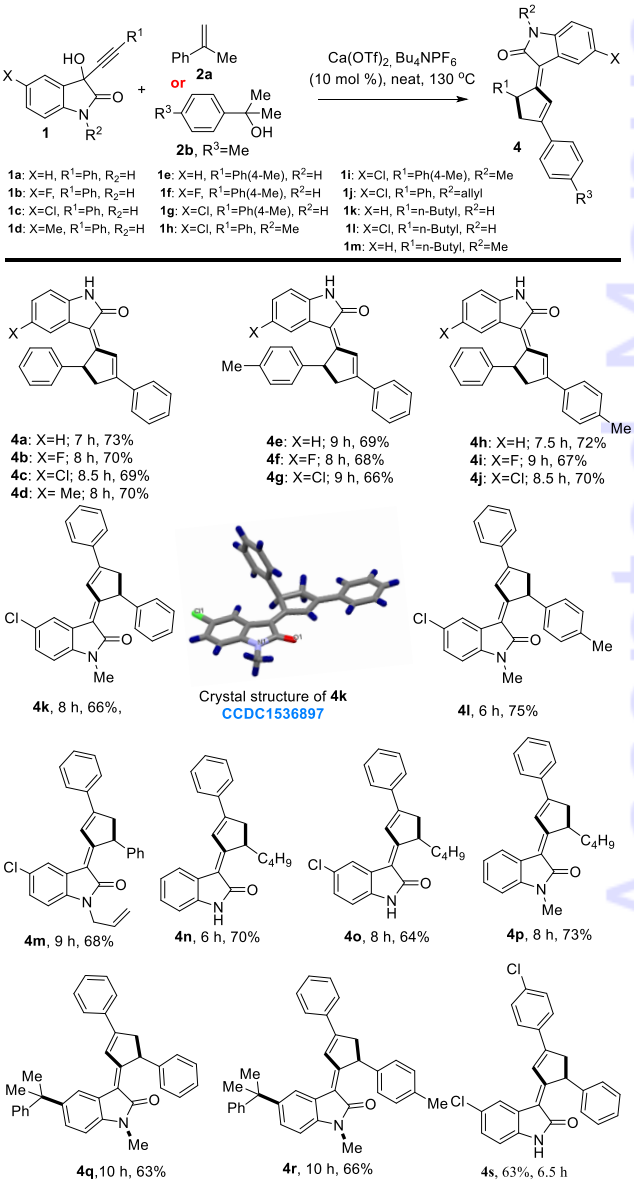
10.1002/adsc.201700569

group the yield of **3h** (1.5 h, 87%) is slightly higher than that of **3g** (2.5 h, 81%), Table 1.

Encouraged by this result, we decided to check the scope of the Ca(II) catalyzed tandem 1,5-enyne formation and its cycloisomerization to synthesize structurally diversified cyclopentenylidenes as showed in the Table 2. Thus, alkynol derivatives **1b** (5-fluoro), **1c** (5-chloro) and **1d** (5-methyl) were heated independently with styrene **2a** under standard conditions to furnish the respective cyclopentenylidenes **4b**, **4c** and **4d** in good yields. 3-hydroxy-3-(p-tolylethynyl)indolin-2-one derivatives **1e**, **1f** and **1g** also furnished respective cp-derivatives **4e**, **4f** and **4g** in good yields as shown in the Table 2. Interestingly, when α-methyl styrene **2a** was replaced with 2-(p-tolyl)propan-2-ol (**2b**) and treated with alkynol (**1**) the reaction proceeded with the same ease and yielded the respective products **4h**, **4i** and **4j**. Here the tertiary alcohol (**2b**) has undergone a calcium (II) catalyzed E_1 elimination to furnish the styryl derivative, which further took part in the dehydrative cross coupling. N-alkyl derivatives of **1**, such as **1h**, **1i** and **1j** reacted with **2a** to furnish **4k**, **4l** and **4m** in very good yields (Table 2, second row). The scope of aliphatic alkynols (**1k**, **1l** and **1m)** was also successfully demonstrated by synthesizing the cp-derivatives **4n**, **4o** and **4p** in good yields. Interestingly, when 3-hydroxy-1-methyl-3-(phenylethynyl)indolin-2-one (**1n**) was treated with **2a** under standard conditions, we observed that after the formation of cyclopentenylidene, a Friedel-Crafts type reaction took place on the 5-position of oxindole with the excess styrene to yield **4q** in 63% after 10 h. This domino approach was further reproduced with alkynol **1o** while synthesizing **4r** in 66% yield. α-methylstyrene bearing electron acceptor group such as 1-chloro-4-(prop-1-en-2-yl)benzene gave 63% of **4s** in 6.5 h.

It was observed that the cycloisomerization of 1,5-enyne (**3**) proceeded through a spirocyclic hexadiene intermediate (**3ab**) to furnish cyclopentenylidene **4**. Since **3ab** is thermally unstable it has undergone a rearrangement to furnish the cyclopentenylidene **4**. Taking the advantage of thermal instability of **3ab**, we anticipated that the spirocyclic compound **3ab** can also undergo a thermal-oxidative- ring rearrangement to furnish phenanthridinone **5.** Phenanthridinone is a key structural motif present in many of the biologically active natural alkaloids and pharmaceuticals with a broad range of activities such as antitumor, antivirus and as DNA topoisomerase inhibitor.[11] Owing to these reasons, the synthesis of this motif has been intensively pursued during the past decade.[12] In order to implement our idea, **1a** and **2a** were heated at 110 °C with 10 mol% of $Ca(OTf)_2/Bu_4NPF_6$ for 2 h and then chloranil was added to the reaction mixture at 150 °C.[13] After continuing the reaction for 4.5 h, we were glad to isolate the 7,9-diphenylphenanthridin-6(5H)-one **5a** in 72% yield (Table 3).[14] Encouraged by this results, we also demonstrated the substrate scope of this strategy (Table 3). The substitutions on the isatin aryl ring (**1a**) with 5-chloro, 5-flouro, 5-methyl, 7-fluoro were equally tolerated by this protocol and yielded the respective phenanthridinones **5b**, **5c**, **5d** and **5e** in good yields. N-methyl isatin derivative **1n** gave 74% of **5f**. Another styryl derivative 1-methyl-4-(prop-1-en-2-yl)benzene also showed good reactivity in the one-pot, tandem dehydrative cross-coupling/cycloisomerization/thermal-oxidative ring rearrangement to furnish the phenanthridinones **5g**, **5h** and **5i** in moderate to good yields. Thus this protocol would be the superior to all the existing methods for the synthesis of phenanthridinones due to its simple operation conditions, easily available starting materials, one-pot and tandem process with atom and step economy.

Table 2. One-pot 1,5-enyne synthesis and cycloisomerization to furnish 3-(cyclopent-2-en-1-ylidene)indolin-2-ones *via* a Ca(II) catalysis.[a]

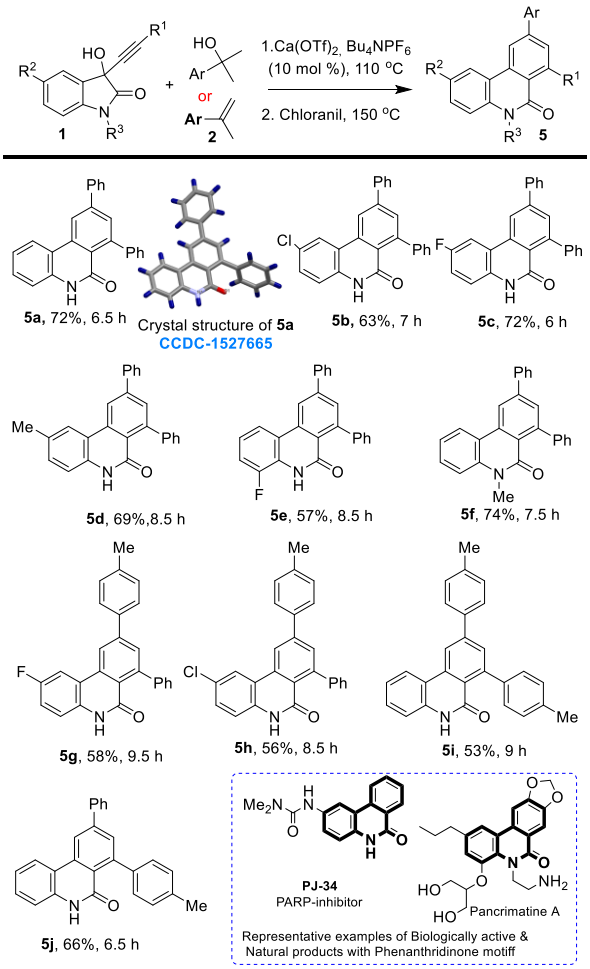


[a]General conditions:1 equiv. of **1a**, 2.2 equiv. of **2a**, 10 mol% of $Ca(OTf)_2$, 10 mol% of Bu_4NPF_6. Isolated yields.

10.1002/adsc.201700569

Encouraged by the successful utilization of spirocyclic-hexadiene **3ab** for the synthesis of phenanthridinone (Table 3), strategically we planned to trap this diene intermediate **3ab** into a thermal [4+2] cycloaddition reaction (Diels-Alder)[15] and to study the stereoselectivity of the adduct. In order to execute the concept, **1a** and **2a** were heated at 110 °C with 10 mol% of $Ca(OTf)_2$/Bu_4NPF_6 for 2 h (formation of diene **3ab** was observed by TLC) then maleic anhydride (enophile) was added to the reaction and then the temperature was raised to 150 °C. To our delight and as proposed we were able to isolate the exo adduct **6a** as the single diastereomer in 67%.[16] The scope of substituted isatin derivatives (**1**) was demonstrated in this cascade reaction by using 5-chloro, N-methyl, N-allyl, N-benzyl and 5-chloro-N-benzyl derivatives to furnish the single exo isomers **6b**, **6c**, **6d**, **6e** and **6f** in good yields as described in the Table 4. The scope of styryl derivatives has also been demonstrated by synthesizing the Diels-Alder adducts **6g**, **6h**, **6i**, **6j**, **6k** and **6l** in moderate to good yields (Table 4).

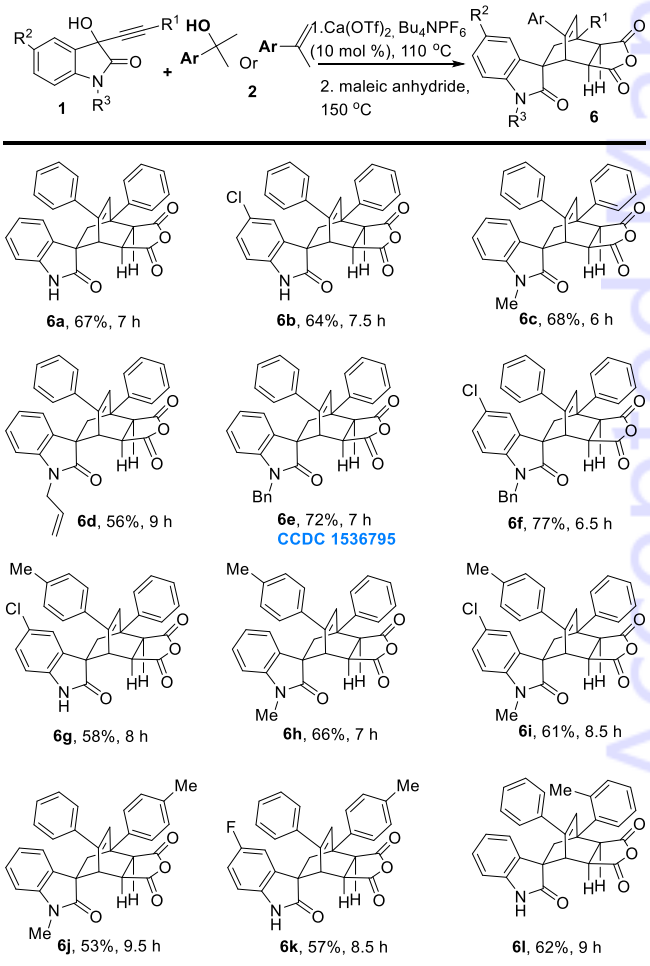
Table 3. Synthesis of phenanthridinones through a cascade 1,5-enyne formation/ cycloisomerization/ oxidative ring-rearrangement.[a]



[a]General conditions:1 equiv. of **1a,** 2.2 equiv. of **2a,** 10 mol% of $Ca(OTf)_2$, 10 mol% of Bu_4NPF_6. After 2 h at 110 °C chloranil (2.2 equiv) was added and the temperature raised to 150 °C. Isolated yields.

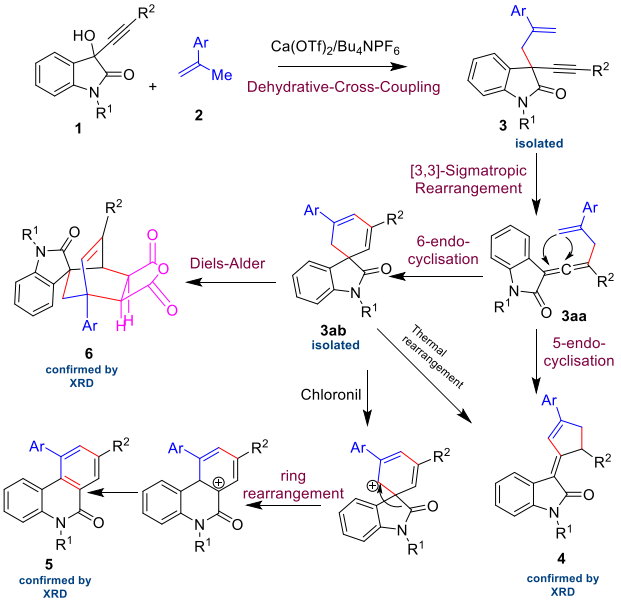
The detailed mechanism for this tandem process has been delineated in the Scheme 3. Initially, a calcium(II) mediated dehydrative cross coupling reaction takes place between propargyl alcohol **1** and α-methylstyrene **2** to furnish the 1,5-enyne **3**. Then the enyne **3** would undergo a thermal [3,3]-sigmatropic rearrangement at 130 °C and furnish the allene intermediate **3aa**,[17] which could immediately cycloisomerizes to the trisubstituted cyclopentenylidene **4**.[18] **3aa** can also undergo exocyclization to furnish the spirohexadiene **3ab** which can further rearrange to a stable cyclopentenylidene **4**. In presence of enophile such as maleic anhydride, spirocyclohexadiene **3ab** can be trapped into a [4+2] cycloaddition (Diels-Alder) reaction to furnish the DA-adduct **6**. When treated with oxidative agents such as chloranil, **3ab** underwent oxidative ring rearrangement (benzannulation) to furnish the phenanthridinone **5.**

Table 4. Ca(II)-catalyzed one-pot, regioselective dehydrative cross-coupling/cycloisomerization/Diels-Alder cascade.[a]



[a]General conditions:1 equiv. of **1a,** 2.2 equiv. of **2a,** 10 mol% of $Ca(OTf)_2$, 10 mol% of Bu_4NPF_6. After 2 h at 110 °C maleic anhydride (2.2 equiv) was added and temperature raised to 150 °C. Isolated yields. [b]structure confirmed by X-ray analysis.

In summary, we have developed a Ca(II)-catalyzed highly regioselective, atom & step economical, one-pot cascade strategy for the oxindole-derived 1,5-enyne synthesis and their cycloisomerization reactions to furnish trisubstituted cyclopentenylidenes, benzannulation to yield phenanthridinones and Diels-Alder cycloadditions to furnish the stereoselective 3-spirocyclic indolin-2-one derivatives. For the first time, we have expanded the scope of oxindole-derived 1,5-enyne isomerization to furnish new chemical entities which may be useful in organic, medicinal and materials chemistry.



Scheme 3. Plausible mechanism for the Ca(II) catalyzed synthesis of 1,5-enynes and their cycloisomerization

Experimental Section

General procedure for the synthesis of 3-(cyclopentenylidene)indolin-2-ones (4):

A mixture of propargyl alcohol **1a** (100 mg, 0.4 mmol), α-methyl styrene **2** (104.2 mg, 0.88 mmol) along with $Ca(OTf)_2$ (13.6 mg, 0.04 mmol), Bu_4NPF_6 (15.6 mg, 0.04 mmol) were heated in 10 mL round bottom flask at 130 °C for 8-10 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the resulting mixture was diluted with water and extracted with ethyl acetate (thrice). Combined organic layers were washed with brine solution and dried over anhydrous Na_2SO_4 and the solvent was evaporated to get the crude product. The crude product was purified by silica gel column chromatography to furnish the pure product **4a** in 73% (101 mg) yield.

General procedure for the synthesis of phenanthridinones (5):

A mixture of propargyl alcohol **1a** (100 mg, 0.4 mmol), α-methyl styrene **2a** (104.2 mg, 0.88 mmol) along with $Ca(OTf)_2$ (13.6 mg, 0.04 mmol), Bu_4NPF_6 (15.6 mg, 0.04 mmol) were heated in 10 ml round bottom flask at 110 °C for 2 h, then chloranil (243.9 mg, 1 mmol) was added and the reaction was further heated at 150 °C for 4-5 h. The progress of reaction was monitored by TLC. After completion of the reaction, the resulting mixture was diluted with water and extracted with ethyl acetate (thrice). Combined organic layers were washed with brine solution and dried over anhydrous Na_2SO_4 and the solvent was evaporated to get the crude product. The crude product was purified by silica gel column chromatography to furnish the pure product **5a** in 72% (100.3 mg) yield.

General procedure for the synthesis of Diels-Alder adduct (6):

A mixture of propargyl alcohol **1a** (100 mg, 0.4 mmol), α-methyl styrene **2a** (104.2 mg, 0.88 mmol) along with $Ca(OTf)_2$ (13.6 mg, 0.04 mmol), Bu_4NPF_6 (15.6 mg, 0.04 mmol) was heated at the 110 °C for 2 h then maleic anhydride (98.0 mg, 1 mmol) added further heated in 10 ml round bottom flask at 150 °C for 4-5 h. The progress of reaction was monitored by TLC. After completion of the reaction, the resulting mixture was diluted with water and extracted with ethyl acetate (thrice). Combined organic layers were washed with brine solution and dried over anhydrous Na_2SO_4 and the solvent was evaporated to get the crude product. The crude product was purified by silica gel column chromatography to furnish the pure product **6a** in 67% (120.2 mg) yield.

Supporting Information

Detailed descriptions of experimental procedures and their spectroscopic data as well as the crystal structures are presented in the Supporting Information. CCDC 1536897 (**4k**), 1527665 (**5a**) and CCDC 1536795 (**6e**) contain the supplementary 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.

Acknowledgements

This work is partially supported by SERB (SB/FT/CS-149/2012) and CSIR (02/200/14/EMR-II) India. AP and RD thank Central University of Rajasthan for the fellowships. Authors are grateful to Dr. Gopal K and Mr. Sudhir M for the technical support in solving the crystal structures.

References

[1] For reviews, see: a) B. M. Trost, F. D. Toste, A. B. Pinkerton, *Chem. Rev.* **2001**, *101*, 2067; b) B. M. Trost, M. J. Krische, *Synlett* **1998**, 1; c) Guy C. Lloyd-Jones, *Org. Biomol. Chem.* **2003**, *1*, 215; d) C. Aubert, O. Buisine, M. Malacria, *Chem. Rev.* **2002**, *102*, 813; e) B. M. Trost, *Chem. Eur. J.* **1998**, *4*, 2405; f) I. Ojima, M.

Tzamarioudaki, Z. Y. Li, R. J. Donovan, *Chem. Rev.* **1996**, *96*, 635; g) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180; h) Eloísa Jiménez-Núñez, et al. *Chem. Commun*. **2007**, *333; i)* A. S. K. Hashmi, *Angew. Chem. Int. Ed*. **2006**, *45*, 7896; j) A. Furstner, P. Hannen, *Chem. Eur. J.* **2006**, *12*, 3006; k) C. Fehr, J. Galindo, *Angew. Chem. Int. Ed.* **2006**, *45*, 2901.

[2] a) A. M. Echavarren, C. Nevado, *Chem. Soc. Rev*. **2004**, *33*, 431; b) L. Aorbe, G. Domnguez, J. Prez-Castells, *Chem. Eur. J*. **2004**, *10*, 4938; c) C. Bruneau, *Angew. Chem.* **2005**, *117*, 2380; d) L. Zhang, J. Sun, S. A. Kozmin, *Adv. Synth. Catal*. **2006**, *348*, 2271; e) A. Frustner, P. W. Davies, *Angew. Chem.* **2007**, 119, 3478; f) E. Jimnez-Nfflez, A. M. Echavarren, *Chem. Rev*. **2008**, *108*, 3326; g) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev*. **2008**, *108*, 3351; h) *V. Michelet, P.Y. Toullec, J.-P. GenÞt, Angew. Chem.* **2008**, *120*, 4338; i) V. Michelet, P. Y. Toullec, J. P. Genet, *Angew. Chem. Int. Ed*. **2008**, *47*, 4268; j) L. Zhang, J. Sun, S. A. Kozmin, *Adv. Synth. Catal*. **2006**, *348*, 2271; k) G. C. Lloyd-Jones, *Org. Biomol. Chem*. **2003**, *1*, 215; l) E. Soriano and J. Marco-Contelles, *Acc. Chem. Res.* **2009**, *42*, 1026; m) I. J. S. Fairlamb, *Angew. Chem. Int. Ed.* **2004**, *43*, 1048; n) B. M. Trost, *Acc. Chem. Res.* **1990**, *23*, 34; o) S. T. Diver and A. J. Giessert, *Chem. Rev.* **2004**, *104*, 1317; p) I. Ojima, M. Tzamarioudaki, Z. Li, R. J. Donovan, *Chem. Rev*. **1996**, *96*, 635; q) V. Michelet, P. Y. Toullec, J.-P. Genet, *Angew. Chem. Int. Ed*. **2008**, *47*, 4268; r) A. R. Chianese, S. J. Lee, M. R. Gagne, *Angew. Chem. Int. Ed.* **2007**, *46*, 4042; s) S. I. Lee, N. Chatani, *Chem. Commun.* **2009**, 371; t) C. Aubert, L. Fensterbank, P. Garcia, M. Malacria, A. Simonneau, *Chem. Rev*. **2011**, *111*, 1954; u) P. Belmont, E. Parker, *Eur. J. Org. Chem.* **2009**, 6075.

[3]a) V. Mamane, T. Gress, H. Krause, A. F. Mrstner, *J. Am. Chem. Soc.* **2004**, *126*, 8654; b) Y. Harrak, C. Blaszykowski, M. Bernard, K. Cariou, E. Mainetti, V. Mouries, A. L. Dhimane, L. Fensterbank, M. Malacria, *J. Am. Chem. Soc.* **2004**, *126*, 8656; c) Y. Nishibayashi, M. Yoshikawa, Y. Inada, M. Hidai, S. Uemura, *J. Am. Chem. Soc.* **2004**, *126*, 16066; d) N. Marion, P. Fremont, G. Lemiere, E. D. Stevens, L. Fensterbank, M. Malacria, S. P. Nolan, *Chem. Commun.* **2006**, 2048; e) M. R. Luzung, J. P. Markham, F. D. Toste, *J. Am. Chem. Soc.* **2004**, *126*, 10858; f) L. Zhang, S. A. Kozmin, *J. Am. Chem. Soc*. **2005**, *127*, 6962.

[4] C. Blaszykowski, Y. Harrak, M. Goncalves, J. Cloarec, A. Dhimane, L. Fensterbank, M. Malacria, *Org. Lett*. **2004**, *6*, 3771.

[5] a) S. Wang, L. Zhang, *J. Am. Chem. Soc.* **2006**, *128*, 14274; b) J. Sun, M. P. Conley, L. Zhang, S. A. Kozmin, *J. Am. Chem. Soc.* **2006**, *128*, 9705; c) L. Zhang, S. A. Kozmin, *J. Am. Chem. Soc*. **2004**, *126*, 11806; d) K. Fukamizu, Y. Miyake, Y. Nishibayashi, *Angew. Chem. Int. Ed.* **2009**, *48*, 2534; e) J. Blum, H. Beer-Krafts, Y. Badrieh, *J. Org. Chem.* **1995**, *60*, 5567; f) A. Frstner, H. Szillat, F. Stelzer, *J. Am. Chem. Soc.* **2000**, *122*, 6785; g) V. Mamane, T. Gress, H. Krause, A. Frstner, *J. Am. Chem. Soc.* **2004**, *126*, 8654.

[6] F. Gagosz, *Org. Lett.* **2005**, *7*, 4129.

[7] Cycloisomerization reactions are inherently atom economic due to the intramolecular bond formation proceeding with quantitative atom economy. See for atom economy: See: a) B. M. Trost, *Acc. Chem. Res.* **2002**, *35*, 695; b) B. M. Trost, *Angew. Chem. Int. Ed.* **1995**, *34*, 259; c) B. M. Trost, *Science*, **1991**, *254*, 1471.

[8] a) S. A. Martin, G. Mehta, H. Hopf, A. Krief, *Nature Chem.* **2015**, *7*, 941; b) S. A. Martin, G. Mehta, H. Hopf, A. Krief, *Nature Chem.* **2016**, *8*, 393.

[9] a) S. Yaragorla, A. Pareek, R. Dada *Tetrahedron Lett.* **2016**, *57*, 5841; b) S. Yaragorla, P. L. Saini, G. Singh, *Tetrahedron Lett*. **2015**, *56*, 1649; c) S. Yaragorla, A. Pareek, R. Dada, *Tetrahedron Lett*. **2015**, *56*, 4770.

[10] a) S. Yaragorla, R. Dada, G. Singh, A. Pareek, M. Rana, A. K. Sharma, *Chemistry Select*, **2016**, *1*, 6902; b) A. Pareek, R. Dada, M. Rana, A. K. Sharma, S. Yaragorla, *RSC Adv*. **2016**, *6*, 89732; c) S. Yaragorla, R. Dada, A. Pareek, G. Singh, *RSC Adv*. **2016**, *6*, 28865.

[11] a) T. Harayama, H. Akamatsu, K, Okamura, T. Miyagoe, T. Akiyama, H. Abe, Y. Takeuchi, *J. Chem. Soc. Perkin Trans. 1* **2001**, 523; b) T. Harayama, T. Akiyama, Y. Nakano, K. Shibaike, H. Akamatsu, A. Hori, H. Abe, Y. Takeuchi, *Synthesis* **2002**, 237; c) D. Bellocchi, A. Macchiarulo, G. Costantino, R. Pellicciari, *Bioorg. Med. Chem.* **2005**, *13*, 1151; d) J. Ishida, K. Hattori, H. Yamamoto, A. Iwashita, K. Mihara, N. Matsuoka, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 4221.

[12] a) T. Furuta, Y. Kitamura, A. Hashimoto, S. Fujii, K. Tanaka, T. Kan, *Org. Lett.* **2007**, *9*, 183; b) T. N. Le, S. G. Gang, W.-J. Cho, *J. Org. Chem*. **2004**, *69*, 2768; c) B. O. Ashburn, R. G. Carter, L. N. Zakharov, *J. Org. Chem.* **2008**, *73*, 7305; d) H. Gilman, J. Eisch, *J. Am. Chem. Soc*. **1957**, *79*, 5479.

[13] a) B. M. Barclay, N. Campbell. *J. Chem. Soc.* **1945**, 530; b) A. I. Kosak, R. J. F. Palchak, W. A. Steele, C. M. Selwitz. *J. Am.Chem. Soc.* **1954**, *76*, 4450; c) W. E. Noland, S. R. Wann. *J. Org. Chem.* **1979**, *44*, 4402; d) R. B. Carlin, M. S. Moores, *J. Am.Chem. Soc.* **1962**, *84*, 4107; e) B. D. Tilak, H. S. Desai, S. S. Gupta. *Tetrahedron Lett.* **1964**, *5*, 1609.

[14] CCDC 1536897 (**4k**), 1527665 (**5a**) and 1536795 (**6e**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/data_request/cif. The single crystal X-ray structures of **4k**, **5a** and **6e** are included in the supporting information.

[15] a) B. Saroja, P. C. Srinivasan, *Synthesis* **1986**, 748; b) U. Pindur, *Heterocycles* **1988**, *27*, 1253; c) E. M. Beccalli, A. Marchesini, T. Pilati, *Tetrahedron* **1996**, *52*, 3029; d) C. Gioia, A. Hauville, L. Bernardi, F. Fini, A. Ricci, *Angew. Chem. Int. Ed*. **2008**, 47, 9236.

[16] a). W. R. Roush, B. B. Brown, *J. Org. Chem*. **1992**, *57***,** 3380; b) M. Node, K. Nishide, H. Imazato, R. Kurosaki, T. Inoue, T. Ikariya, *Chem. Commun*. **1996**, 2559; c) S. A. Kozmin, V. H. Rawal, *J. Org. Chem*. **1997,** *62*, 5252; d) M. E. Jung, N. Nishimura, N. *J. Am. Chem. Soc*. **1999**, *121*, 3529; e) F. Fotiadu, O. Pardigon, G.

10.1002/adsc.201700569

Buono, M. L. Corre, A. Hercouët, *Tetrahedron Lett*. **1999,** *40*, 867.

[17] a) B. D. Sherry, F. D. Toste, *J. Am. Chem. Soc.* **2004**, *126*, 15978; b) B. D. Sherry, L. Maus, B. N. Laforteza, F. D. Toste, *J. Am. Chem. Soc.* **2006**, *128*, 8132.

[18] Refer to the supporting information for the details on control experiments.

10.1002/adsc.201700569

COMMUNICATION

Cycloisomerization of Oxindole-derived 1,5-enynes: A Calcium(II) catalyzed one-pot, solvent-free synthesis of Phenanthridinones, 3-(cyclopentenylidene)indolin-2-ones and 3-spirocyclic indolin-2-ones

Adv. Synth. Catal. **Year**, *Volume*, Page – Page

Srinivasarao Yaragorla,*[a,b] Abhishek Pareek[a,b] and Ravikrishna Dada[a,b]