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Nitromethane as a Recursive Carbanion Source for Domino Benzoannulation with Ynones: One-pot Synthesis of Polyfunctional Naphthalenes and a Total Synthesis of Macarpine

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Abstract: A one-pot, transition-metal-free, domino Michael-S_NAr protocol of general applicability has been devised for the regioselective synthesis of polyfunctional naphthalenes employing nitromethane and *ortho*-haloaryl ynones. Utilization of nitromethane as one carbon recursive carbanion source that is subsumed into a variety of ynones to end up as aromatic nitro substituent has been demonstrated. Besides many interesting examples, the application of this domino process towards a total synthesis of polycyclic alkaloid macarpine vouch for the efficacy of this methodology. The conceptually simple approach to affect regioselective, multifunctional benzoannulation of ynones displays wide substrate scope and functional group tolerance and has been implemented with substituted nitromethanes, reacting through a 'split and subsume' process, as well as with alicyclic *o*-haloynones.

Highly functionalized naphthalenes are common, widely distributed structural motifs which are encountered in many important and diverse bioactive natural products and pharmaceuticals, (Figure 1).[1] Recently, substituted naphthalenes have also drawn traction as building blocks for electronic materials, particularly as organic field-effect transistors for a variety of applications that range from large area flexible displays, smart cards and sensors.[2] Consequently, short, versatile syntheses of substituted naphthalenes have been engaging widespread attention during the past several decades with many notable developments.[3] These include various functionalizations and cross coupling maneuvers on preexisting naphthalene platform,[4]Diels Alder cycloaddition[5] or Wulff-Dötz benzannulation[6] on appropriately pre-assembled substrates, transition-metal/Lewis acid catalyzed cyclizations,[7] annulations employing arynes or ring-closing metathesis[8], rearrangements of strained rings[9] and photo-catalyzed[10] reactions among others.[11] From this vast repertoire, a selection of newer approaches, reported during the preceding decade, are captured in Scheme 1.

Although many of the existing methods for the synthesis of polyfunctional naphthalenes have their own merits and importance, there is a void in terms of methods of general applicability and broad substrate scope that can be executed using operationally simple procedure (metal free, one-pot reaction), bench-top building blocks and reagents and can generate diverse functionalities in a regioselective manner.

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Herein, we disclose a *de novo* effort via domino[12]/tandem Michael-S_NAr strategy [13] that fills the gap and provides a versatile entry to polyfunctional naphthalenes with the embedment of the desirable functional elements. We further demonstrate efficacy of classical tactics to amplify functionality on the naphthalene framework and as an application disclose a total synthesis of phenanthridine alkaloid macarpine.[1e] We have also extended the domino/tandem Michael-S_NAr strategy to access diverse benzoannulated carbocycles.

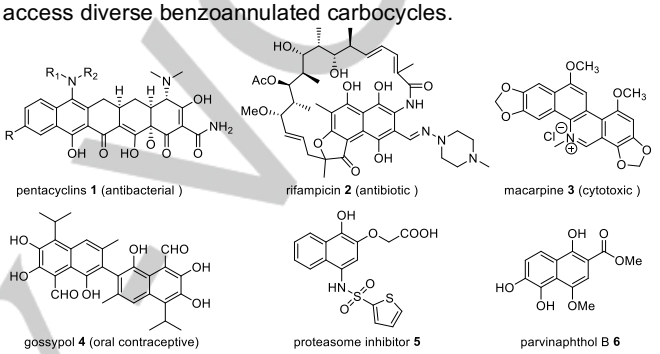
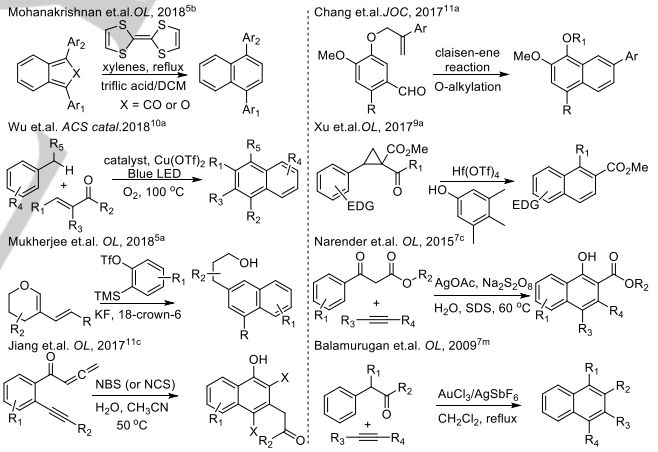
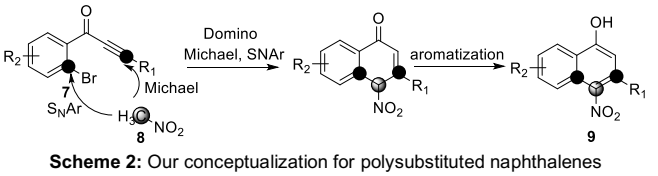


Figure 1: Representative bioactive naphthalene containing natural products



Scheme 1: Representative recent synthesis of polysubstituted naphthalenes

Conceptual foundation of our new naphthalene synthesis was based on sequential, one pot union, of two entities involving *ortho*-haloarylynone moiety **7** as a dual acceptor for tandem Michael addition and S_NAr substitution and nitromethane partner[14] **8** as one carbon recursive carbanion source, see, Scheme 2. In this process, two new C-C bonds are formed along with concomitant aromatization and nitromethane, as a dual donor, is completely subsumed to show up as aromatic nitro group in the target structure **9**. Such incorporation of nitromethane as a source of aromatic nitration, visualized here, is quite new and has the potential for wider applications.



Scheme 2: Our conceptualization for polysubstituted naphthalenes

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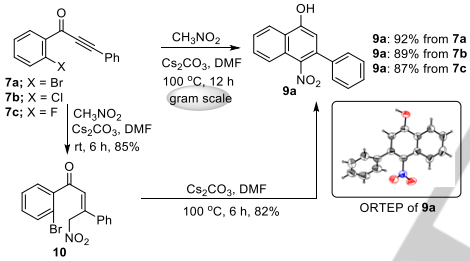
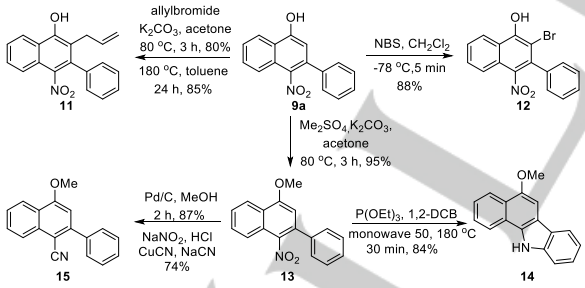
To implement the conceptual framework depicted in Scheme 2, reaction between a model *o*-bromoaryl ynone [1-(2-bromophenyl)-3-phenylprop-2-yn-1-one] **7a** and nitromethane **8** was performed. Several bases like Na_2CO_3, K_2CO_3, Cs_2CO_3 and DBU were explored but under optimized conditions {Cs_2CO_3 (2.0 equiv), DMF, 100 °C, 12 h, see Supporting Information (SI)}, the reaction afforded, as projected, 4-nitro-α-naphthol product **9a** in 92% yield (Scheme 3). It was also established that 4-nitro-α-naphthol (**9a**) formation proceeded with equal felicity employing other *o*-halogen substituted aryl ynones **7b** (X = Cl) and **7c** (X = F) to deliver naphthalene derivative **9a**. To glean validating evidence about the involvement of the proposed tandem Michael addition - S_NAr steps in the formation of **9a**, the reaction of **7a** leading to **9a** was performed at ambient temperature using same reagents and solvent. This protocol delivered the intermediate Michael addition product **10** in 85% yield and its further exposure to Cs_2CO_3 (1.0 equiv) at higher temperature, under optimized conditions, led to naphthalene derivative **9a**. Indeed, this 4-nitro-3-phenyl-1 naphthol **9a** can be readily prepared on gram scale, enabling further useful explorations, particularly amplification and tuning of functionality employing classical manipulations around it, as displayed in Scheme 4. This includes reductive insertion of the nitro group in the methyl ether **13** into the pendant aryl ring *via* Cadogan cyclisation[15] to furnish benzocarbazole **14**.

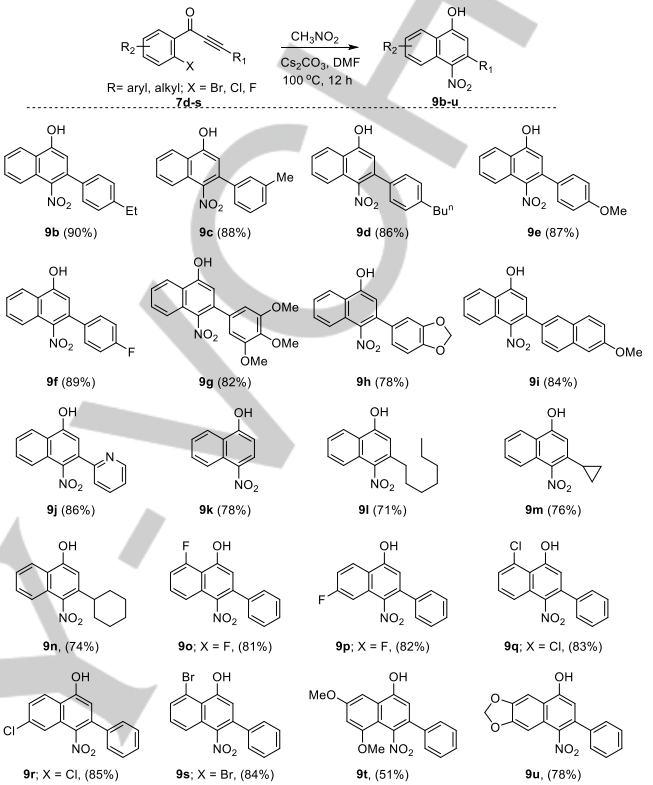


Scheme 3: Synthesis of polysubstituted naphthols

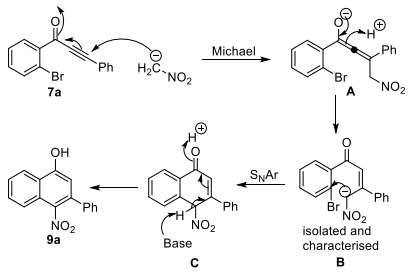


Scheme 4: Selected transformations of **9a**

At this stage, it was important to demonstrate the generality and substrate scope of this domino Michael-S_NAr reaction. Towards this end, we have explored the substrate scope employing *o*-bromoaryl ynones (**7d-p**) having diverse substitutions (aryl, pyridyl, naphthyl, alkyl, hydrogen) attached to triple bond leading to the formation of functionalized naphthalenes (**9b-n**) respectively (Scheme 5). To amplify functional group density and diversity of substitution pattern on the naphthalenes, variously substituted *o*-haloaryl ynones (**7q-w**) were engaged with nitromethane under the standard conditions to furnish the corresponding polyfunctional naphthalenes **9o-u**. During these studies, it was observed, not quite unexpectedly, that the nitromethane insertion to furnish highly substituted naphthalenes **9t** and **9u**, respectively, was less efficient with electron rich ynones **7v** and **7w** (Scheme 5).



Scheme 5: Reaction of nitromethane with various substituted *o*-haloaryl ynones

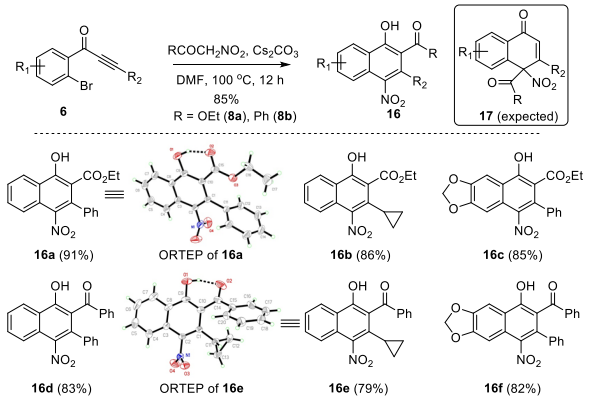


Scheme 6: Possible reaction mechanism

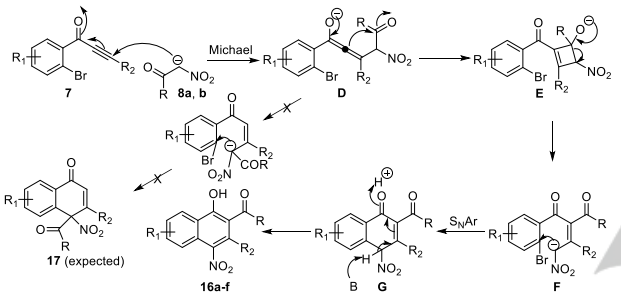
A plausible reaction mechanism for the new domino process is indicated in Scheme 6. An initial Michael addition of nitromethane anion onto ynone **7a** leads to intermediate **A** which tautomerises to enone **B** (isolated and characterized). Reiterative carbanion generated from **B** displaces the aromatic bromide in a S_NAr reaction to deliver intermediate **C**, which aromatizes to substituted naphthalene **9a**.

To further leverage the advantageous outcome with the recursive carbanion from nitromethane for naphthalene synthesis, it was of interest to deploy its activated derivatives like ethyl nitroacetate **8a** and benzoyl nitromethane **8b** as reaction partners with *o*-bromoaryl ynones **7a**, **p**, **w**. Under the optimized conditions, the reaction occurred smoothly, but took an unexpected deviant course to deliver highly substituted naphthalenes **16a-f** instead of the expected products like **17**. This stratagem has paved a way for one-pot benzoannulation

with four different functional groups (hydroxy, ester/benzoate, aryl/alkyl and nitro) on four consecutive sp^2-carbons to deliver poly-substituted naphthalenes, (scheme 7).

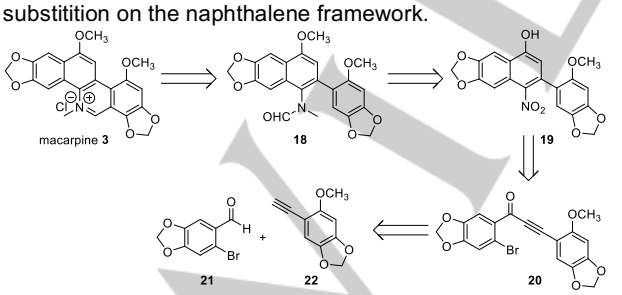


Scheme 7: Synthesis of highly substituted naphthalenes



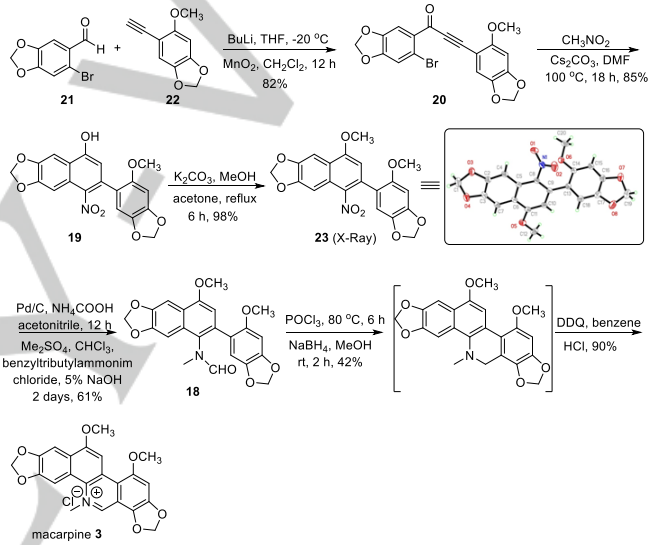
Scheme 8: Possible reaction mechanism

A possible mechanism for the formation of **16a-f** involves Michael addition of anion derived from activated nitromethane (**8a**, **b**) to ynone **7** to afford intermediate **D**, which readily collapses to strained cyclobutene[13d-f] intermediate **E** before C-C bond cleavage to deliver enone **F**. The recursive carbanion from Intermediate **F** undergoes S_NAr reaction to bicyclic intermediate **G** enroute aromatization to tetrasubstituted naphthalene **16a-f**, Scheme 8. Overall, in this deviant albeit interesting reaction course, directed by a bystander carbonyl group (**D**→**E**) the two functionalities of activated ethyl nitroacetate **8a** and benzoyl nitromethane **8b** are 'split', subsumed and show up as 1,3-substitition on the naphthalene framework.



Scheme9: Retrosynthetic analysis of macarpine**3**

The ease and efficacy of this new naphthalene synthesis opened the avenues for diverse natural product synthesis embodying this motif. As a demonstrator in this quest, we targeted bioactive, polyoxygenated benzo[c]phenanthridine alkaloid natural product macarpine **3**, embodying a naphthalene moiety as a total synthesis objective. This tetracyclic alkaloid was isolated from *Macleaya cordata* and other papaveraceous plants and displayed cytotoxic activity against HeLa S3 tumor cell lines with an IC_{50} of 0.192 mg/mL.[1e] Our synthetic approach to macarpine **3** was delineated through a retrosynthetic analysis in which 4-nitronaphthalene derivative **19** was to serve as a pivotal intermediate, Scheme 9. Accordingly, macarpine **3** could be synthesized from the known *N*-methylated aldehyde **18** via cyclization and dehydration reaction sequence. Aldehyde **18** inturn could be generated from the pivotal naphthalene derivative **19** via nitro group reduction and to amine and *N*-substitution reactions. The key functionalized naphthalene **19** was to be accessed via the domino Michael-S_NAr reaction of nitromethane with suitably crafted ynone precursor **20**, which could be assembled from aldehyde **21** and alkyne **22**.

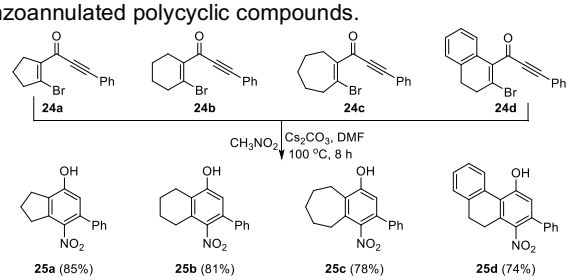


Scheme 10: Total synthesis of macarpine **3**

The synthesis was initiated by synthesizing the suitable ynone **20** through the addition of alkyne **22** to *o*-bromo-aldehyde **21** further oxidation to ynone **20**. The key Michael-S_NAr benzoannulation reaction between ynone **20** and nitromethane was performed under optimized conditions to furnish 4-nitro-α-naphthol **19** in good yield and was further *O*-methylated to **23**. The nitro functionality in **23** was directly transformed to *N*-CHO in one-pot protocol[16] using Pd/C and NH_4COOH and was further *N*-methylated to provide the known compound **18**. By following the precedented steps,[1e] **18** was elaborated to the natural product macarpine **3** and its spectral data was in complete agreement with those reported in the literature, (Scheme10).

Is our benzoannulation protocol an exclusive preserve of *o*-haloaryl ynone substrates or has wider implications? To probe this question, we have investigated β-bromoalkenylynone[13c]-nitromethane domino reaction, an alicyclic equivalent of our *o*-bromoaryl ynone based naphthalene synthesis. Four different carbocyclic ynones (**24a-d**) were readily assembled and their banzoannulation with nitromethane under optimized conditions proceeded flawlessly and efficiently to deliver functionalized indane **25a**, tetralin **25b**, benzosuberane **25c** and 9,10-

dihydrophenanthrene **25d**, respectively, Scheme 11. Clearly insertion of recursive carbanion into suitably crafted ynones is a general reaction and may have wider ramifications in the synthesis of natural products and accessing diverse benzoannulated polycyclic compounds.



Scheme 11: Synthesis of various benzoannulated carbocycles

In summary, we have successfully harnessed the utility of nitromethane as a recursive carbanion source/nitrating agent to stitch *o*-haloaryl ynones through a new domino process to regioselectively furnish highly substituted nitronaphthalenes. This one pot methodology has been applied to achieve a total synthesis of benzo[c]phenanthridine alkaloid macarpine and further extended to substituted nitromethanes which react through a 'split and subsume' process to amplify functional diversity pattern and to alicyclic *o*-haloynones to deliver various benzocarbocylic scaffolds. We believe that the methodology unveiled here will be a convenient and efficacious enabler for accessing a range of polycyclic aromatics for bio- and materials applications.

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Keywords: nitromethane• domino reaction•S_NAr reaction• substituted naphthalenes• macarpine• benzocarbazoles•

†Both the authors contributed equally

[1] a) N. Abdissa, F. Pan, A. Gruhonjic, J. Grafenstein, P. A. Fitzpatrick, G. Landberg, K. Rissanen, A. Yenesew, M. Erdelyi, *J. Nat. Prod.* **2016**, *79*, 2181–2187; b) Y. Ge, A. Kazi, F. Marsilio, Y. Luo, S. Jain, W. Brooks, K. G. Daniel, W. C. Guida, S. M. Sebti, H.R. Lawrence, *J. Med. Chem.* **2012**, *55*, 1978–1998; c) C. Sun, D. K. Hunt, R. B. Clark, D. Lofland, W.J. O'Brien, L. Plamondon, X.-Y. Xiao, *J. Med. Chem.* **2011**, *54*, 3704–3731; d) C. Sun, Q. Wang, J. D. Brubaker, P. M. Wright, C. D. Lerner, K. Noson, M. Charest, D. R. Siegel, Y. –M. Wang, A. G. Myers. *J. Am. Chem. Soc.* **2008**, *130*, 17913–17927; d) E. M. Coutinho, *Contraception* **2002**, *65*, 259–263; e) T. Ishikawa, T. Saito, H Ishii, *Tetrahedron* **1995**, *51*, 8447–8458; f) P. Sensi, *Rev. Infect. Dis.***1983**, *5*, S402–S406; g) J. Slavik, L. Slavikova, *Coil. Czech. Chem. Commun.* **1955**, *20*, 356–361.

[2] For reviews see:a) W. Wu, Y. Liu, D. Zhu, *Chem. Soc. Rev.* **2010**, 39, 1489–1502; b) M. Kertesz, C. H. Choi, S. Yang, *Chem. Rev.* **2005**, *105*, 3448–3481; c) M. D. Watson, A. Fechtenkötter, K. Müllen, *Chem. Rev.* **2001**, *101*, 1267–1300; d) A. J. Berresheim, M. Muller, K. Mullen, *Chem. Rev.* **1999**, *99*, 1747–1786.

[3] For reviews see:a) S. J. Hein, D. Lehnherr, H. Arslan, F. J. Uribe-Romo, W. R. Dichtel, *Acc. Chem. Res.* **2017**, *50*, 2776–2788; b) R. Remy, C. G.Bochet, *Chem. Rev.* **2016**, *116*, 9816–9849; c) C. B. de Koning, A. L. Rousseau, W. A. L. van Otterlo, *Tetrahedron* **2003**, *59*, 07–36; d) S. Saito, Y. Yamamoto, *Chem. Rev.* **2000**, *100*, 2901–2916; e) C. K. Bradsher, *Chem. Rev.* **1987**, *87*, 1277–1297.

[4] a) M. L. N. Rao, O. Yamozaki, S. Shimada, T. Tanaka, Y. Suzuki, M. Tanaka, *Org. Lett.* **2001**, *3*, 4103–4105; b) D. Zim, V. R. Lando, J. Dupont, A. L. Monteiro, *Org. Lett.* **2001**, *3*, 3049–3051; c) D. D. Hennings, T. Iwama, V. H. Rawel, *Org. Lett.* **1999**, *1*, 1205–1208.

[5] a) N. Hussain, K. Jana, B. Ganguly, D. Mukherjee, *Org. Lett.* **2018**, *20*, 1572–1575; b) J. Karunakaran, A. K. Mohanakrishnan, *Org. Lett.* **2018**, *20*, 966−970.

[6] a) S. Duan, D. K. Sinha-Mahapatra, J. W. Herndon, *Org. Lett.* **2008**, *10*, 1541–1544; b) K. H. Dotz, P. Tomuschat. *Chem. Soc. Rev.* **1999**, *28*, 187–198.

[7] For selected recent examples see: a) M. Xiong, H. Hu, X. Hu, Y. Liu, *Org. Lett.* **2018**, *20*, 3661–3665; b) F. Wagner, K. Harma, U. Koert, *Org. Lett.* **2015**,*17*, 5670–5673; c) G. Naresh, R. Kant, T. Narender. *Org. Lett.* **2015**, *17*, 3446–3449; d) H. Y. Kim, K. Oh, *Org. Lett.* **2014**, *16*, 5934−5936; e) S. Wang, Z. Chai, Y. Wei, X. Zhu, S. Zhou, S. Wang, *Org. Lett.* **2014**, *16*, 3592−3595; f) Y. Xia, P. Qu, Z. Liu, R. Ge, Q. Xiao, Y. Zhang, J. Wang, *Angew. Chem. Int. Ed.* **2013**, *52*, 2543–2546; g) P. Gandeepan, C. –H. Cheng, *Org. Lett.* **2013**,*15*, 2084–2087; h) D. Kang, J. Kim, S. Oh, P. H. Lee, *Org. Lett.* **2012**.*14*, 5636–5639; i) R. Liedtke, M. Harhausen, R. Frohlich, G. Kehr, G. Erker, *Org. Lett.* **2012**,*14*, 1448–1451; j) S. Naoe, Y. Suzuki, K. Hirano, Y. Inaba, S. Oishi, N. Fujii, H. Ohno, *J. Org. Chem.* **2012**, *77*, 4907–4916; k) C. C. Malakar, D. Schmidt, J. Conrad, U. Beifuss, *Org. Lett.*, **2011**,*13*, 1972-1975; l) A. R. Jagdale, J. H. Park, S. W. Youn, *J. Org. Chem.* **2011**, *76*, 7204–7215.

[8] a) W. –M. Shu, S. Liu, J. –X. He, S. Wang, A. –X. Wu, *J. Org. Chem.* **2018**, *83*, 9156–9165; b) K. Okuma, R. Itoyama, A. Sou, N. Nagahora, K. Shioj, *Chem. Commun.* **2012**, *48*, 11145–11147; c) W. A. L. van Otterlo, E. L. Ngidi, M. Coyanis, C. B. de Koning, *Tetrahedron Lett.* **2003**, *44*, 311–313; d) K. –S. Huang, E. –C. Wang, *Tetrahedron Lett.* **2001**, *42*, 6155–6157.

[9] a) H. Ma, X. –Q. Hu, Y. –C. Luo, P. –F. Xu, *Org. Lett.* **2017**, *19*, 6666−6669; b) R. A. Novikov, A. V. Tarasova, D. A. Denisov, D. D. Borisov, V. A. Korolev, V. P. Timofeev, Y. V. Tomilov, *J. Org. Chem.* **2017**, *82*, 2724–2738; c) A. C. Glass, B. B. Morris, L. N. Zakharov, S. –Y. Liu, *Org. Lett.* **2008**, *10*, 4855–4857.

[10] a) H. Liu, L. Ma, R. Zhou, X. Chen, W. Fang, J. Wu, *ACS Catal.* **2018**, *8*, 6224–6229; b) J. –H. Ho, T. –I. Ho, R. S. H. Liu, *Org Lett.* **2001**, *3*, 409–411.

[11] a) C. –K. Chan, Y. –H. Chen, Y. –L. Tsai, M. –Y. Chang, *J. Org. Chem.* **2017**, *82*, 3317–3326; b) E. T. Akin, M. Erdogan, A. Dastan, N. Saracoglu, *Tetrahedron* **2017**, *73*, 5537–5546; c) J.-Y. Wang, P. Zhou, G. Li, W. –J. Hao, S. –J. Tu, B. Jiang, *Org. Lett.* **2017**,*19*, 6682–6685; d) N. Koppanathi, K. C. Kumara Swamy, *Org. Biomol. Chem.*, **2016**, *14*, 5079–5087; e) X. Yu, P. Zhu, M. Bao, Y. Yamamoto, A. L. Almansour, N. Arumugam, R. S. Kumar, *Asian J. Org. Chem.* **2016**, *5*, 699–704; f) S. Manojveer, R. Balamurugan, *Org. Lett.* **2014**, *16*, 1712−1715; g) D. Basavaiah, D. M. Reddy, *RSC Adv.* **2014**, *4*, 23966–23970; h) J. –G. Wang, M. Wang, J. –C. Xiang, Y. –P. Zhu, W. –J. Xue, A. –X. Wu, *Org. Lett.* **2012**, *14*, 6060-6063.

[12] L. F. Tietze, *Chem. Rev.***1996**, *96*,115–136.

[13] a) B. Alcaide, P. Almendros, C. Lazaro-Milla, P. Delgado-Martinez, *Chem. Eur. J.* **2018**, *24*, 8186–8194; b) Q. Yao, L. Kong, M. Wang, Y. Yuan, R. Sun, Y. Li, *Org. Lett.* **2018**, *20*, 1744–1747; c) R. Samineni, J. Madapa, P. Srihari, G. Mehta, *Org. Lett.* **2017**, *19*, 6152–6155; d) F. Zhang, Q. Yao, Y. Yuan, M. Xu, L. Kong, Y. Li, *Org. Biomol. Chem.*

2017, *15*, 2497–2500; e) Y. Zhou, X. Tao, Q. Yao, Y. Zhao, Y. Li, *Chem. Eur. J*. **2016**, *22*, 17936–17939; f) X. Cheng, Y. Zhou, F. Zhang, K. Zhu, Y. Liu, Y. Li, *Chem. Eur. J*. **2016**, *22*, 12655–12659.

[14] A. Y. Sukhorukov, A. A. Sukhanova, S. G. Zlotin. *Tetrahedron* **2016**, *72*, 6191–6281.

[15] a) J. I. G. Cadogan, M. Carmeron-Wood, R. K. Makie, R. J. G. Searle, *J. Chem. Soc*. **1965**, 4831–4837; b) J. I. G. Cadogan, *Organophosphorus Reagents in Organic Synthesis; Academic Press Inc*.: London, **1979**, 269.

[16] T. V. Pratap, S. Baskaran,*Tetrahedron Lett*. **2001**, *42*, 1983–1985.

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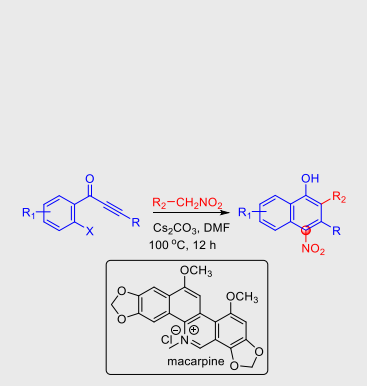
Layout 1:

COMMUNICATION

A one-pot, transition-metal-free, domino Michael-S_NAr protocol of general applicability has been devised for the regioselective synthesis of polyfunctional naphthalenes employing nitromethane and *ortho*-haloaryl ynones. Utilization of nitromethane as one carbon recursive carbanion source that is subsumed into a variety of ynones to end up as aromatic nitro substituent has been demonstrated. Besides many interesting examples, the application of this domino process towards a total synthesis of polycyclic alkaloid macarpine vouch for the efficacy of this methodology. The conceptually simple approach to affect regioselective, multifunctional benzoannulation of ynones displays wide substrate scope and functional group tolerance and has been implemented with substituted nitromethanes, reacting through a 'split and subsume' process, as well as with alicyclic *o*-haloynones.



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Nitromethane as a Recursive Carbanion Source for Domino Benzoannulation with Ynones: One-pot Synthesis of Polyfunctional Naphthalenes and a Total Synthesis of Macarpine