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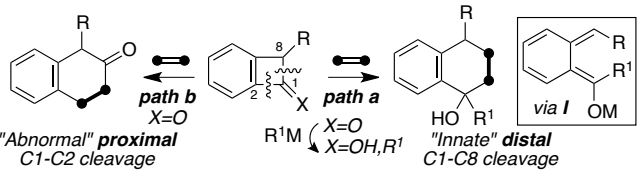
Ni-catalyzed Mild Chemo-, Regio- and Diastereoselective Bond-Formation via Proximal C–C Cleavage of Benzocyclobutenones

Francisco Juliá-Hernández,[a] Asraa Ziadi,[a] Akira Nishimura[a] and Ruben Martin*[a],[b]

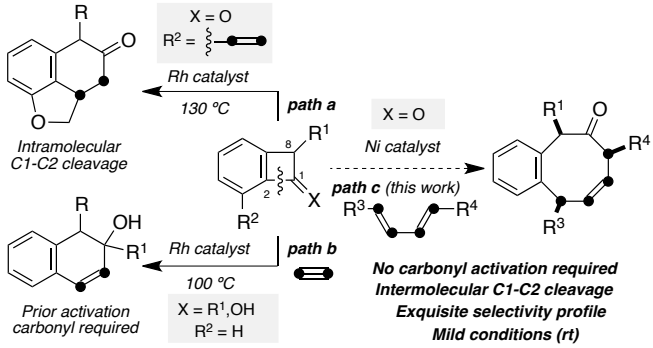
Abstract: The first catalytic intermolecular *proximal* C1-C2 cleavage of benzocyclobutenones (BCB) without prior carbonyl activation or employing noble metals has been developed. This protocol operates at room temperature and is characterized by an exquisite chemo-, regio- and diastereoselectivity profile, constituting a unique platform for preparing an array of elusive carbocyclic skeletons.

The development of metal-catalyzed C–C bond-cleavage reactions has recently received considerable attention, holding great promise to revolutionize approaches towards the elaboration of complex molecules.[1] Among these, molecules such as cyclobutanes possessing a high ring strain have shown to be particularly effective for such purposes, providing the necessary driving force for the targeted C–C bond-cleavage.[2] Although oftentimes visualized as exotic cyclobutane analogues, benzocyclobutenones (BCB) have shown to be superb reaction intermediates in a myriad of transformations,[3] even in the context of natural product synthesis.[4] At present, the reactivity of BCB remain primarily confined to their proclivity for *distal* C1–C8 cleavage via retro-4π cyclization (Scheme 1, *via* **I**).[3] Unfortunately, such scenarios commonly require an initial pre-activation of the carbonyl group (*path a*), thus constituting a drawback from a practical and step-economical standpoint.[3]



Scheme 1. Innate reactivity of BCB for C1–C8 cleavage.

Despite the advances realized, the means to alter the innate *distal* C1–C8 cleavage of BCB has been virtually unexplored (Scheme 1, *path b*), thus representing a unique opportunity for chemists to increase our ever-expanding chemical portfolio and flexibility in synthetic design. Recently, Dong[5] and Murakami[6] independently reported an elegant solution to tackle the "*abnormal*" *proximal* C1–C2 cleavage by *intramolecular* techniques (Scheme 2, *path a*)[5] or via *prior carbonyl activation* using alkyne partners (Scheme 2, *path b*).[6],[7] While no doubt a significant step-forward, these techniques unfortunately require expensive noble metals (Rh) and high temperatures, illustrating the inertness of *proximal* C1–C2 bonds.[8] Ideally, this field should include unconventional intermolecular proximal C1–C2 cleavage strategies that operate under mild conditions without employing noble metals or prior carbonyl activation platforms, thus opening up new vistas in the C–C cleavage arena. Although we anticipated that such scenario would be far from trivial due to the ability of closely related unsaturated cyclobutanones to trigger *catalytic distal C–C cleavage with exceptional ease*,[9] we were attracted to the challenge. As part of our interest in BCB[10] and C–C bond-cleavage,[11] we report herein the *first intermolecular bond-formation via proximal C1–C2 cleavage of BCB using non-precious noble Ni(0) catalysts and without prior activation of carbonyl groups* (Scheme 2, *path c*). This method is inherently modular, allowing for preparing a variety of otherwise inaccessible carbocyclic skeletons depending on the synthon utilized, including elusive benzofused eight-membered rings.[12],[13] The reaction operates at *rt*, constituting the *lowest temperature achieved for catalytic C–C cleavage events of BCB reported to date.* Importantly, our proximal C1–C2 cleavage event is distinguished by an exquisite chemo-, regio- and diastereoselectivity profile.



Scheme 2. Catalytic *proximal* C1–C2 cleavage strategies.

We started our investigations by evaluating the reaction of **1a**[14] with **2a** en route to rather elusive benzofused eight-membered rings (**3a**), molecules that display significant biological properties.[15] After systematic evaluation of all reaction parameters, we identified promising results with $Ni(COD)_2$ as precatalyst at *room temperature* (Scheme 3). While the utilization of **2a** as a two-carbon synthon might result in a formal [4+2]-cycloaddition (**3a'**), we anticipated that the nature of the ligand might exert a profound influence on both reactivity and selectivity. As shown in Scheme 3, this turned out to be the case. Among all the ligands examined, we found that **L3** was particularly suited for our purposes, giving rise to **3a** in 98% yield in 30 minutes with traces of **3a'** in the crude mixtures (entry

[a] Dr. F. Juliá-Hernández, Dr. A. Ziadi, Dr. A. Nishimura, Prof. R. Martin
Institute of Chemical Research of Catalonia (ICIQ)
Av. Països Catalans 16, 43007, Tarragona (Spain)
E-mail: rmartinromo@iciq.es
[b] Prof. R. Martin
Catalan Institution for Research and Advanced Studies (ICREA)
Passeig Lluïs Companys, 23, 08010, Barcelona (Spain)

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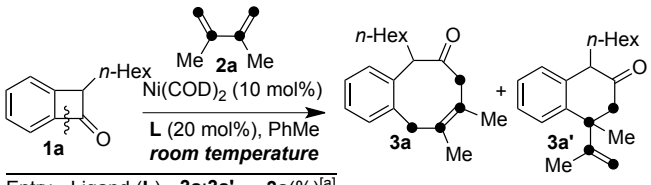
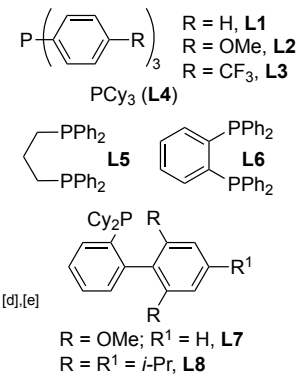
3).[16] Notably, the reaction could even be performed in the absence of solvent in identical yield (entry 4). Interestingly, the inclusion of electron-rich triarylphosphines significantly eroded the selectivity profile (entry 2).[17] Likewise, little reactivity, if any, was observed when operating with bulkier ligands or bidentate phosphines (entries 5-9), thus suggesting an intimate interplay of stereoelectronic effects on the ligand backbone with both reactivity and selectivity. As expected, control experiments revealed that all reaction parameters were critical for success (entries 10-11). In order to put these results into perspective, we found no reaction under previously reported Rh-catalyzed conditions for *proximal* C1–C2 cleavage with π-systems (entry 12).[5],[6] We believe these results show the unique features of our novel Ni-catalyzed intermolecular protocol compared to other *distal bond-cleavage events*,[9] intramolecular reactions[5] or via prior carbonyl activation (Scheme 2, *paths a* and *b*).[6]



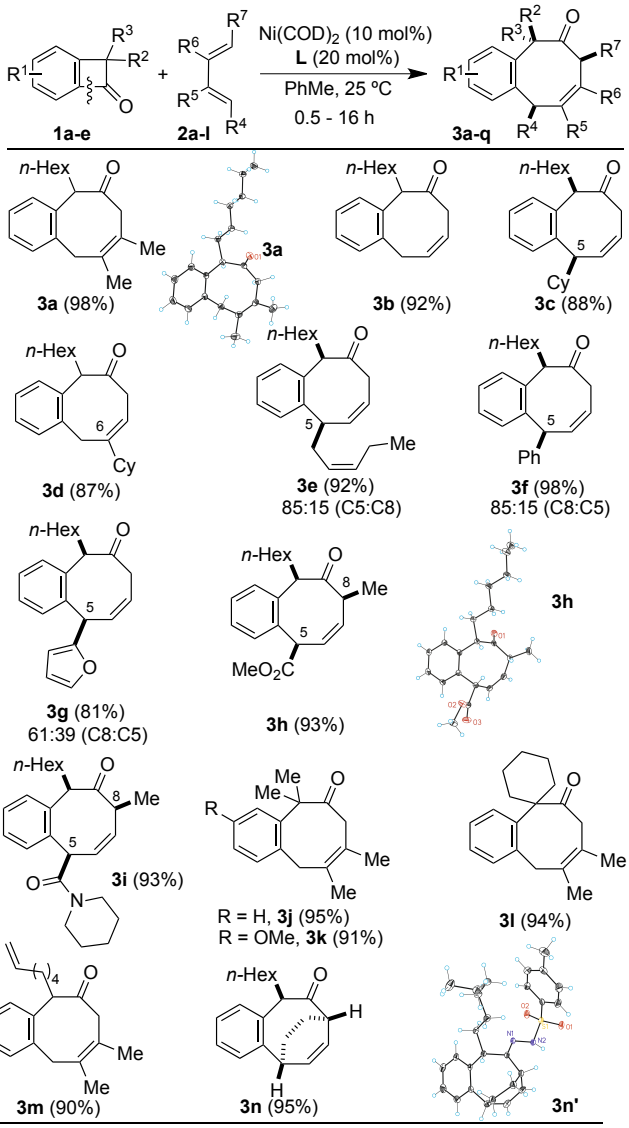
Entry	Ligand (**L**)	**3a**:**3a'**	**3a**(%)[a]
1	**L1**	87:13	71
2	**L2**	78:22	62
3	***L3***	***97:3***	***98***[b]
4	**L3**	96:4	98[b],[c]
5	**L4**	46:54	5
6	**L5**	0	0
7	**L6**	0	0
8	**L7**	0	0
9	**L8**	0	0
10	**L3**	98:2	22[d], 31[d],[e]
11	-	0	0
12	-	0	0[f]



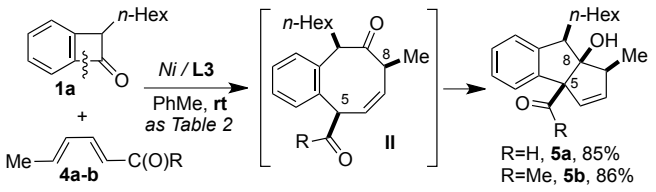
Scheme 3. Optimization of the Ni-catalyzed [4+4]-cycloaddition via *proximal* C1–C2 cleavage of **1a.** Reaction conditions: **1a** (0.35 mmol), **2a** (0.45 mmol), $Ni(COD)_2$ (10 mol%), ligand (20 mol%), toluene (2 mL), 25 ºC, 16 h. [a] GC yield using dodecane as internal standard. [b] Isolated yield, 30 min. [c] No solvent. [d] **L3** (10 mol%). [e] $Ni(COD)_2$ (5 mol%). [f] Conditions of ref. 5 and 6.

We next turned our attention to examine the scope of our Ni-catalyzed intermolecular [4+4]-cycloaddition via *proximal* C1–C2 bond-cleavage. As shown in Scheme 4, substrates with aromatic as well as aliphatic backbones on the 1,3-diene motif reacted equally well under our optimized protocol. Importantly, the reaction showed an excellent chemoselectivity profile, as heterocycles (**3g**), amides (**3i**), esters (**3h**) and alkenes (**3e, 3m**) were perfectly accommodated. Although we anticipated selectivity issues with unsymmetrical 1,3-dienes,[11] we found an unexpected exquisite regio- and diastereoselectivity profile. Specifically, a single diastereoisomer with *syn* configuration was obtained in all cases analyzed (**3c-3g**). Notably, the electronic nature of the substituents on the 1,3-diene core did not exert a profound influence on regioselectivity, invariably locating the larger residues at either C5 or C6 (**3c**-**3i**). While tentative, these results suggest that steric effects might dictate the regioselectivity pattern.[18] Such argument goes in line with the observation that **3e-3g** were obtained as mixtures of regioisomers with a slight preference for C5-selectivity.[19] Notably, the presence of a pending alkene on both BCB (**2m**) and 1,3-diene core (**2e**) did not result in a competitive intramolecular [4+2]-cycloaddition. Of particular interest was the observation that unsymmetrically disubstituted 1,3-dienes could be coupled with excellent yields and as single regio- and diastereoisomers (**3h** and **3i**), with **3h** unambiguously characterized by X-ray analysis.[19] Gratifyingly, cyclic 1,3-dienes could also participate in the ring-expansion event (**3n**); in sharp contrast with acyclic 1,3-dienes, however, we observed an opposite *anti*-diastereoselectivity pattern.[20] Although such observation was evident by extensive NMR spectroscopical studies, we univocally assigned the structure of **3n** by comparison with the corresponding tosyl hydrazone **3n'** by X-ray crystallography.[21]

Scheme 4. [4+4]-cycloaddition via Ni-catalyzed *proximal* C–C cleavage at rt.

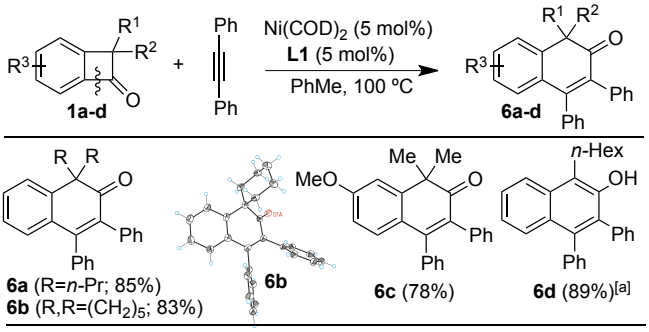


Reaction conditions: as for Scheme 3, entry 3; Isolated yields, average of at least two independent runs. In all cases analyzed, traces (<5%) of [4+2]-cycloadducts were observed in the crude mixtures.



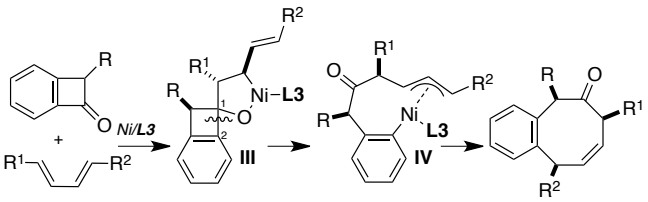
Scheme 5. Tricyclic skeletons via C1–C2 bond-cleavage of **1a**.

In light of these results, we wondered whether our Ni-catalyzed intermolecular *proximal* C1–C2 bond-cleavage of BCB could be utilized for the synthesis of other polycyclic skeletons. Specifically, we hypothesized that intramolecular transannular aldol reactions[22] from *in situ* generated benzofused eight-membered rings **II** (Scheme 5) would be within reach when utilizing 1,3-dienes substituted with carbonyl groups with relatively acidic α–hydrogens. As shown in Scheme 5, this was indeed the case, obtaining exclusively tricyclic **5a** and **5b** as single regioisomers and diastereoisomers under otherwise identical reaction conditions to that shown in Scheme 4.[23],[24]



Scheme 6. [4+2]-Cycloaddition via Ni-catalyzed *proximal* C1–C2 cleavage. Conditions: **1a-d** (0.35 mmol), diphenylacetylene (0.525 mmol), $Ni(COD)_2$ (5 mol%), PPh_3 (5 mol%), in PhMe at 100 ºC Isolated yields, average of at least two independent runs. [c] $Ni(COD)_2$ (10 mol%), PPh_3 (10 mol%).

As becomes evident from the results compiled in Scheme 6, [4+2]-cycloadducts could easily be obtained upon exposure of **1a-1d** with alkyne counterparts to a protocol based on a $Ni(COD)_2$/**L1** couple. By definition, such transformation constitutes an straightforward alternative to the elegant [4+2]-cycloaddition technique recently reported by Murakami using BCB and noble Rh catalysts, but without requiring prior activation of the carbonyl group (Scheme 2, *path b*).[6],[25] In all cases analysed, **6a-6d** were obtained in high yields as single regioisomers resulting from a *proximal* C1–C2 bond-cleavage event, as illustrated by X-ray crystallographical analysis of **6b**.[26] In all cases analysed, not even traces of the corresponding *distal* C–C cleavage were detected in the crude reaction mixtures.[9] Interestingly, spontaneous aromatization occurred with α-monosubstituted BCB, hence leading the exclusive formation of naphthol derivatives (**6d**). Overall, we believe the results in Schemes 4-6 tacitly suggest that *non-precious* noble Ni-catalysts might pave the way for preparing a priori inaccessible polycyclic structures via unconventional C–C bond-cleavage disconnections.



Scheme 7. Mechanistic rationale.

Although a full mechanistic picture should await further studies, we propose a mechanistic scenario consisting of an initial coordination of the 1,3-diene and BCB to a low valent Ni complex that precedes oxidative cyclization (**III**, Scheme 7).[27],[28] A subsequent β-carbon elimination event[29] might lead to the formation of putative π-allyl Ni(II) metallacycle (**IV**) that ultimately undergoes reductive elimination to form the corresponding benzofused eight-membered ring. An otherwise similar rationale might account for [4+2]-cycloadducts utilizing alkyne counterparts (Scheme 6).[30]

In conclusion, we have described the first intermolecular catalytic bond-formation via *proximal* C1–C2 cleavage of benzocyclobutenones without prior carbonyl activation or employing noble metals. This procedure is characterized by its exceptional mild conditions and exquisite chemo-, regio- and diastereoselectivity profile using non-precious noble Ni catalysts, allowing for the preparation of a variety of otherwise inaccessible carbocyclic skeletons in a straightforward manner. The asymmetric version and further investigations of other related transformations are currently underway in our laboratories.

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Keywords: nickel catalysis • C–C activation • Benzocyclobutenones• strain rings •

[1] a) M. Murakami; T. Matsuda, *Chem. Commun.* **2011**, *47*, 1100; b) T. Seiser; N. Cramer, *Org. Biomol. Chem.* **2009**, *7*, 2835; c) M. Rubin; M. Rubina; V. Gevorgyan, *Chem. Rev.* **2007**, *107,* 3117; d) T. Nishimura; S. Uemura *Synlett,* **2004**, 201; e) M. E. van der Boom; D. Milstein, *Chem. Rev.* **2003**, *103,* 1759, and references therein.

[2] a) T. Seiser; T. Saget; D. N. Tran, N. Cramer, *Angew. Chem. Int. Ed.* **2011**, *50*, 7740; *Angew. Chem.* **2011**, *123*, 7884-7896; b) H. Nemoto, *Chem. Pharm. Bull.* **2007**, *55*, 961, and references therein.

[3] a) A. Flores-Gaspar, R. Martin, *Synthesis* **2013**, *45*, 0563; b) A. K. Sadana, R. K. Saini, W. E. Billups, *Chem. Rev.* **2003**, *103*, 1539; c) D. Bellus, B. Ernst, *Angew. Chem. Int. Ed.* **1988**, *27*, 797; *Angew. Chem.* **1988**, *100*, 820-850, and references therein.

[4] For selected examples: a) N. Takahashi, T. Kanayama, K. Okuyama, H. Kataoka, H. Fukaya, K. Suzuki, T. Matsumoto, *Chem. Asian. J.* **2011**, *6*, 1752; b) K. Mori, K. Ohmori, K. Suzuki, *Angew. Chem. Int. Ed.* **2009**, *48*, 5633; *Angew. Chem.* **2009**, *121*, 5743-5747; c) T. Suzuki, T. Hamura, K. Suzuki, *Angew. Chem. Int. Ed.* **2008**, *47*, 2248; *Angew. Chem.* **2008**, *120*, 2280-2284.

[5] a) T. Xu, G. Dong, *Angew. Chem. Int. Ed.* **2012**, *51*, 7567; *Angew. Chem.* **2012**, *124*, 7685-7689; b) T. Xu, H. M. Ko, N. A. Savage, G. Dong, *J. Am. Chem. Soc.* **2012**, *134*, 20005; c) T. Xu, G. Dong, *Angew. Chem. Int. Ed.* **2014**, *53*, 10733; *Angew. Chem.* **2014**, *126*, 10909-10912; d) T. Xu, N. A. Savage, G. Dong, *Angew. Chem. Int. Ed.* **2014**, *53*, 1891; *Angew. Chem.* **2014**, *126*, 1922-1926.

[6] a) N. Ishida, N. Ishikawa, S. Sawano, Y. Masuda, M. Murakami, *Chem. Commun.* **2015**, *51*, 1882; b) L. Ding; N. Ishida, M. Murakami, K. Morokuma, *J. Am. Chem. Soc.* **2014**, *136*, 169; c) N. Ishida, S. Sawano, Y. Masuda, M. Murakami, *J. Am. Chem. Soc.* **2012**, *2012*, 17502.

[7] For a Pd-catalyzed C1–C2 bond-arylation approach via prior activation of the carbonyl group: A. Chtchemelinine, D. Rosa, A. Orellana, *J. Org. Chem.* **2011**, *76*, 9157.

[8] a) Y. Masuda, M. Hasegawa, M. Yamashita, K. Nozaki, N. Ishida, M. Murakami, *J. Am. Chem. Soc.* **2013**, *135*, 7142; b) M. A. Huffman, L. S. Liebeskind, W. T. Pennington, *Organometallics* **1992**, *11*, 255; c) M. A. Huffman, L. S. Liebeskind, *Organometallics* **1990**, *9*, 2194. d) L. S. Liebeskind, S. L. Baysdon, M. S. South, J. F. Blount, *J. Organomet. Chem.* **1980**, *202*, C73

[9] *For distal (not proximal)* C–C bond-cleavage of otherwise related unsaturated cyclobutanones via [4+2]-cycloaddition: a) T. Stalling, W. R. R. Harker, A.-L. Auvinet, E. J. Cornel, J. P. A. Harrity, *Chem. Eur. J.* **2015**, *21*, 2701. b) M. A. Huffman, L. S. Liebeskind, *J. Am. Chem. Soc.* **1991**, *113*, 2771. c) M. A. Huffman, L. S. Liebeskind, *J. Am. Chem. Soc.* **1990**, *112*, 8617.

[10] a) P. Alvarez-Bercedo, A. Flores-Gaspar, A. Correa, R. Martin, *J. Am. Chem. Soc.* **2010**, *132*, 466; b) A. Flores-Gaspar, A. Gutierrez-Bonet, R. Martin, *Org. Lett.* **2012**, *14*, 5234.

[11] a) A. Ziadi, R. Martin, *Org. Lett.* **2012**, *14*, 1266; b) A. Ziadi, A. Correa, R. Martin, *Chem. Commun.* **2013**, *49*, 4286; c) A. Gutierrez-Bonet, A. Flores-Gaspar, R. Martin, *J. Am. Chem. Soc.* **2013**, *135*, 12576; d) X. Wang, J. Gallardo-Donaire, R. Martin, *Angew. Chem. Int. Ed.* **2014**, *53*, 11084; *Angew. Chem.* **2014**, *126*, 11264-11267

[12] Recently, an elegant [4+4]-cycloaddition of 3-azetidinones and 1,3-dienes has been described. Unfortunately, *this procedure was conducted at high temperatures and was limited to symmetrical 3-azetidinones and symmetrical 1,3-dienes*: A. Thakur, M. E. Facer, J. Louie, *Angew. Chem. Int. Ed.* **2013**, *52*, 12161; *Angew. Chem.* **2013**, *125*, 12383-12387.

[13] For selected examples dealing with the metal-catalyzed synthesis of benzofused eight-membered rings, see: a) X.-F. Fu, Y. Xiang, Z.-X. Yu, *Chem. Eur. J.* **2015**, *21*, 4242; b) D. Crepin, J. Dawick, C. Aïssa, *Angew. Chem. Int. Ed.* **2010**, *49*, 620; *Angew. Chem.* **2010**, *122*, 630-633; c) M. Murakami, S. Kadowaki, A. Fujimoto, M. Ishibashi, T. Matsuda, *Org. Lett.* **2005**, *7*, 2059.

[14] All BCB used in this work were easily and rapidly prepared in multigram scale using previous protocols from our group (ref. 10 and A. Flores-Gaspar, R. Martin, *Org. Synth.* **2012**, *89*, 159) or via Weinreb amides: I. S. Aidhen, J. R. Ahuja, *Tetrahedron Lett.* **1992**, *33*, 5431.

[15] a) J. Chang, J. Reiner, J. Xie, *Chem. Rev.* **2005**, *105*, 4581; b) S.-Y. Li, M.-D. Wu, C.-W. Wang, Y.-H. Kuo, R.-L. Huang, K.-H. Lee, *Chem. Pharm. Bull.* **2000**, *48*, 1992.

[16] No [4+4]-cycloadducts were obtained via Ni-catalyzed homodimerization of 1,3-dienes: R. Benn, B. Bussemeier, S. Holle, P. W. Jolly, R. Mynott, I. Tkatchenko, G. Wilke, *J. Organomet. Chem.* **1985**, *279*, 63.

[17] At present we do not have a rationale explanation for such behaviour.

[18] The utilization of BCB lacking a-substituents gave statistical mixtures of [4+4]- and [4+2]-cycloadducts via C1–C2 & C1–C8 cleavage.

[19] For the assignment of the corresponding regio- and diastereoisomers, see supporting information for details

[20] CCDC 1059521 (**3a**) and CCDC 1059522 (**3h**) contain the supplementary crystallographic data for this paper and can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac/uk/data_request/cif

[21] These results are tentatively ascribed to the preferred *s-cis* conformation for cyclic 1,3-dienes.

[22] CCDC 1059523 (**3n'**) contain the supplementary crystallographic data for this paper and can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac/uk/data_request/cif

[23] For selected reviews: a) E. Marsault, A. Toró, P. Nowak, P. Deslongchamps, *Tetrahedron* **2001**, *57*, 4243; b) P. A. Clarke, A. T. Reeder, J. Winn, *Synthesis* **2009**, *5*, 691.

[24] At present, we believe that the lack of transannular aldol reaction in otherwise related **3h** and **3i** (Scheme 4) might be attributed to the higher pKa values of α-hydrogens of esters and amides as compared to those in aldehydes or ketones

[25] We cannot rule out the possibility that the transannular aldol reaction might also be a Ni-catalyzed event: N. Shida, Y. Kubota, H. Fukui, N. Asao, I. Kadota, Y. Yamamoto, *Tetrahedron Lett.* **1995**, *36*, 5023.

[26] For related [4+2]-cycloaddition techniques that do not employ as coupling partners benzocyclobutenones or unsaturated cyclobutenones, see: a) ref. 9. b) N. Ishida, T. Yuhki, M. Murakami, *Org. Lett.* **2012**, *14*, 3898; c) P. Kumar, J. Louie, *Org. Lett.* **2012**, *14*, 2026; d) K. Y. T. Ho, C. Aïssa, *Chem. Eur. J.* **2012**, *18*, 3486.

[27] CCDC 1059524 (**6b**) contain the supplementary crystallographic data for this paper and can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac/uk/data_request/cif

[28] For elegant stoichiometric studies regarding the coordination of alkenes and carbonyl compounds to low valent Ni(0) complexes, see: a) S. Ogoshi, T. Arai, M. Ohashi, H. Kurosawa, *Chem. Commun.* **2008**, 1347; b) S. Ogoshi, K. Tonomori, M. Oka, H. Kurosawa, *J. Am. Chem. Soc.* **2006**, *128*, 7077; c) S. Ogoshi, M.-A. Oka, H. Kurosawa, *J. Am. Chem. Soc.* **2004**, *126*, 11802.

[29] a) L. Liu, N. Ishida, M. Murakami, *Angew. Chem. Int. Ed.* **2012**, *51*, 2485; *Angew. Chem.* **2012**, *124*, 2535-2538; b) M. Murakami, S. Ashida, T. Matsuda, *Tetrahedron* **2006**, *62*, 7540; c) M. Murakami, S. Ashida, T. Matsuda, *J. Am. Chem. Soc.* **2005**, *127*, 6932.

[30] For reviews dealing with β-carbon elimination, see: a) T. Seiser, T. Saget, D. N. Tran, N. Cramer, *Angew. Chem. Int. Ed.* **2011**, *50*, 7740; *Angew. Chem.* **2011**, *123*, 7884-7896; b) C. Aïssa, *Synthesis* **2011**, 3389; c) M. Murakami, M. Makino, S. Ashida, T. Matsuda, *Bull. Chem. Soc. Jpn.* **2006**, *79*, 1315

[31] For reviews dealing with Ni-catalyzed reactions via simultaneous η^2-coordination of carbonyl compounds and π-components, see: a) S. Z. Tasker, E. A. Standley, T. F. Jamison, *Nature* **2014**, *509*, 299. b) J. Montgomery, Organonickel Chemistry. *In Organometallics in Synthesis;* B. H. Lipshutz, Ed.; John Wiley & Sons, Inc.; Hoboken, **2013**; pp 319-428. c) K. Tanaka, Y. Tajima, *Eur. J. Org. Chem.* **2012**, 3715.

*Francisco Juliá-Hernández, Asraa Ziadi, Akira Nishimura and Ruben Martin**
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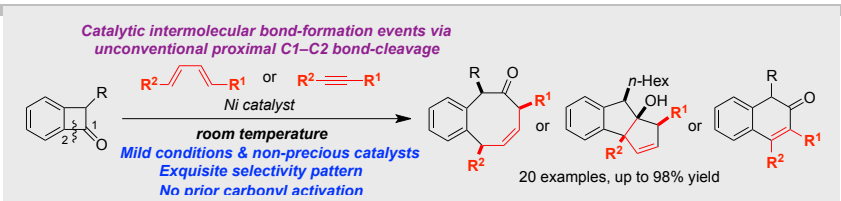

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