JOC Article

Stereo- and Regioselectivity of Pd^0/InI-Mediated Allylic Additions to Aldehydes and Ketones. *In Situ* Generation of Allylindium(III) Intermediates from *N*-Acylnitroso Diels−Alder Cycloadducts and 1-Amino-4-acetoxycyclopentenes

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Acylnitroso Diels−Alder cycloadduct (**11**, **37**, and **45**)- and cyclopentenyl acetate (**8** and **9**)-derived allylindium(III) species were generated *in situ* from palladium(0) catalysts and indium(I) iodide, and the stereo- and regiochemistry of their additions to aldehydes and ketones were investigated. Solvent, catalyst, and ionic effects were examined for the reaction of *N*-acetyl cycloadduct (**11**) and benzyloxyacetaldehyde (**10**). The solvent mixture of THF/H_2O with $Pd(OAc)_2$·PPh_3 catalysis was found to be optimal. The addition of *N*-acetyl cycloadduct to aliphatic aldehydes afforded products in good yields and high regio- and stereoselectivity, with the *cis*-1,4-isomers constituting 90−95% of the products. The reactions with *N*-Boc (**37a**) and *N*-methylcarbamate (**37b**) cycloadducts also gave the *cis*-1,4-products predominantly. The same regio- and stereoselectivity applied to the reactions of 4-acetoxy-1-(*N*-hydroxyphenyacetamido)cyclopentene (**8**). 4-Acetoxy-1-phenylacetamidocyclopentene (**9**), however, afforded *trans*-1,4-products exclusively. Mechanistic speculations involving chelated transition states are described.

Indium-mediated allylation, being tolerant of water and having demonstrated regio- and stereoselectivities, has gained recognition as a powerful and environmentally friendly tool in carbon−carbon bond formation.[1−3] The allylindium reagents used in most studies in this area were generated from the oxidative addition of indium powder to allylic halides. A more versatile preparative method was reported recently in which allylindium(III) reagents were formed by reductive transmetalation of π-allylpalladium(II) complexes with indium(I) iodide.[1e] This methodology allows for the preparation of allylindium(III) reagents from a new variety of allylic compounds including vinyloxiranes[1a] and vinylaziridines[1c] as well as conventional allylic acetates and carbonates.

Acylnitroso-derived hetero Diels−Alder cycloadducts have been shown to be susceptible to the catalysis of palladium(0) to open the cycloadduct ring systems and form π-allyl complexes (**1**) (Scheme 1).[4,5] The π-allyl complexes (**1**), when trapped by a variety of nucleophiles, afforded *cis*-1,4-cycloalkanes. It was envisioned that when a π-allylpalladium(II) complex (**1**) was treated with indium(I) iodide, a reductive transmetalation would occur to generate allylindium(III) species **2**, **3**, and/or **4**, which upon treatment with electrophiles such as aldehydes and ketones would lead to disubstituted cyclopentenes (**5**−**7**, Scheme 1). We anticipated that the hydroxamate group generated after ring opening would have a directing effect perhaps by chelating with the indium and, therefore, bias the result toward *cis*-1,4-products (**5**). The premise of this directing effect could be further tested by reacting

(1) (a) Araki, S.; Kameda, K.; Tanaka, J.; Hirashita, T.; Yamamura, H.; Kawai, M. *J. Org. Chem.* **2001**, *66*, 7919. (b) Lu, W.; Chan, T. H. *J. Org. Chem.* **2001**, *66*, 3467. (c) Takemoto, Y.; Anzai, M.; Yanada, R.; Nobutaka, F.; Ohno, H.; Ibuka, T. *Tetrahedron Lett.* **2001**, *42*, 1725. (d) Cha, J. H.; Pae, A. N.; Choi, K. I. I.; Cho, Y. S.; Koh, H. Y.; Lee, E. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2079. (e) Araki, S.; Kamei, T.; Hirashita, T.; Yamamura, H.; Kawai, M. *Org. Lett.* **2000**, *2*, 847. (f) Kumar, H. M. S.; Anjaneyulu, S.; Reddy, E. J.; Yadav, J. S. *Tetrahedron Lett.* **2000**, *41*, 9311. (g) Klaps, E.; Schmid, W. *J. Org. Chem.* **1999**, *64*, 7537. (h) Fujiwara, N.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 4095. (i) Araki, S.; Kamei, T.; Igarashi, Y.; Hirashita, T.; Yamamura, H.; Kawai, M. *Tetrahedron Lett.* **1999**, *40*, 7999. (j) Araki, S.; Horie, T.; Kato, M.; Hirashita, T.; Yamamura, H.; Kawai, M. *Tetrahedron Lett.* **1999**, *40*, 2331. (k) Chan, T. H.; Lu, W. *Tetrahedron Lett.* **1998**, *39*, 8605. (l) Araki, S.; Nakano, H.; Subburaj, K.; Hirashita, T.; Shibutani, K.; Yamamura, H.; Kawai, M.; Butsugan, Y. *Tetrahedron Lett.* **1998**, *39*, 6327. (m) Araki, S.; Usui, H.; Kato, M.; Butsugan, Y. *J. Am. Chem. Soc.* **1996**, *118*, 4699. (n) Araki, S.; Imai, A.; Shimizu, K.; Butsugan, Y. *Tetrahedron Lett.* **1992**, *33*, 2581. (o) Araki, S.; Ito, H.; Katsumura, N.; Butsugan, Y. *J. Organomet. Chem.* **1989**, *369*, 291. (p) Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem.* **1988**, *53*, 1831. Also see a recent review of indium-mediated reactions in aqueous solution: Li, C.-J.; Chan, T.-H. *Tetrahedron* **1999**, *55*, 11149.

(2) Paquette, L. A. In *Green Chemistry: Frontiers in Benign Chemical Synthesis and Processing*; Anastas, P., Williamson, T., Eds.; Oxford University Press: New York, 1998.

(3) (a) Paquette, L. A.; Rothhaar, R. R. *J. Org. Chem.* **1999**, *64*, 217. (b) Paquette, L. A.; Bennett, G. D.; Chhatriwalla, A.; Isaac, M. B. *J. Org. Chem.* **1997**, *62*, 3370. (c) Paquette, L. A.; Mitzel, T. M. *J. Org. Chem.* **1996**, *61*, 8799. (d) Paquette, L. A.; Lobben, P. C. *J. Am. Chem. Soc.* **1996**, *118*, 1917. (e) Paquette, L. A.; Mitzel, T. M. *J. Am. Chem. Soc.* **1996**, *118*, 1931.

(4) (a) Mulvihill, M. J.; Surman, M. D.; Miller, M. J. *J. Org. Chem.* **1998**, *63*, 4874. (b) Surman, M. D.; Miller, M. J. *Org. Lett.* **2001**, *3*, 519. (c) Surman, M. D.; Miller, M. J. *J. Org. Chem.* **2001**, *66*, 2466.

(5) (a) Miller, A.; Procter, G. *Tetrahedron Lett.* **1990**, *31*, 1043. (b) Cowart, M.; Bennett, M. J.; Kerwin, J. F., Jr. *J. Org. Chem.* **1999**, *64*, 2240.

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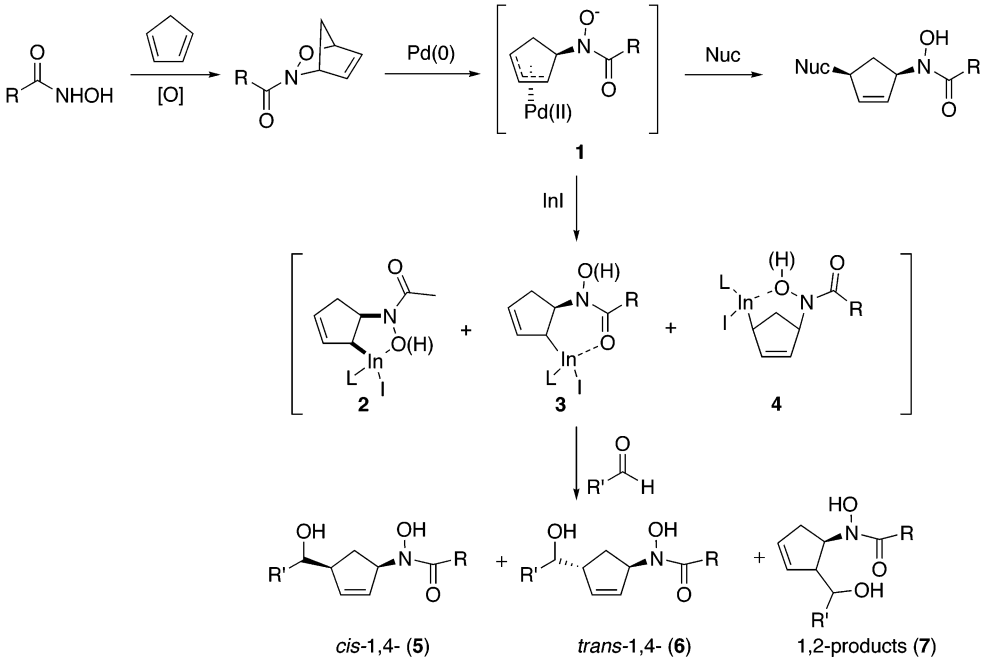
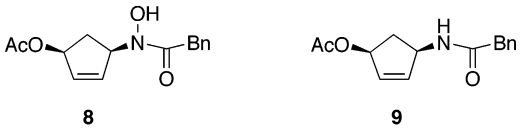
SCHEME 1





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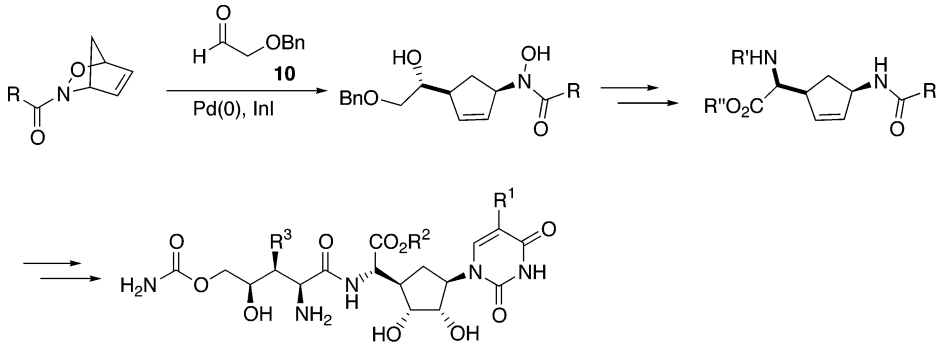


Carbocyclic polyoxins and nikkomycins

cyclopentenyl acetates **8** and **9** with aldehydes and ketones under similar conditions involving Pd^0/InI. It was expected that compound **8**, containing a hydroxamic acid, would provide *cis*-1,4-products (**5**) as the major isomers, whereas compound **9** could give predominantly *trans*-1,4-products. Regio- and diastereoselectivity for the *cis*-1,4-products (**5**), if obtained as anticipated, would provide a facile synthesis of various carbocyclic nucleosides, potential antifungal and antiviral agents.[6]

Results and Discussion

Benzyloxyacetaldehyde (**10**) was chosen as the electrophile in our exploratory experiments due to its key role in the synthesis of carbocyclic polyoxins and nikkomycins (Scheme 2), which have been of our particular interest.[7] Treatment of benzyloxyacetaldehyde **10** and *N*-acetyl cycloadduct (**11**)[8] with Pd^0 catalyst (generated in situ from an equimolar amount of $Pd(OAc)_2$ and PPh_3)[9] and InI indeed resulted in addition products, and the

(6) (a) Kaneko, M. *J. Synth. Org. Chem. Jpn.* **1991**, *49*, 989. (b) Boehme, R. E.; Borthwick, A. D.; Wyatt, P. G. *Annu. Rep. Med. Chem.* **1994**, *29*, 145. (c) Marquez, V. E. Lim, M.-I. *Med. Res. Rev.* **1986**, *6*, 1. (d) Borthwick, A. D.; Biggadike, K. *Tetrahedron* **1992**, *48*, 571. (e) Agrofoglio, L.; Suhas, E.; Farese, A.; Condom, R.; Chailand, S. R.; Earl, R. A.; Guedj, R. *Tetrahedron* **1994**, *50*, 10611. (f) Crimmins, M. T. *Tetrahedron* **1998**, *54*, 9229.

(7) Zhang, D.; Miller, M. J. *J. Org. Chem.* **1998**, *63*, 755.

(8) The acylnitroso Diels−Alder cycloadducts used in this report were all racemic, and therefore all the products generated were racemic as well. Only one enantiomer was shown for every compound to simplify the schemes and tables.

(9) Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1999**, *64*, 5201.

SCHEME 3

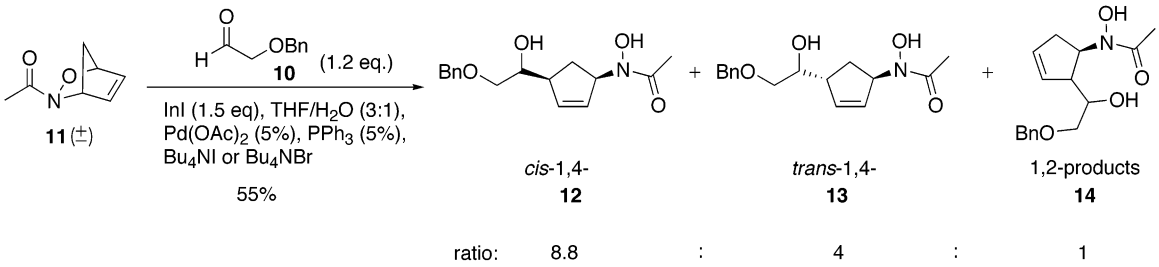
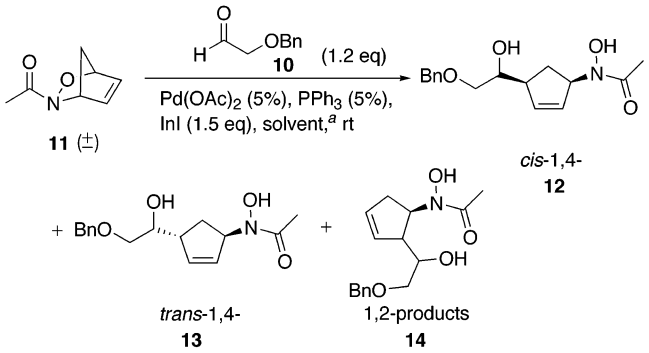


TABLE 1. Solvent Effect on Pd⁰/InI-Mediated Addition of *N*-Acetyl Cycloadduct 11 to Benzyloxyacetaldehyde 10



entry	solvent	yield[b] (%)	product ratio[c] **12/13/14**
1	THF/H_2O (3:1)	62	14:1:1
2	THF/H_2O (1:1)	62	10:1:trace
3	THF (anhydrous)	75	4.8:4.5:1
4	CH_2Cl_2/H_2O (3:1)[d]	74	3:2:1
5	CH_3CN/H_2O (3:1)	33	4.5:4.5:1
6	Et_2O/H_2O (3:1)[d]	<36[e]	1:4:3.6
7	MeOH	34	1.7:trace:1
8	NMP	63	1.8:1.1:1
9	THF/pH 7.0, 1 M phosphate buffer (3:1)	27	trace:1:1
10	THF/pH 7.5, 1 M phosphate buffer (3:1)	51	trace:1:1.4
11	THF/pH 6.5, 1 M phosphate buffer (3:1)	N.D.	complex mixture

[a] The reactions were all run at 0.1 M concentration. [b] Total yield of all isomers. [c] Determined by ^{1}H NMR integration. [d] 0.3 equiv of Bu_4NI was added. [e] Contaminated by some inseparable impurity.

solvent effect on the product distribution was explored (Table 1). Water was employed as a cosolvent in many of our experiments (entries 1−2 and 4−6, Table 1) as it was reported as a beneficial solvent/cosolvent in indium chemistry.[1,3] Mixtures of THF/H_2O (entries 1 and 2, Table 1) afforded the best selectivity of *cis*-1,4-products. Unexpectedly, anhydrous THF afforded the highest yield (75%), albeit with lower selectivity relative to THF/H_2O (entry 3, Table 1). This high yield could be rationalized by invoking competitive formation of the hydrate of benzyloxyacetaldehyde **10**, which exists to a lesser degree in anhydrous THF. The use of 3:1 CH_2Cl_2/H_2O (entry 4, Table 1) gave a better yield (74%); however, the selectivity suffered significantly, yielding a 3:2 ratio of *cis*-1,4- and *trans*-1,4-products. Acetonitrile/H_2O, ether/H_2O, and methanol appeared to be inferior solvents as they produced lower yields and lower selectivity (entries 5−7, Table 1). Use of *N*-methylpyrrolidinone (NMP, entry 8, Table 1) as solvent gave a satisfactory yield but a deteriorated selectivity.

Paquette and co-workers noted that the pH of their indium-promoted allylation performed in water or aqueous THF dropped below 4.0 as the reactions progressed.[3e] The effect of aqueous phosphate buffer as cosolvent on the reaction outcome was, therefore, explored (entries 9−11, Table 1). The addition of pH 7.0 or pH 7.5 phosphate buffer dramatically shifted the selectivity away from *cis*-1,4-products, giving approximately a 1:1 ratio of *trans*-1,4- and 1,2-products (entries 9 and 10, Table 1). The slightly acidic pH 6.5 phosphate buffer, however, yielded a complex mixture of products (entry 11, Table 1), which might be attributed to the quenching of InI in acidic conditions.

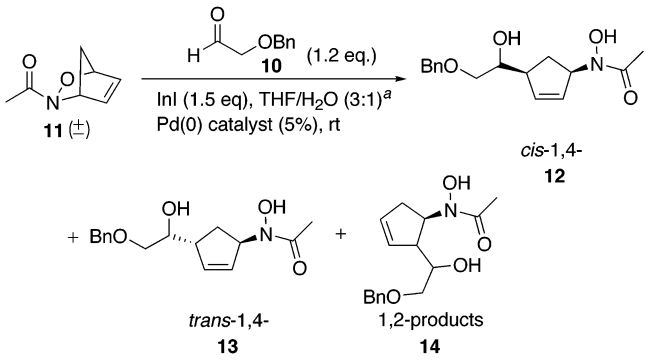
The product distribution change in neutral or slightly basic phosphate buffers may not result from the pH per se but rather an ionic effect[3e] of the phosphate ion. Two separate reactions were performed in which Bu_4NI and Bu_4NBr were added to the reaction mixtures (Scheme 3). The *cis*-1,4-products were still favored, however, with increased percentages of the other two isomers. Although there appears to be some indication of ionic (or salt) effect on the reactions of acylnitroso cycloadducts derived allylindium reagents, more studies will be needed to determine the role of ions (or salts).

The effect of varying the palladium catalyst was next examined, and the results are depicted in Table 2. The use of 5% $Pd(OAc)_2$·PPh_3 afforded *cis*-1,4-products in good yield and with the best selectivity (entry 1, Table 2). Neither increasing the amount of PPh_3 (entries 2 and 3, Table 2) nor using a different ligand, tri-2-furylphosphine (entry 4, Table 2), had significant advantage over 5% PPh_3 (entry 1). The combination of $Pd_2(dba)_3$ and tri-2-furylphosphine ligand (entries 5 and 6, Table 2) gave comparable results to 5% $Pd(OAc)_2$ and 5% PPh_3. $PdCl_2$-(dppf) afforded the desired *cis*-1,4-isomers predominantly, but the yield was poor and the products were contaminated with inseparable impurities (entry 7, Table 2). Finally, the use of $Pd(PPh_3)_4$ gave both a lower yield and deteriorated selectivity (entry 8, Table 2).

To further explore our methodology, a variety of aliphatic aldehydes and *N*-acetyl cycloadduct **11** were subjected to the optimized reaction condition of 5% Pd-$(OAc)_2$·PPh_3 and 1.5 equiv of InI in 3:1 THF/H_2O (Table 3). Gratifyingly, all reactions gave excellent selectivity for the *cis*-1,4-isomers[10] (90−95% of the total products) in chemical yields ranging from 56% to 64%.[11] The diastereomeric ratio on the newly formed C6 stereocenter (determined by ^{1}H NMR) ranged from ∼1:1 for less hindered aldehydes to 7:1 for bulkier aldehydes.

The reactions of aromatic aldehydes with *N*-acetylcycloadduct **11** were also investigated (Table 4). The *cis*-1,4-isomers still constituted a major percentage of the products, however, selectivities were not as good as with

TABLE 2. Catalyst Effect on Pd⁰/InI-Mediated Addition of *N*-Acetyl Cycloadduct 11 to Benzyloxyacetaldehyde 10



entry	Pd^0 catalyst	yield[b] (%)	product ratio[c] **12**/**13**/**14**
1	$Pd(OAc)_2$ (5%), PPh_3 (5%)	62	14:1:1
2	$Pd(OAc)_2$ (5%), PPh_3 (10%)	68	16:3:1
3	$Pd(OAc)_2$ (5%), PPh_3 (15%)	55	8.4:3.6:1
4	$Pd(OAc)_2$ (5%), tri-2-furylphosphine (5%)	58	12:1:trace
5	$Pd_2(dba)_3$ (2.5%), tri-2-furylphosphine (5%)	67	16.6:3.4:1
6	$Pd_2(dba)_3$ (2.5%), tri-2-furylphosphine (10%)	67	10:1:trace
7	$PdCl_2$(dppf) (5%)	<17[d]	2.9:2.2:1
8	$Pd(PPh_3)_4$ (5%)[e]	50	12.6:5.7:1

[a] The reactions were all run at 0.1 M concentration. [b] Total yield of all isomers. [c] Determined by ^1H NMR integration. [d] Contaminated by some inseparable impurity. [e] The solvent used was THF/H_2O (2:1). dba = dibenzylideneacetone. dppf = 1,1′-bis(diphenylphosphino)ferrocene.

aliphatic aldehydes. Significant quantities of *trans*-1,4-products were detected in all three entries.

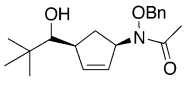
The X-ray crystal structure of the major component of compound **19** was obtained, and the newly formed C6 stereocenter was found to have the *S* configuration (for the enantiomer shown in Table 3, see the Supporting Information). It also provided confirmation of the *cis*-1,4-configuration assigned to the molecules based on ^1H NMR. The C6 stereochemistry of the major products of all the other compounds was therefore tentatively assigned as the *S* configuration (for the enantiomers shown).

Inspection of the regio- and stereochemistry for these acylnitroso Diels−Alder cycloadduct-derived allylindium reactions has led to the postulated mechanism in Scheme 4. Initial Pd^0-catalyzed ring opening of cycloadduct **11** is followed by reductive transmetalation with InI. The resultant allylindium(III) species can exist in four possible configurations (**26**−**29**, Scheme 4), with chelation operating between the indium and one of the oxygens on the hydroxamate.[12] Although some investigators doubted chelation in aqueous solvents, numerous reports have provided extensive experimental support for chelated transition states operating in water.[3,13] Allylindium species **28**, when treated with an aldehyde, can lead to transition states that involve another chelation between the indium and the carbonyl group of the aldehyde (**30** and **31**, Scheme 4).[14] The aldehydic R group assumes either an equatorial position (**30**) or an axial position (**31**) of the chair conformation. The transition state **30** should be preferred when the aldehydic R group is bulky, resulting in a greater proportion of diastereomer **32**. When R is small, little preference for **30** or **31** exists. It is also possible that products **32** and **33** arise from the allylindium species **27** through similar transition states.

trans-1,4-Products could result from aldehyde approaching from the opposite face of the cyclopentene ring of **28** (or **27**, Scheme 5). Alternatively, species **26** with indium chelated to the carbonyl oxygen of the hydroxamate in a *trans* fashion can react with the aldehyde and presumably afford the *trans*-1,4-products (**34**) through chelated transition states **35** and **36** (Scheme 5). The 1,2-products most likely result from the allylindium species **29**. The observed selectivity for *cis*-1,4-isomers indicated a preference for the allylindium species **28**, which may be attributed to stronger Lewis acid−base interaction between indium and the hydroxamate oxygen in **28**.

The results from the exploratory reactions with cycloadduct **11** prompted us to examine the applicability of this methodology to the *N*-Boc-protected cycloadduct (**37a**) (Table 5). This compound also reacted with a variety of aldehydes to afford predominantly the *cis*-1,4-products with generally good yields for aliphatic aldehydes (**38a**−**42a**, entries 1−5) and somewhat lower yields for aromatic aldehydes (**43a**−**44a**, entries 6 and 7). However, the selectivity was not as high as with the *N*-actetylcycloadduct (**11**). Significant amounts of *trans*-1,4-isomers were found in every case except the one with pivalaldehyde (**40a**, entry 3), which yielded only the *cis*-1,4-products.

(10) The stereochemistry of product **18** (entry 4, Table 3) was initially questioned because of its disparate ^1H NMR pattern. The *O*-benzyl derivative (**20**) was, therefore, prepared and the cyclopentene ring structure was unequivocally assigned as *cis*-1,4-configuration judging by the ^1H NMR. The bulky *tert*-butyl group in **18** may have had a significant effect on the conformation of the molecule, leading to the unusual NMR pattern.



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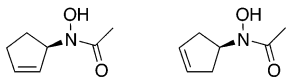
(11) It was noticed that the yields of these reactions were modest in many cases. We did not observe any significant amount of the quenched products **21** and **22**. However, before the workup of the reaction, we observed an $FeCl_3^+$ spot (i.e. indicating the presence of hydroxamic acid) around the baseline on the TLC plate. This spot disappeared after the acidic aqueous workup. We suspected that a portion of the π-allyl intermediates polymerized to generate this very polar $FeCl_3^+$ spot and the reaction yields were affected.



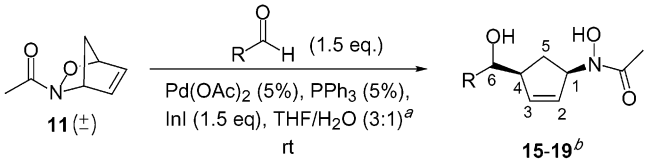
21 **22**

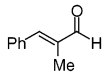
(12) There is no direct evidence to date as to how reductive transmetalation between InI and palladium π-allyl complex occurs (i.e., whether InI approaches from the same or opposite face of the palladium). However, an indication that the allylindium species are at equilibrium has been observed from our results with the *N*-carbamate protected cycloadducts (vide infra).

(13) (a) Chen, X.; Hortelano, E. R.; Eliel, E. L.; Frye, S. V. *J. Am. Chem. Soc.* **1990**, *112*, 6130. (b) Chen, X.; Hortelano, E. R.; Eliel, E. L.; Frye, S. V. *J. Am. Chem. Soc.* **1992**, *114*, 1778. (c) Frye, S. V.; Eliel, E. L.; Cloux, R. *J. Am. Chem. Soc.* **1987**, *109*, 1862. (d) Chan, T.-H.; Li, C.-J. *J. Chem. Soc., Chem. Commun.* **1992**, 747. (e) Carda, M.; Castillo, E.; Rodriquez, S.; Murga, J.; Marco, J. A. *Tetrahedron: Asymmetry* **1998**, *9*, 1117.

(14) For the lack of a better way to clarify the drawing of the transition states, we actually used the mirror image of **28** in transition states **30** and **31**. Since the compounds are racemic, it does not affect the results.

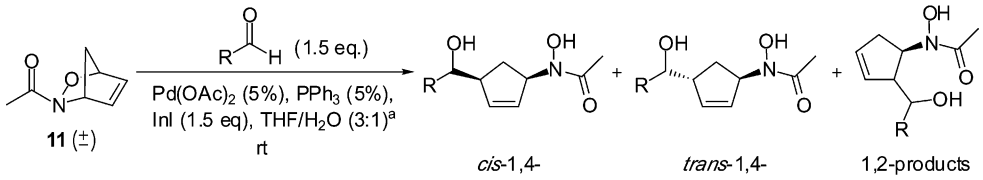
TABLE 3. Pd⁰/InI-Mediated Addition of *N*-Acetyl Cycloadduct 11 to Aliphatic Aldehydes

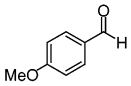
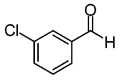


Entry	Aldehyde	Yield (%)[c]	Product	*dr* on C6[d]
1		59	**15**	1.9:1
2		56	**16**	1.3:1
3		57	**17**	1.1:1
4		64	**18**	6:1
5		59	**19**	7:1

[a] The reactions were all run at 0.1 M concentration. [b] The *cis*-1,4-products constituted 90−95% of the total products, and the rest 5−10% was a mixture of the other isomers. [c] Total yield of all isomers. [d] Determined by ^{1}H NMR integration.

TABLE 4. Pd⁰/InI-Mediated Addition of *N*-Acetyl Cycloadduct 11 to Aromatic Aldehydes



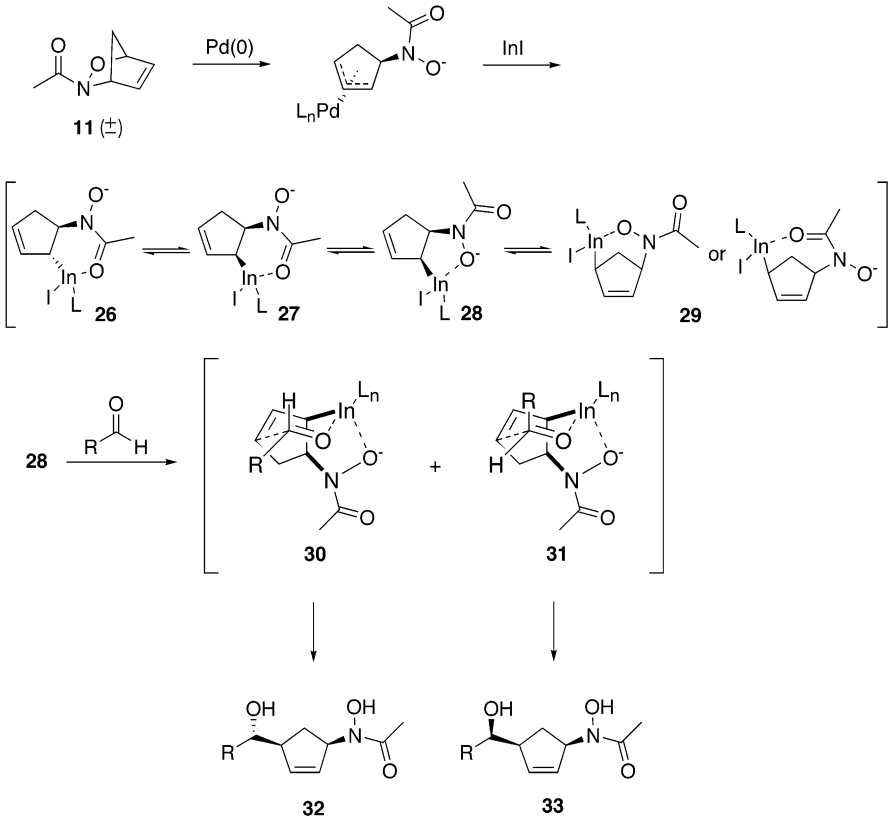
Entry	Aldehyde	Yield (%)[b]	Product	Ratio[c] *cis*-1,4-:*trans*-1,4-:1,2-products
1		65	**23**	8.5:3.5:1
2		52	**24**	N.D.[d]
3		58	**25**	8.1:5.5:1

[a] The reactions were all run at 0.1 M concentration. [b] Total yield of all isomers. [c] Determined by ^{1}H NMR integration. [d] Although we could tell that the *cis*-1,4-products were the major components from the ^{1}H NMR, the ratio could not be determined due to overlapping of the peaks.

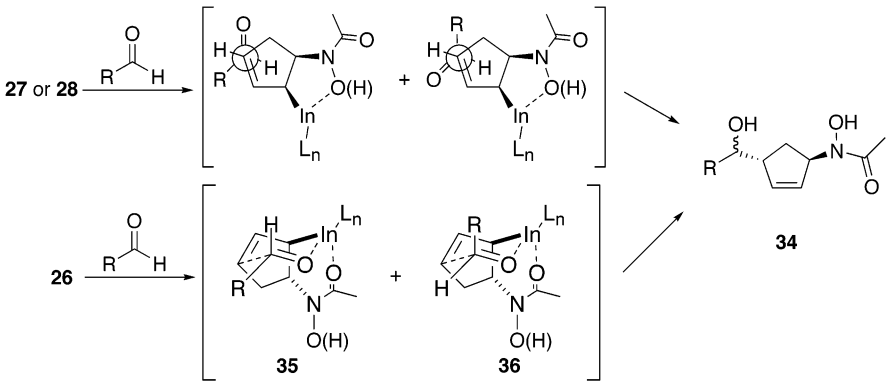
The preference of *cis*-1,4-products could be explained by analogous transition states depicted in Scheme 4, but we were not certain at this point of the reason for the eroded selectivity. It could be caused by either the steric influence of the Boc group and/or by the electronic effect of a carbamate (as opposed to the amide in the *N*-acetyl cycloadduct **11**). It would seem logical to examine the reactivity of a cycloadduct containing a smaller carbamate protecting group. *N*-Methylcarbamate cycloadduct (**37b**) was subjected to similar reactions as the *N*-Boc cycloadduct and the results are shown in Table 5 (i.e., series **b**). As with the *N*-Boc cycloadduct, all reactions afforded the *cis*-1,4-products predominantly, albeit in somewhat diminished total yields. Also similar to the *N*-Boc cycloadduct was the generation of a significant amount of *trans*-1,4-isomers (all entries, Table 5). For aldehydes with a primary α-carbon or benzaldehyde (**38b**, **41b**, and **43b**, entries 1, 4, and 6), 1,2-products were present as well. Analogous allylindium species can be drawn for the *N*-carbamate-protected cycloadducts (see Scheme 4). The lowered *cis*-1,4-selectivity is suggestive of an influence by the slightly higher pK_a of *N*-carbamate hydroxamic acids than that of *N*-acetylhydroxamic acid.

A trend emerged from Table 5 concerning aliphatic aldehydes: selectivity for *cis*-1,4-products improved with increasing bulk at the aldehydic α-carbon (i.e., selectiv-

SCHEME 4



SCHEME 5

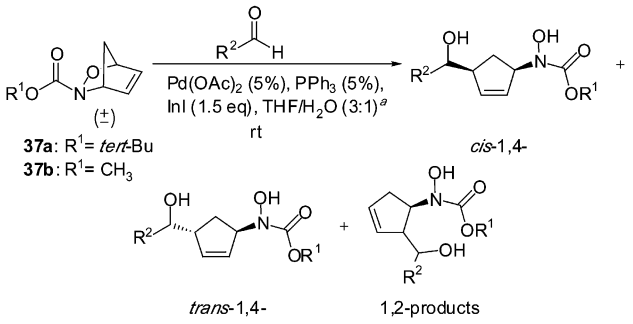


ity: entry 3 > entry 5 > entry 2 > entry 4 > entry 1, Table 5). This phenomenon is suggestive of a Curtin−Hammett situation where the π-allylindium(III) intermediates (e.g., **26**−**29**) are at equilibrium. With a bulky, and hence, less reactive aldehyde, the activation energy from any of the π-allylindium(III) intermediates to its products becomes larger than the activation energy for the interconversion of the π-allylindium(III) intermediates. The reaction is, therefore, driven toward the one leading to the *cis*-1,4-products which may have energetically favored transition states.

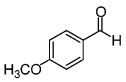
To further explore the present allylindium reactions, a second series of Pd^0/InI mediated additions were carried out using *N*-phenylacetyl cycloadduct **45** and *cis*-1-amino-4-acetoxy-cyclopentenes **8** and **9** (Table 6). Four electrophiles including acetone, benzaldehyde, formaldehyde, and acidic proton (i.e., 1 N HCl quench of the allylindium(III) species) were employed. The addition products of *N*-phenylacetyl cycloadduct **45** and cyclopentenyl acetate **8** with acetone and benzaldehyde paralleled the findings for *N*-acetyl cycloadduct **11**, with *cis*-1,4-isomers isolated as the major products (entries 1, 2, 5, and 6). Reactions with formaldehyde, unfortunately, resulted in a low yield of all possible isomers (entries 3 and 7). Acidic quench of the allylindium(III) species of **8** and **45** generated cyclopentene **46a** (electrophile = H^+, entries 4 and 8). This selective formation of **46a** rather than **47a** indicated a preference for the unbridged chelated forms of the allylindium species (i.e., **2** and **3**, but not **4**).

The *cis*-1,4-regio- and steroselectivity observed so far for acylnitroso cycloadducts and hydroxamic acid-containing **8** supported the anticipated directing effect of the hydroxamate group. To further verify this directing effect, cyclopentenyl acetate **9** (without hydroxamic acid, R_1 = Bn in Scheme 6) was subjected to similar Pd^0/InI-mediated addition to the four electrophiles used in Table

TABLE 5. Pd⁰/InI-Mediated Addition of *N*-Carbamate Cycloadducts to Aldehydes



38a-44a: R¹= *tert*-Bu
38b-44b: R¹= CH_3

Entry	Aldehyde	Product (%Yield)[b]	Ratio[c] products *cis*-1,4-:*trans*-1,4-:1,2
1		**38a** (70)	2.1:1:trace (**38a**)
		38b (61)	5.0:3.5:1 (**38b**)
2		**39a** (63)	3.8:1:trace (**39a**)
		39b (48)	2.2:1:trace (**39b**)
3		**40a** (54)	1:trace:trace (**40a**)
		40b (49)	7.3:1:trace (**40b**)
4		**41a** (73)	3.3:2.9:1 (**41a**)
		41b (54)	3.0:2.1:1 (**41b**)
5		**42a** (66)	5.7:1:trace (**42a**)
		42b (49)	2.6:1:trace (**42b**)
6		**43a** (39)	1.3:1:trace (**43a**)
		43b (49)	3.6:3.2:1 (**43b**)
7		**44a** (55)	3.5:1:trace (**44a**)
		44b (58)	2.2:1:trace (**44b**)

[a] The reactions were all run at 0.1 M concentration. [b] Total yield of all isomers. [c] Determined by ^{1}H NMR integration.

6. Treatment of **9** with benzaldehyde and formaldehyde (entries 10 and 11, Table 6) under similar conditions resulted exclusively in *trans*-1,4-products. The use of acetone, surprisingly, resulted only in cyclopentenes **46b** and **47b** (entry 9). Acidic quench of the allylindium(III) species generated a 3:1 mixture of **46b** and **47b** (entry 12), again indicating a preference for unbridged chelated forms of the allylindium species. Despite the two abnormalities (i.e., entries 7 and 9), an indication of *cis*-1,4-directing effect of the hydroxamate group was, nevertheless, prominent from the opposite results of compounds **8** and **9**.

The predominance of *trans*-1,4-products originated from compound **9** is rationalized mechanistically in Scheme 6. After *trans*-substituted palladium π-allyl complex **53** formation and reductive transmetalation with indium(I) iodide, the chelated allyindium(III) species **54** is formed. This species then reacts with aldehydes to yield *trans*-1,4-products through transition states **55**. In the absence of a strong Lewis acid−base interaction as exhibited in **28**, the indium of **54** stays at the *trans* face rather than isomerizing to the *cis*-chelated form. Thus, no *cis*-1,4-products are generated.

The present studies have demonstrated that acylnitroso Diels−Alder derived cycloadducts can undergo Pd⁰/InI-mediated ring opening, umpolung, and subsequent allylic addition to aldehydes with a heightened degree of regio- and stereoselection. As we anticipated, the hydroxamate generated after the ring opening asserted a directing effect, yielding *cis*-1,4-products predominantly. The *N*-acetylcycloadduct afforded excellent selectivity, with the *cis*-1,4-isomers constituting 90−95% of the total products for aliphatic aldehydes. As for the *N*-carbamate-protected cycloadducts (*N*-Boc- and *N*-methylcarbamate), *cis*-1,4-products still predominated, albeit with lower selectivity. With bulkier aldehydes, the *cis*-1,4-/*trans*-1,4-ratio became larger, indicative of a Curtin−Hammett situation where equilibrium existed among allylindium species. The opposite selectivities obtained from cyclopentenyl acetate **8** (hydroxamic acid-containing) and **9** (no hydroxamic acid) further supported the suggested directing effect of hydroxamate group.[15] This methodology should hold great potential for its synthetic utility as a wide variety of electrophiles could be used to provide facile synthesis of alkylated aminocycloalkanes.

Experimental Section

General Methods. Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were obtained on a 300 or a 500 MHz spectrometer. Analytical TLC was carried out using Merck aluminum-backed 0.2 mm silica gel 60 F-254 plates. Column chromatography was conducted using Merck silica gel 60 (230−400 mesh). Anhydrous tetrahydrofuran was freshly distilled from sodium benzoquinone ketyl, and indium(I) iodide was prepared as reported by Marshall and Grant.[16] All other purchased reagents were of reagent grade quality and were used without further purification.

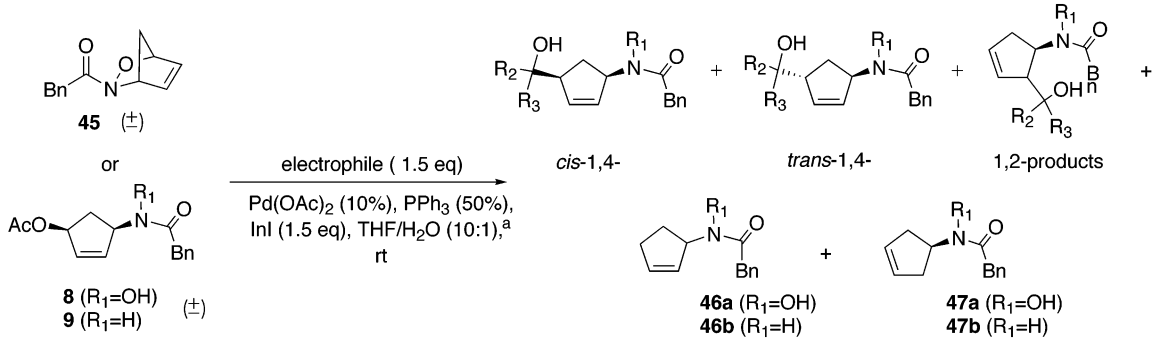
General Procedure A. A round-bottomed flask was charged with the *N*-acetyl cycloadduct (28 mg, 0.2 mmol), the aldehyde (0.24 mmol), freshly distilled THF (0.5 mL), InI (72 mg, 0.3 mmol), and water (0.5 mL). The resultant mixture was purged with Ar, and to this mixture was added a premixed solution of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol) and PPh_3 (2.6 mg, 0.01 mmol) in THF (freshly distilled, 0.5 mL + 0.5 mL wash) via cannula. The resultant mixture was purged with Ar again and stirred under Ar at room temperature overnight. HCl (1 M, ∼3−5 mL) was added to quench the reaction. The mixture was diluted with EtOAc and water and transferred to a separatory funnel. The layers were separated, and the aqueous solution was extracted with another two portions of EtOAc. The combined EtOAc portions were washed with water and brine and then dried over $MgSO_4$. The solvent was removed *in vacuo*, and the products were purified by flash column chromatography (silica gel, gradient 100% CH_2Cl_2 → 100:1 CH_2Cl_2/MeOH → 70:1 CH_2Cl_2/MeOH → 50:1 CH_2Cl_2/MeOH → 20:1 CH_2Cl_2/MeOH) to give the product as a mixture of *cis*-1,4-, *trans*-1,4-, and 1,2-products in various ratios.

***cis*-4-(2-Benzyloxy-1-hydroxyethyl)-1-(*N*-hydroxyacetamido)cyclopent-2-ene (12).** ^{1}H NMR (DMSO-d_6): (major C6 diastereomer) δ 1.75 (overlapping ddd, 1H, J = 7.0, 7.0,

(15) During the preparation of this manuscript, Cook et. al. reported in an ACS abstract the Pd⁰/InI-mediated allylation of aldehydes from *N*-acyl cyclohexeneoxazolidinones and related allylic substrates containing cyclohexene ring system. The *trans* products were obtained predominantly. Cook, G. R.; Hallman, J. *Abstr. Pap. Am. Chem. Soc.* paper 650, Org. Chem. Division, Aug 18, 2002.

(16) Marshall, J. A.; Grant, C. M. *J. Org. Chem.* **1999**, *64*, 8214.

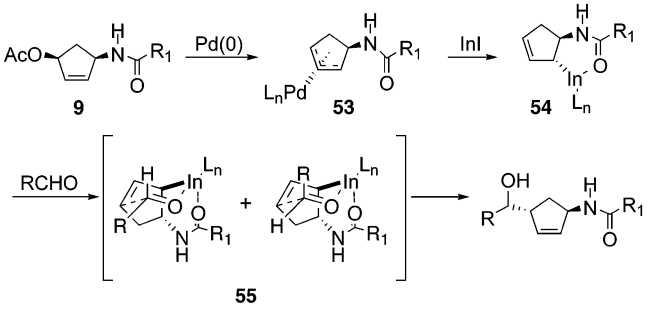
TABLE 6. Pd⁰/InI-Mediated Addition of *N*-Phenylacetyl Cycloadduct 45, 8, or 9 to a Variety of Electrophiles



entry	substrate	electrophile	yield[b] (%)	product (R_1, R_2, R_3)	ratio[c] *cis*-1,4-/*trans*-1,4-/1,2-/**46**/**47**
1	**45**	acetone	96	**48** (OH, CH_3, CH_3)	2.2:0:0:1:0
2	**45**	benzaldehyde	76	**49** (OH, H, Ph)	1.6:1:0:0:0
3	**45**	formaldehyde	30	**50** (OH, H, H)	1:1:1:0:0
4	**45**	H^+	51	**46a**	(0:0:0):1:0
5	**8**	acetone	82	**48** (OH, CH_3, CH_3)	1.4:0:0:1:0
6	**8**	benzaldehyde	63	**49** (OH, H, Ph)	1.9:1:0:0:0
7	**8**	formaldehyde	30	**50** (OH, H, H)	1:1:1:0:0
8	**8**	H^+	86	**46a**	(0:0:0):1:0
9	**9**	acetone	24	**46b** + **47b**	0:0:0:1:1
10	**9**	benzaldehyde	60	**51** (H, H, Ph)	0:1:0:0:0
11	**9**	formaldehyde	10	**52** (H, H, H)	0:1:0:0:0
12	**9**	H^+	98	**46b** + **47b**	(0:0:0):3:1

[a] The reactions were all run at 0.1 M concentration. [b] Total yield of all products including **46** and **47**. [c] Determined by ^{1}H NMR integration.

SCHEME 6



13.0 Hz), 1.99 (s, 3H), 2.09 (overlapping ddd, 1H, J = 8.0, 8.0, 13.0 Hz), 2.70 (m, 1H), 3.38−3.51 (m, 2H), 3.59 (m, 1H), 4.48−4.54 (m, 2H), 4.74 (d, 1H, J = 5.5 Hz), 5.44 (m, 1H), 5.58 (m, 1H), 5.84 (m, 1H), 7.28−7.37 (m, 5H), 9.38 (s, 1H); (minor C6 diastereomer) δ 1.53 (overlapping ddd, 1H, J = 7.0, 7.0, 13.5 Hz), 1.99 (s, 3H), 1.95−2.12 (m, 1H), 2.65 (m, 1H), 3.38−3.51 (m, 2H), 3.59 (m, 1H), 4.48−4.55 (m, 2H), 4.87 (d, 1H, J = 5.0 Hz), 5.44 (m, 1H), 5.58 (m, 1H), 6.02 (m, 1H), 7.28−7.37 (m, 5H), 9.38 (s, 1H). ^{13}C NMR (DMSO-d_6): (major C6 diastereomer) δ 20.85, 28.75, 48.13, 60.16, 72.33, 72.95, 73.44, 127.39, 127.54, 128.25, 131.18, 135.41, 138.63, 170.29; (minor C6 diastereomer) δ 20.85, 28.98, 47.60, 60.67, 72.07, 72.95, 73.62, 127.38, 127.52, 128.25, 130.52, 135.86, 138.65, 170.29. FAB HRMS: 292.1531 (MH^+, calcd for $C_{16}H_{22}NO_4$, 292.1549).

***cis*-4-(2,2-Dimethyl-1-hydroxypropyl)-1-(*N*-hydroxyacetamido)cyclopent-2-ene (18).** Prepared and purified according to general procedure A to give the *cis*-1,4-products as a mixture of two inseparable C6 diastereomers (dr = 6:1, brown paste, 29 mg, 64%). ^{1}H NMR (DMSO-d_6): (major C6 diastereomer) δ 0.88 (s, 9H), 1.91−1.99 (overlapping s and m, 5H), 2.80 (m, 1H), 3.31 (m, 1H), 4.25 (d, 1H, J = 4.5 Hz), 5.41 (m, 1H), 5.56 (m, 1H), 5.77 (m, 1H), 9.39 (bs, 1H); (minor C6 diastereomer) δ 0.88 (s, 9H), 1.63 (overlapping ddd, 1H, J = 7.5, 7.5, 13.0 Hz), 1.97 (s, 3H), 2.13 (m, 1H), 2.71 (m, 1H), 2.95 (m, 1H), 4.47 (d, 1H, J = 6.0 Hz), 5.41 (m, 1H), 5.56 (m, 1H), 5.98 (m, 1H), 9.34 (bs, 1H). ^{13}C NMR (DMSO-d_6): (major C6 diastereomer) δ 20.84, 26.92, 28.13, 35.44, 45.88, 61.13, 78.38, 130.08, 138.73, 170.11; (minor C6 diastereomer) δ 20.84, 26.64, 31.27, 35.54, 46.10, 60.62, 81.00, 130.01, 137.13, 170.11. FAB HRMS: 228.1608 (MH^+, calcd for $C_{12}H_{22}NO_3$ 228.1600).

***cis*-1-(*N*-Benzyloxyacetamido)-4-(2,2-dimethyl-1-hydroxypropyl)cyclopent-2-ene (20).** To the solution of **18** (26 mg, 0.114 mmol) in DMF (2 mL) was added K_2CO_3 solid (32 mg, 0.229 mmol) and benzyl bromide (24 μL, 0.206 mmol, via syringe). The resultant mixture was stirred at room temperature overnight. The mixture was diluted with EtOAc and water and transferred to a separatory funnel. The layers were separated, and the organic solution was washed with another portion of water and brine and then dried over $MgSO_4$. The major product (UV (+)/$FeCl_3$ (+) after heating of the TLC) was purified by flash column chromatography (silica gel, 4:1 hexane/ethyl acetate, then 2:1 hexane/ethyl acetate) to yield a colorless paste (31 mg, 86%), which consisted of a mixture of two inseparable C6 diastereomers. ^{1}H NMR ($CDCl_3$): (major C6 diastereomer) δ 0.96 (s, 9H), 2.14 (overlapping ddd, 1H, J = 6.6, 6.6, 13.5 Hz), 2.16 (s, 3H), 2.17 (s, 1H), 2.32 (overlapping ddd, 1H, J = 9.0, 9.0, 13.5 Hz), 3.02 (m, 1H), 3.54 (d, 1H, J = 1.5 Hz), 4.88 (d, 1H, J = 9.9 Hz), 4.95 (d, 1H, J = 9.9 Hz), 5.42 (m, 1H), 5.87 (m, 2H), 7.41 (bs, 5H); (minor C6 diastereomer) δ 0.96 (s, 9H), 1.88 (overlapping ddd, 1H, J = 6.6, 6.6, 13.5 Hz), 2.16 (s, 3H), 2.17 (s, 1H), 2.52 (overlapping ddd, 1H, J = 9.0, 9.0, 13.5 Hz), 3.02 (m, 1H), 3.22 (d, 1H, J = 3.3 Hz), 4.88 (d, 1H, J = 9.9 Hz), 4.95 (d, 1H, J = 9.9 Hz), 5.42 (m, 1H), 6.08 (m, 2H), 7.41 (bs, 5H). ^{13}C NMR ($CDCl_3$): (major C6 diastereomer) δ 26.94, 27.91, 29.92, 35.66, 46.43, 65.56, 79.11, 80.39, 128.95, 129.24, 129.56, 130.47, 134.48, 139.04, 173.61; (minor C6 diastereomer) δ 26.75, 27.91, 29.92, 35.81, 46.15, 63.75, 79.16, 82.75, 128.92, 129.24, 129.54, 131.61, 136.35,

139.04, 173.61. FAB HRMS: 318.2051 (MH^+, calcd for $C_{19}H_{28}NO_3$, 318.2069).

***cis*-1-(*N*-Hydroxyacetamido)-4-(1-hydroxy-1-phenylmethyl)cyclopent-2-ene (23).** Prepared and purified according to general procedure A to give an inseparable 8.5:3.5:1 mixture of *cis*-1,4-, *trans*-1,4-, and 1,2-products (light brown paste, 31 mg, 62%). ^{1}H NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 1.86 (overlapping ddd, J = 6.0, 6.0, 12.0 Hz), 2.01 (s, 3H), 2.15 (m, 1H), 2.82 (m, 1H), 4.37 (m, 1H), 5.29−6.20 (m, 4H), 7.24−7.32 (m, 5H), 9.47 (bs, 1H); (*trans*-1,4-product, major C6 diastereomer) δ 1.81−2.15 (overlapping m and s, 5H), 3.08 (m, 1H), 4.27−4.44 (m, 1H), 5.02−6.20 (m, 4H), 7.24−7.32 (m, 5H), 9.34 (bs, 1H). ^{13}C NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 20.90, 30.01, 52.64, 60.44, 76.33, 126.52, 126.99, 128.06, 131.32, 135.31, 145.01, 170.37; (*trans*-1,4-product, major C6 diastereomer) δ 20.85, 29.29, 53.31, 60.37, 75.37, 126.43, 126.85, 127.93, 130.83, 136.64, 144.94, 170.37. FAB HRMS: 248.1290 (MH^+, calcd for $C_{14}H_{18}NO_3$, 248.1287).

General Procedure B. A round-bottomed flask was charged with the *N*-Boc cycloadduct (**37a**) (47 mg, 0.24 mmol) or *N*-methylcarbamate cycloadduct (**37b**) (37 mg, 0.24 mmol), the aldehyde (0.2 mmol, purified either by redistillation or through its sodium bisulfite derivative), freshly distilled THF (0.5 mL), InI (72 mg, 0.3 mmol), and water (0.5 mL). The resultant mixture was purged with Ar, and to this mixture was added a premixed solution of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol) and PPh_3 (2.6 mg, 0.01 mmol) in THF (freshly distilled, 0.5 mL + 0.5 mL wash) via cannula. The resultant mixture was purged with Ar again and stirred under Ar at room temperature for 4−4.5 h. The reaction mixture was layered with ethyl acetate and water, and the resultant mixture was transferred to a separatory funnel containing some crushed ice. HCl (1 M, ∼10 mL) was added, and the layers were separated after vigorous mixing of the two layers in the funnel. The aqueous solution was extracted with another two portions of EtOAc. The combined EtOAc portions were washed with water and brine and then dried over $MgSO_4$. The solvent was removed *in vacuo*, and the product was purified by flash column chromatography (silica gel, slow gradient 100% CH_2Cl_2 → 4:1 CH_2Cl_2/EtOAc, then 96:4 CH_2Cl_2/2-propanol) to give the product as a mixture of *cis*-1,4-, *trans*-1,4-, and 1,2-products in various ratios.

***cis*-4-(1-Hydroxy-*n*-butyl)-1-(*N*-hydroxy-*N*-butyloxycarbonylamino)cyclopent-2-ene (38a).** Prepared according to the general procedure B, and the product was obtained as a brown paste (38 mg, 70%), which consisted of a 2.1:1 mixture of inseparable *cis*-1,4- and *trans*-1,4-products. The 1,2-products constituted only a very trace amount. ^{1}H NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 0.86 (t, 3H, J = 7.0 Hz), 1.19−1.49 (overlapping s and m, 13H), 1.67 (overlapping ddd, 1H, J = 7.1, 7.1, 13.0 Hz), 2.08 (overlapping ddd, 1H, J = 8.5, 8.5, 13.0 Hz), 2.51 (m, 1H), 3.30 (m, 1H), 4.32 (d, 1H, J = 6.0 Hz), 4.98−5.06 (m, 1H), 5.55−5.59 (m, 1H), 5.76 (overlapping ddd, 1H, J = 2.0, 2.0, 6.0 Hz), 8.81 (s, 1H); (*cis*-1,4-product, minor C6 diastereomer) δ 0.88 (t, 3H, J = 7.0 Hz), 1.19−1.49 (overlapping s and m, 14H), 2.03 (overlapping ddd, 1H, J = 8.5, 8.5, 12.5 Hz), 2.45 (m, 1H), 3.25−3.35 (m, 1H), 4.50 (d, 1H, J = 6.0 Hz), 4.98−5.06 (m, 1H), 5.55−5.59 (m, 1H), 5.96 (overlapping ddd, 1H, J = 2.0, 2.0, 6.0 Hz), 8.83 (s, 1H); (*trans*-1,4-product, major C6 diastereomer) δ 0.86 (t, 3H, J = 7.0 Hz), 1.19−1.49 (overlapping s and m, 13H), 1.70 (overlapping ddd, 1H, J = 4.5, 8.5, 13.0 Hz), 1.90 (overlapping ddd, 1H, J = 4.5, 8.5, 13.0 Hz), 2.71−2.76 (m, 1H), 3.17 (m, 1H), 4.40 (d, 1H, J = 6.0 Hz), 4.98−5.06 (m, 1H), 5.55−5.59 (m, 1H), 5.800 (overlapping ddd, 1H, J = 2.0, 2.0, 6.0 Hz), 8.76 (s, 1H); (*trans*-1,4-product, minor C6 diastereomer) δ 0.86 (t, 3H, J = 7.0 Hz), 1.19−1.49 (overlapping s and m, 13H), 1.80 (overlapping ddd, 1H, J = 5.0, 9.0, 14.0 Hz), 1.82 (overlapping ddd, 1H, J = 5.0, 9.0, 14.0 Hz), 2.71−2.76 (m, 1H), 3.17 (m, 1H), 4.35 (bs, 1H), 4.98−5.06 (m, 1H), 5.55−5.59 (m, 1H), 5.96 (overlapping ddd, 1H, J = 2.0, 2.0, 6.0 Hz), 8.77 (s, 1H). ^{13}C NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 14.14, 18.57, 28.09, 29.02, 36.80, 51.12, 64.17, 72.47, 79.45, 131.43, 134.93, 155.96. Due to the complexity of the spectrum, the ^{13}C NMR (DMSO-d_6) of the minor diastereomer of the *cis*-1,4-products and the two diastereomers of the *trans*-1,4-products are not differentiated in the following description: δ 14.11, 14.11, 14.14, 18.40, 18.64, 18.68, 28.09, 28.09, 28.09, 28.58, 28.88, 29.84, 37.23, 37.26, 37.29, 51.03, 51.71, 51.72, 64.17, 64.30, 64.48, 72.05, 73.01, 73.26, 79.29, 79.40, 79.48, 129.79, 130.39, 130.61, 135.64, 136.74, 136.89, 155.85, 155.88, 155.92. FAB HRMS: 272.1849 (MH^+, calcd for $C_{14}H_{26}NO_4$, 272.1862).

***cis*-4-(1-Hydroxy-*n*-butyl)-1-(*N*-hydroxy-*N*-methoxycarbonylamino)cyclopent-2-ene (38b).** Prepared according to the general procedure B, and the product was obtained as a brownish yellow oil (28 mg, 61%), which consisted of a mixture of inseparable *cis*-1,4-, *trans*-1,4-, and 1,2-products (ratio 5.0:3.5:1). Due to the complexity of the spectra, the relatively scarce 1,2-products are not included in the following description. ^{1}H NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 0.82−0.88 (m, 3H), 1.18−1.49 (m, 4H), 1.69 (overlapping ddd, 1H, J = 7.0, 7.0, 13.5 Hz), 2.08 (overlapping ddd, 1H, J = 8.5, 8.5, 13.5 Hz), 2.53 (m, 1H), 3.18 (m, 1H), 3.61 (s, 3H), 4.33 (d, 1H, J = 5.7 Hz), 5.03−5.10 (m, 1H), 5.56−5.59 (m, 1H), 5.79 (overlapping ddd, 1H, J = 2.0, 2.0, 6.0 Hz), 9.05 (s, 1H); (*cis*-1,4-product, minor C6 diastereomer) δ 0.82−0.88 (m, 3H), 1.18−1.49 (m, 5H), 2.04 (overlapping ddd, 1H, J = 8.5, 8.5, 13.0 Hz), 2.46 (m, 1H), 3.14−3.47 (m, 1H), 3.60−3.61 (s, 3H), 4.51 (d, 1H, J = 5.7 Hz), 5.03−5.10 (m, 1H), 5.56−5.59 (m, 1H), 5.97−6.00 (m, 1H), 9.06 (s, 1H); (*trans*-1,4-product, major C6 diastereomer) δ 0.82−0.88 (m, 3H), 1.18−1.49 (m, 4H), 1.72 (overlapping ddd, 1H, J = 5.0, 9.0, 14.0 Hz), 1.92 (overlapping ddd, 1H, J = 4.5, 8.5, 13.5 Hz), 2.74 (m, 1H), 3.14−3.47 (m, 1H), 3.60−3.61 (s, 3H), 4.38 (d, 1H, J = 6.0 Hz), 5.03−5.10 (m, 1H), 5.52−5.68 (m, 1H), 5.82 (overlapping ddd, 1H, J = 2.0, 2.0, 5.5 Hz), 9.00 (s, 1H); (*trans*-1,4-product, minor C6 diastereomer) δ 0.82−0.88 (m, 3H), 1.18−1.49 (m, 4H), 1.81 (overlapping ddd, 1H, J = 4.5, 8.5, 13.0 Hz), 1.84 (overlapping ddd, 1H, J = 4.5, 8.5, 13.0 Hz), 2.73−2.88 (m, 1H), 3.14−3.47 (m, 1H), 3.60−3.61 (s, 3H), 4.41 (d, 1H, J = 6.0 Hz), 5.03−5.10 (m, 1H), 5.52−6.00 (m, 2H), 9.01 (s, 1H). ^{13}C NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 14.14, 18.56, 28.91, 36.82, 51.08, 52.35, 64.08, 72.38, 131.12, 135.42, 157.01. Due to the complexity of the spectrum, the minor C6 diastereomer of *cis*-1,4-products and both C6 diastereomers of *trans*-1,4-products are not differentiated in the following description: δ 14.10, 14.11, 14.14, 18.40, 18.65, 18.68, 28.51, 28.89, 29.83, 37.25, 37.26, 37.28, 51.00, 51.63, 51.65, 52.29, 52.33, 52.35, 64.17, 64.29, 64.41, 71.97, 72.96, 73.21, 129.65, 130.19, 130.29, 136.11, 137.05, 137.12, 156.90, 156.94, 156.96: FAB HRMS: 230.1403 (MH^+, calcd for $C_{11}H_{19}NO_4$, 230.1392).

***cis*-4-(2,2-Dimethyl-1-hydroxypropyl)-1-(*N*-hydroxy-*N*-butyloxycarbonylamino)cyclopent-2-ene (40a).** Prepared according to the general procedure B, and the product was obtained as a yellow solid (31 mg, 54%) that consisted of only the *cis*-1,4-products (diastereomeric ratio on C6 = 9:1). ^{1}H NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 0.86 (s, 9H), 1.41 (s, 9H), 1.92 (overlapping ddd, 1H, J = 8.0, 8.0, 12.5 Hz), 1.97 (overlapping ddd, 1H, J = 8.0, 8.0, 12.0 Hz), 2.76 (overlapping dddd, 1H, J = 2.5, 2.5, 8.0, 8.0 Hz), 3.26 (dd, 1H, J = 3.0, 5.5 Hz), 4.08 (d, 1H, J = 5.0 Hz), 5.00 (overlapping ddd, 1H, J = 2.0, 8.0, 8.0 Hz), 5.57 (overlapping ddd, 1H, J = 2.0, 2.0, 5.0 Hz), 5.71 (overlapping ddd, 1H, J = 2.0, 2.0, 5.0 Hz), 8.86 (s, 1H); (*cis*-1,4-product, minor C6 diastereomer) δ 0.86 (s, 9H), 1.41 (s, 9H), 1.62 (overlapping ddd, 1H, J = 7.5, 7.5, 12.5 Hz), 2.13 (overlapping ddd, 1H, J = 8.0, 8.0, 12.5 Hz), 2.67 (m, 1H), 2.92 (overlapping dd, 1H, J = 6.0, 6.0 Hz), 4.40 (d, 1H, J = 6.0 Hz), 5.00 (m, 1H), 5.54−5.58 (m, 1H), 5.95 (overlapping ddd, 1H, J = 2.0, 2.0, 5.5 Hz), 8.88 (s, 1H). ^{13}C NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 27.30, 27.56, 28.80, 36.09, 46.55, 65.49, 79.20, 80.13, 131.13, 138.70, 156.530; (*cis*-1,4-product, minor C6 diastereomer) δ

27.30, 27.56, 28.80, 33.60, 46.72, 65.28, 80.16, 81.66, 130.94, 137.21, 156.53. FAB HRMS: 286.1999 (MH^+, calcd for $C_{15}H_{28}NO_4$, 286.2018).

***cis*-4-(2,2-Dimethyl-1-hydroxypropyl)-1-(*N*-hydroxy-*N*-methoxycarbonylamino)cyclopent-2-ene (40b).** Prepared according to general procedure B, and the product was obtained as a yellow oil (24 mg, 49%) that consisted of a mixture of inseparable *cis*-1,4- and *trans*-1,4-products (ratio 7.3:1). The *trans*-1,4-product is not described in the following data due to its relative scarcity. ^{1}H NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 0.86 (s, 9H), 1.95 (overlapping ddd, 1H, J = 8.0, 8.0, 12.5 Hz), 1.98 (overlapping ddd, 1H, J = 8.0, 8.0, 12.5 Hz), 2.77 (overlapping dddd, 1H, J = 2.5, 2.5, 8.0, 8.0 Hz), 3.28 (dd, 1H, J = 3.0, 5.0 Hz), 3.62 (s, 3H), 4.14 (d, 1H, J = 5.5 Hz), 5.05 (m, 1H), 5.58 (overlapping ddd, 1H, J = 2.5, 2.5, 5.5 Hz), 5.73 (overlapping ddd, 1H, J = 2.0, 2.0, 5.5 Hz), 9.09 (s, 1H); (*cis*-1,4-product, minor C6 diastereomer) δ 0.86 (s, 9H), 1.63 (overlapping ddd, 1H, J = 8.0, 8.0, 12.5 Hz), 2.14 (overlapping ddd, 1H, J = 8.0, 8.0, 12.5 Hz), 2.68 (m, 1H), 2.92 (overlapping dd, 1H, J = 6.0, 6.0 Hz), 3.62 (s, 3H), 4.43 (d, 1H, J = 6.0 Hz), 5.05 (m, 1H), 5.55−5.59 (m, 1H), 5.98 (overlapping ddd, 1H, J = 2.0, 2.0, 6.0 Hz), 9.11 (s, 1H). ^{13}C NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 27.58, 28.67, 36.09, 46.53, 53.04, 65.61, 79.06, 130.80, 139.15, 157.64; (*cis*-1,4-product, minor C6 diastereomer) δ 26.19, 27.28, 33.54, 46.72, 53.04, 65.25, 81.61, 130.61, 137.66, 157.64. FAB HRMS: 244.1544 (MH^+, calcd for $C_{12}H_{22}NO_4$, 244.1549).

***cis*-4-(2-Benzyloxy-1-hydroxyethyl)-1-(*N*-hydroxy-*N*-butyloxycarbonylamino)cyclopent-2-ene (41a).** Prepared according to the general procedure B, and the product was obtained as a yellow solid (51 mg, 73%) that consisted of a mixture of inseparable *cis*-1,4-, *trans*-1,4-, and 1,2-products (ratio 3.3:2.9:1). ^{1}H NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 1.42 (s, 9H), 1.71 (overlapping ddd, 1H, J = 7.0, 7.0, 13.0 Hz), 2.08 (overlapping ddd, 1H, J = 8.5, 8.5, 13.0 Hz), 2.65 (m, 1H), 3.37 (dd, 1H, J = 6.5, 10.0 Hz), 3.48 (dd, 1H, J = 4.5, 10.0 Hz), 3.54 (m, 1H), 4.45−4.53 (m, 2H), 4.67 (d, 1H, J = 5.5 Hz), 4.99−5.06 (m, 1H), 5.58 (overlapping ddd, 1H, J = 2.0, 2.0, 6.0 Hz), 5.76 (overlapping ddd, 1H, J = 2.0, 2.0, 6.0 Hz), 7.26−7.35 (m, 5H), 8.83 (s, 1H); (*cis*-1,4-product, minor C6 diastereomer) δ 1.41 (s, 9H), 1.49 (overlapping ddd, 1H, J = 7.5, 7.5, 13.0 Hz), 2.03 (overlapping ddd, 1H, J = 8.5, 8.5, 13.0 Hz), 2.59 (m, 1H), 3.35−3.49 (m, 2H), 3.54 (m, 1H), 4.45−4.53 (m, 2H), 4.81 (d, 1H, J = 5.0 Hz), 4.99−5.06 (m, 1H), 5.55−5.59 (m, 1H), 5.95 (overlapping ddd, 1H, J = 2.5, 2.5, 5.5 Hz), 7.26−7.35 (m, 5H), 8.85 (s, 1H); (*trans*-1,4-product, major C6 diastereomer) δ 1.41 (s, 9H), 1.80 (overlapping ddd, 1H, J = 4.5, 8.5, 13.5 Hz), 1.94 (overlapping ddd, 1H, J = 4.5, 8.5, 13.5 Hz), 2.87 (m, 1H), 3.34−3.53 (m, 3H), 4.45−4.53 (m, 2H), 4.73 (d, 1H, J = 5.5 Hz), 5.05 (m, 1H), 5.56 (overlapping ddd, 1H, J = 2.5, 2.5, 5.0 Hz), 5.93 (overlapping ddd, 1H, J = 2.0, 2.0, 6.0 Hz), 7.26−7.36 (m, 5H), 8.77 (s, 1H); (*trans*-1,4-product, minor C6 diastereomer) δ 1.41 (s, 9H), 1.77 (overlapping ddd, 1H, J = 5.0, 8.5, 13.5 Hz), 1.83 (overlapping ddd, 1H, J = 4.5, 8.5, 13.5 Hz), 2.87 (m, 1H), 3.34−3.53 (m, 3H), 4.45−4.53 (m, 2H), 4.70 (d, 1H, J = 5.5 Hz), 5.05 (m, 1H), 5.55−5.58 (m, 1H), 5.79 (overlapping ddd, 1H, J = 2.0, 2.0, 5.5 Hz), 7.26−7.36 (m, 5H), 8.78 (s, 1H); (1,2-product, major diastereomer) δ 1.40 (s, 9H), 2.39 (m, 2H), 2.90 (m, 1H), 3.39 (dd, 1H, J = 7.0, 10.0 Hz), 3.43 (dd, 1H, J = 5.5, 10.0 Hz), 3.61 (m, 1H), 4.46 (d, 1H, J = 3.0 Hz), 4.49 (s, 2H), 4.70−4.74 (m, 1H), 5.62 (m, 2H), 7.26−7.36 (m, 5H), 9.00 (s, 1H); (1,2-product, minor diastereomer) δ 1.39 (s, 9H), 2.39 (m, 2H), 2.95 (m, 1H), 3.36−3.46 (m, 2H), 3.74 (m, 1H), 4.43−4.51 (m, 1H), 4.49 (s, 2H), 4.70−4.74 (m, 1H), 5.53 (m, 2H), 7.26−7.36 (m, 5H), 8.96 (s, 1H). ^{13}C NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 28.17, 28.90, 48.19, 64.20, 72.26, 72.38, 73.49, 79.59, 127.43, 127.56, 128.29, 131.55, 134.73, 138.71, 156.09; Due to the complexity of the spectrum, the ^{13}C NMR (DMSO-d_6) of the minor diastereomer of *cis*-1,4-products and the two diastereomers of *trans*-1,4-products are shown indifferentially in the following description: δ 28.17, 28.17, 28.17, 28.90, 29.90, 29,90, 47.67, 48.50, 48.78, 64.35, 64.43, 64.71, 71.56, 72.35, 72.39, 72.41, 72.64, 73.05, 73.60, 73.67, 73.71, 79.53, 79.55, 79.61, 127.40, 127.43, 127.48, 127.53, 127.57, 127.59, 128.29, 128.29, 128.29, 130.67, 130.83, 131.30, 135.30, 136.39, 136.41, 138.67, 138.69, 138.73, 155.99, 156.02, 156.06. FAB HRMS: 350.1960 (MH^+, calcd for $C_{19}H_{28}NO_5$, 350.1967).

***cis*-4-(2-Benzyloxy-1-hydroxyethyl)-1-(*N*-hydroxy-*N*-methoxycarbonylamino)cyclopent-2-ene (41b).** Prepared according to general procedure B, and the product was obtained as a yellow paste (33 mg, 54%) that consisted of an inseparable 3.0:2.1:1 mixture of *cis*-1,4-, *trans*-1,4-, and 1,2-products. Due to the relative scarcity of the 1,2-products, they are not included in the following description. ^{1}H NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 1.75 (overlapping ddd, 1H, J = 7.0, 7.0, 13.5 Hz), 2.09 (overlapping ddd, 1H, J = 8.5, 8.5, 13.5 Hz), 2.67 (m, 1H), 3.35−3.79 (m, 3H), 3.62 (s, 3H), 4.48 (m, 2H), 4.70 (d, 1H, J = 5.5 Hz), 5.05−5.11 (m, 1H), 5.58 (m, 1H), 5.79 (overlapping ddd, 1H, J = 2.5, 2.5, 6.0 Hz), 7.26−7.36 (m, 5H), 9.07 (s, 1H); (*cis*-1,4-product, minor C6 diastereomer) δ 1.53 (overlapping ddd, 1H, J = 7.0, 7.0, 13.5 Hz), 2.04 (overlapping ddd, 1H, J = 8.5, 8.5, 13.5 Hz), 2.61 (m, 1H), 3.35−3.79 (m, 3H), 3.61 (s, 3H), 4.49 (m, 2H), 4.83 (d, 1H, J = 5.0 Hz), 5.05−5.11 (m, 1H), 5.53−5.99 (m, 2H), 7.26−7.36 (m, 5H), 9.08 (s, 1H); (*trans*-1,4-product, major C6 diastereomer) δ 1.82 (overlapping ddd, 1H, J = 5.0, 8.0, 13.0 Hz), 1.85 (overlapping ddd, 1H, J = 4.0, 8.5, 13.0 Hz), 2.89 (m, 1H), 3.35−3.79 (m, 3H), 3.59−3.62 (s, 3H), 4.49 (m, 2H), 4.69−4.78 (m, 1H), 5.05−5.11 (m, 1H), 5.53−5.99 (m, 2H), 7.26−7.36 (m, 5H), 9.01 (s, 1H); (*trans*-1,4-product, minor C6 diastereomer) δ 1.86 (overlapping ddd, 1H, J = 4.5, 8.5, 13.0 Hz), 1.96 (overlapping ddd, 1H, J = 4.5, 9.0, 13.0 Hz), 2.94 (m, 1H), 3.35−3.79 (m, 3H), 3.59−3.62 (s, 3H), 4.49 (m, 2H), 4.69−4.78 (m, 1H), 5.05−5.11 (m, 1H), 5.53−5.99 (m, 2H), 7.26−7.36 (m, 5H), 9.02 (s, 1H). ^{13}C NMR (DMSO-d_6): (all *cis*-1,4- and *trans*-1,4-isomers. Some peaks may contain more than one carbon.) 28.19, 28.75, 28.83, 29.81, 47.55, 48.09, 48.31, 48.62, 51.94, 52.31, 52.36, 52.39, 63.99, 64.22, 64.28, 64.51, 70.08, 70.23, 71.35, 72.08, 72.27, 72.31, 72.45, 72.88, 73.41, 73.51, 73.59, 127.38, 127.50, 127.53, 128.21, 128.24, 130.02, 130.40, 130.46, 131.18, 135.13, 135.68, 136.50, 136.63, 138.63, 138.64, 156.91, 157.03. FAB HRMS: 308.1498 (MH^+, calcd for $C_{16}H_{22}NO_5$, 308.1498).

***cis*-1-(*N*-Hydroxy-*N*-butyloxycarbonylamino)-4-(1-hydroxy-1-phenylmethyl)cyclopent-2-ene (43a).** Prepared according to the general procedure B, and the product was obtained as a yellow solid (24 mg, 39%) that consisted of a mixture of inseparable *cis*-1,4- and *trans*-1,4-products (ratio 1.3:1). ^{1}H NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 1.42 (s, 9H), 1.84 (overlapping ddd, 1H, J = 6.6, 6.6, 13.2 Hz), 2.16 (overlapping ddd, 1H, J = 8.4, 8.4, 13.2 Hz), 2.76 (m, 1H), 4.31 (dd, 1H, J = 4.2, 8.4 Hz), 5.04 (m, 1H), 5.24 (d, 1H, J = 4.8 Hz), 5.27 (m, 1H), 5.56 (m, 1H), 7.21−7.34 (m, 5H), 8.93 (s, 1H); (*trans*-1,4-product, major C6 diastereomer) δ 1.39 (s, 9H), 1.80 (overlapping ddd, 1H, J = 4.8, 8.1, 13.2 Hz), 1.97 (overlapping ddd, 1H, J = 4.8, 8.4, 13.2 Hz), 3.04 (m, 1H), 4.36 (dd, 1H, J = 4.2, 6.6 Hz), 4.96 (m, 1H), 5.27 (d, 1H, J = 4.8 Hz), 5.56 (m, 2H), 7.21−7.34 (m, 5H), 8.79 (s, 1H). ^{13}C NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 28.14, 30.16, 52.64, 64.38, 76.41, 79.61, 126.53, 126.97, 128.05, 131.63, 134.58, 145.06, 156.02; (*trans*-1,4-product, major C6 diastereomer) δ 28.13, 29.21, 53.24, 64.23, 75.44, 79.52, 126.49, 126.83, 127.88, 131.04, 136.08, 144.83, 155.95. FAB HRMS: 306.1718 (MH^+, calcd for $C_{17}H_{24}NO_4$, 306.1705).

***cis*-1-(*N*-Hydroxy-*N*-methoxycarbonylamino)-4-(1-hydroxy-1-phenylmethyl)cyclopent-2-ene (43b).** Prepared according to general procedure B, and the product was obtained as a yellow paste (26 mg, 49%) that consisted of a 3.6:3.2:1 mixture of inseparable *cis*-1,4-, *trans*-1,4-, and 1,2-products. Due to the relative scarcity of the minor C6 diastereomers of all products, they are not included in the following

description. ^{1}H NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 1.87 (overlapping ddd, 1H, J = 6.9, 6.9, 13.2 Hz), 2.17 (overlapping ddd, 1H, J = 8.4, 8.4, 13.2 Hz), 2.79 (m, 1H), 3.63 (s, 3H), 4.34 (dd, 1H, J = 4.8, 8.4 Hz), 5.01−5.11 (m, 1H), 5.27 (d, 1H, J = 4.8 Hz), 5.30−5.32 (m, 1H), 5.55−5.58 (m, 1H), 7.19−7.35 (m, 5H), 9.18 (s, 1H); (*trans*-1,4-product, major C6 diastereomer) δ 1.83 (overlapping ddd, 1H, J = 4.8, 8.4, 13.2 Hz), 2.01 (overlapping ddd, 1H, J = 4.8, 8.4, 13.2 Hz), 3.05 (m, 1H), 3.60 (s, 3H), 4.37 (dd, 1H, J = 4.2, 6.0 Hz), 5.01−5.11 (m, 1H), 5.30 (d, 1H, J = 4.8 Hz), 5.30−5.32 (m, 1H), 5.55−5.58 (m, 1H), 7.19−7.35 (m, 5H), 9.05 (s, 1H); (1,2-product) δ 2.34 (m, 2H), 3.22 (m, 1H), 3.58 (s, 3H), 4.48 (dd, 1H, J = 4.0, 6.0 Hz), 4.66 (overlapping ddd, 1H, J = 6.0, 6.0, 8.4 Hz), 5.27−5.37 (m, 1H), 5.40 (m, 1H), 5.55−5.60 (m, 1H), 7.19−7.35 (m, 5H), 9.21 (s, 1H). ^{13}C NMR (DMSO-d_6): (*cis*-1,4-product, major C6 diastereomer) δ 30.07, 52.52, 53.33, 64.36, 76.39, 126.57, 127.04, 128.11, 130.81, 136.58, 145.04, 157.15; (*trans*-1,4-product, major C6 diastereomer) δ 29.18, 52.47, 52.66, 64.27, 75.38, 126.47, 126.94, 127.98, 131.39, 135.08, 144.95, 157.06; (1,2-product) δ 35.35, 52.39, 55.64, 59.07, 74.39, 126.83, 126.90, 127.79, 132.29, 132.97, 143.93, 156.70. FAB HRMS: 264.1216 (MH^+, calcd for $C_{14}H_{18}NO_4$, 264.1236).

General Procedure C. In a 25 mL flask, allylic substrate **45**, **8**, or **9** (0.20 mmol) was dissolved in THF/H_2O (0.8 mL/0.2 mL). Electrophile (acetone, benzaldehyde, or formaldehyde (37wt % aqueous solution) 0.30 mmol) and InI (0.26 mmol) were added. The reaction mixture was flushed by Ar gas before addition of the solution of $Pd(PPh_3)_4$ [preformed from $Pd(OAc)_2$ (0.02 mmol) and PPh_3 (0.10 mmol) in 1 mL THF] at room temperature. The reaction was quenched with 1 N aqueous HCl solution, and the mixture was extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a yellow oil compound. The crude compound was purified by flash chromatography (3% MeOH−CH_2Cl_2).

1-(*N*-Hydroxyphenylacetamido)cyclopent-2-ene (46a). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.78 (m, 1H), 1.98 (m, 1H), 2.23 (m, 1H), 2.39 (m, 1H), 3.68 (s, 2H), 5.46 (bs, 1H), 5.53 (bs, 1H), 5.96 (bs, 1H), 7.18−7.29 (m, 5H), 9.51 (bs, 1H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 25.8, 31.1, 38.8, 61.1, 126.0, 127.9, 128.8, 134.7, 135. 8, 170.6. HRMS (FAB): calcd for $C_{13}H_{15}O_2N$ (MH^+) 218.1181, found 218.1191.

1-Phenylacetamidocyclopent-2-ene (46b) and 1-Phenylacetamidocyclopent-3-ene (47b). ^{1}H NMR ($CDCl_3$, 300 MHz) (compound **46b**): δ 1.38−1.42 (m, 2H), 2.30−2.40 (m, 2H), 3.53 (s, 2H), 4.90−5.00 (m, 1H), 5.50−5.60 (m, 1H), 5.60 (m, 1H), 5.90 (m, 1H), 7.22−7.36 (m, 5H); (compound **47b**) δ 2.05 (dd, J = 3.6, 15.6 Hz, 2H), 2.72 (dd, J = 7.8, 15.6 Hz, 2H), 3.55 (s, 2H), 4.50−4.60 (m, 1H), 5.30−5.40 (m, 1H), 5.64 (s, 2H), 7.22−7.36 (m, 5H); Due to the complexity of the spectrum, the ^{13}C NMR ($CDCl_3$) of these diastereomers were not differentiated in the following description. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 31.3, 31.6, 40.4, 44.1, 49.2, 56.0, 127.5, 129.0, 129.2, 129.6, 131.1, 135.0, 135.2, 170.7, 170.8. IR: 1639, 2914, 3061, 3275 cm^{-1}. MS (FAB): m/z 202 (MH^+). HRMS (FAB): calcd for $C_{13}H_{16}ON$ (MH^+) 202.1232, found 202.1215.

***cis*-4-(1-Hydroxyisopropyl)-1-(*N*-hydroxyphenylacetamido)cyclopent-2-ene (48).** Prepared according to general procedure C. ^{1}H NMR (DMSO-d_6, 300 MHz): (*cis*-1,4-product) δ 1.02 (s, 6H), 1.61 (ddd, J = 8.2, 8.2, 12.6 Hz, 1H), 1.99 (ddd, J = 7.8, 7.8, 12.6 Hz, 1H), 2.58 (m, 1H), 3.69 (s, 2H), 4.27 (bs, 1H), 5.42 (m, 1H), 5.55 (m, 1H), 5.89 (m, 1H), 7.19−7.30 (m, 5H), 9.49 (bs, 1H). ^{13}C NMR (DMSO-d_6, 75 MHz): (*cis*-1,4-product) δ 26.5, 27.5, 28.2, 38.8, 55.7, 60.9, 70.6, 126.2, 128.0, 129.4, 130.9, 135.5, 135.9, 170.7. HRMS (FAB): calcd for $C_{16}H_{21}O_3N$ (MH^+) 276.1600, found 276.1604.

***cis*-4-(1-Hydroxybenzyl)-1-(*N*-hydroxyphenylacetamido)cyclopent-2-ene (49).** Prepared according to general procedure C. ^{1}H NMR (DMSO-d_6, 300 MHz): (*cis*-1,4-product) δ 1.84 (ddd, J = 6.6, 6.6, 13.2 Hz, 1H), 2.12 (ddd, J = 8.5, 8.5, 13.2 Hz, 1H), 2.78 (m, 1H), 3.71 (s, 2H), 4.33 (dd, J = 4.0, 8.0 Hz, 1H), 5.28 (d, J = 4.0 Hz, 1H), 5.34 (m, 1H), 5.43 (m, 1H), 5.53 (m, 1H), 7.20−7.30 (m, 10H), 9.61 (bs, 1H); (*trans*-1,4-product) δ 1.81 (ddd, J = 5.0, 8.4, 13.2 Hz, 1H), 2.01 (ddd, J = 4.2, 8.7, 13.2 Hz, 1H), 3.10 (m, 1H), 3.68 (d, J = 3.3 Hz, 2H), 4.40 (dd, J = 4.5, 6.0 Hz, 1H), 5.32 (d, J = 4.5 Hz, 1H), 5.43 (m, 1H), 5.57 (m, 1H), 5.61 (m, 1H), 7.20−7.35 (m, 10H), 9.53 (bs, 1H). ^{13}C NMR (DMSO-d_6, 75 MHz): (*cis*-1,4-product) δ 29.9, 38.8, 52.5, 60.8, 76.2, 126.2, 126.4, 126.9, 127.9,128.0, 129.4, 131.1, 135.3, 135.9, 144.9, 170.7. MS (FAB): m/z 137, 152, 169, 306, 324 (MH^+). HRMS (FAB): calcd for $C_{20}H_{21}O_3N$ (MH^+) 324.1600, found 324.1613.

***cis*-4-(1-Hydroxymethyl)-1-(*N*-hydroxyphenylacetamido)cyclopent-2-ene (50).** Prepared according to general procedure C. ^{1}H NMR (DMSO-d_6, 300 MHz): (*cis*-1,4-product and *trans*-1,4-product) δ 1.47 (m, 1H), 1.71 (m, 1H), 1.88 (ddd, J = 4.8, 9.0, 13.8 Hz, 1H, *trans*-1,4-adduct), 2.10 (ddd, J = 6.9, 6.9, 13.8 Hz, 1H, *cis*-1,4-adduct), 2.67 (m, 1H), 2.88 (m, 1H), 3.38 (m, 4H), 3.70 (s, 4H), 4.60 (m, 2H), 5.46 (m, 2H), 5.54 (m, 2H), 5.92 (m, 2H), 7.20−7.30 (m, 10H), 9.47 (bs, 1H), 9.49 (bs, 1H); (*trans*-1,2-product) δ 2.41 (m, 2H), 2.90 (m, 1H), 3.71 (s, 2H), 4.55 (m, 1H), 4.83 (m, 1H), 5.66 (s, 2H), 7.20−7.35 (m, 5H), 9.67 (bs, 1H). ^{13}C NMR (DMSO-d_6, 75 MHz): (*cis*-1,4-product and *trans*-1,4-product) δ 29.9, 30.5, 39.5, 48.0, 48.2, 48.6, 61.5, 65.5, 65.7, 67.0, 126.9, 127.6, 128.8, 129.2, 129.3, 130.1, 130.6, 131.1, 135.9, 136.6, 136.8, 138.1, 171.5, 171.5. HRMS (FAB): calcd for $C_{14}H_{18}O_3N$ (MH^+) 248.1287, found 248.1286.

***trans*-4-(1-Hydroxybenzyl)-1-phenylacetamidocyclopent-2-ene (51).** Prepared according to general procedure C. ^{1}H NMR (DMSO-d_6, 500 MHz): (*trans*-1,4-product) δ 1.54 (ddd, J = 5.0, 8.5, 13.0 Hz, 1H), 2.15 (ddd, J = 4.0, 7.5, 13.0 Hz, 1H), 3.06 (m, 1H), 3.33 (s, 2H), 4.37 (dd, J = 4.5, 6.5 Hz, 1H), 4.66 (m, 1H), 5.29 (d, J = 4.5 Hz, 1H), 5.51 (m, 1H), 5.65 (m, 1H), 7.19−7.34 (m, 10H), 8.10 (d, J = 7.5, 1H). ^{13}C NMR (DMSO-d_6, 75 MHz): (*trans*-1,4-product) δ 34.4, 42.9, 53.4, 55.0, 75.8, 126.9, 127.1, 127.5, 128.6, 128.9, 129.6, 133.8, 135.7, 137.3, 145.6, 170.1. HRMS (FAB): calcd for $C_{20}H_{22}O_2N$ (MH^+) 308.1651, found 308.1679.

***trans*-4-(1-Hydroxymethyl)-1-phenylacetamidocyclopent-2-ene (52).** Prepared according to general procedure C. ^{1}H NMR (DMSO-d_6, 300 MHz): (*trans*-1,4-product) δ 1.57 (ddd, J = 5.1, 7.8, 13.0 Hz, 1H), 1.87 (ddd, J = 4.2, 8.7, 13.0 Hz, 1H), 2.87 (m, 1H), 3.26 (d, J = 5.4 Hz, 1H), 3.28 (d, J = 5.4 Hz, 1H), 3.35 (s, 2H), 4.59 (dd, J = 5.4, 5.4 Hz, 1H), 4.72 (m, 1H), 5.65 (m, 1H), 5.86 (m, 1H), 7.19−7.30 (m, 5H), 8.11 (d, J = 7.5, 1H). ^{13}C NMR (DMSO-d_6, 75 MHz): (*trans*-1,4-product) δ 34.9, 43.0, 48.0, 55.0, 65.3, 126.9, 128.9, 129.6, 133.2, 136.4, 137.3, 170.1. MS (FAB): m/z 137, 169, 232 (MH^+). HRMS (FAB): calcd for $C_{14}H_{18}O_2N$ (MH^+) 232.13376, found 232.13493.

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Supporting Information Available: The full characterization of compounds **15**−**17**, **19**, **24**, **25**, **39a**,**b**, **42a**,**b**, and **44a**,**b**, the X-ray crystal structure of compound **19**, and ^{1}H and ^{13}C NMR of compounds **12**, **15**−**20**, **23**−**25**, **38**−**44**, and **46**−**52**. This material is available free of charge via the Internet at http://pubs.acs.org.

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