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Tandem Sequence of Phenol Oxidation and Intramolecular Addition as a Method in Building Heterocycles

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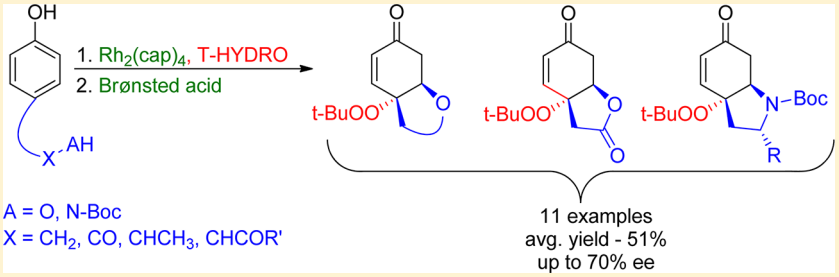
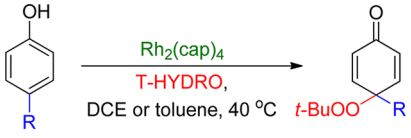
Supporting Information



ABSTRACT: A tandem phenol oxidation−Michael addition furnishing oxo- and -aza-heterocycles has been developed. Dirhodium caprolactamate [Rh_2(cap)$_4$] catalyzed oxidation by T-HYDRO of phenols with alcohols, ketones, amides, carboxylic acids, and *N*-Boc protected amines tethered to their 4-position afforded 4-(*tert*-butylperoxy)cyclohexa-2,5-dienones that undergo Brønsted acid catalyzed intramolecular Michael addition in one-pot to produce oxo- and -aza-heterocycles in moderate to good yields. The scope of the developed methodology includes dipeptides Boc-Tyr-Gly-OEt and Boc-Tyr-Phe-Me and provides a pathway for understanding the possible transformations arising from oxidative stress of tyrosine residues. A novel method of selective cleavage of O−O bond in hindered internal peroxide using $TiCl_4$ has been discovered in efforts directed to the construction of cleroindicin F, whose synthesis was completed in 50% yield over just 3 steps from tyrosol using the developed methodology.

INTRODUCTION

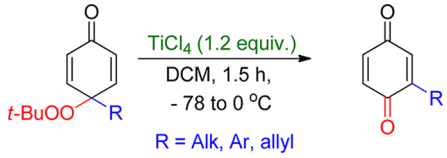
Recently, we reported dirhodium caprolactamate [Rh_2(cap)$_4$] catalyzed oxidation of 4-subtituted phenols by 70% aqueous solution of *tert*-butyl hydroperoxide (T-HYDRO).[1] This protocol furnishes 4-(*tert*-butyldioxy)cyclohexa-2,5-dienones in yields generally above 70% (eq 1). The radical nature of



(1)

the oxidation tolerates a variety of alkyl, aryl, and carboxylate groups and is insensitive to nucleophiles or dioxygen. 4-Substituted 2,5-dienone scaffolds are prepared by Rh_2(cap)$_4$ catalyzed oxidation by T-HYDRO with yields higher than those achieved with Oxone[2] and with fewer byproducts than are generated with hypervalent iodine reagents.[2,3] The versatility and stated advantages of phenol oxidation by T-HYDRO and commercial availability of 4-substituted phenols prompted us to explore applications of phenol oxidation in synthesis.

4-(Alkylperoxy)cyclohexa-2,5-dienones are synthetically useful fragments[4] and are known to form under oxidative stress in lipid cell membranes.[5] Murahashi has shown that 4-(*tert*-butyldioxy)cyclohexa-2,5-dienones afford 2-substituted *p*-quinones upon treatment with $TiCl_4$ (eq 2),[4b] with 4-substituents that include alkyl, cycloalkyls, and allyl. This protocol was



(2)

recently applied to the syntheses from *p*-cresol of vitamin K_1 (36% yield, 5 steps) and vitamin K_3 (79% yield, 4 steps).[6] In a more recent study, Rovis employed 4-hydroperoxy-2,5-dienones in an enantioselective cascade acetylation−oxo-Michael addition tandem sequence for the synthesis of anticancer agents bearing the peroxide functionality (Scheme 1).[4a]

We envisioned that the 4-substituent of 2,5-dienone could serve as a functional handle for syntheses of bicyclic products bearing the peroxide functionality. Furthermore, the versatility of the Rh_2(cap)$_4$ oxidative system[1,7] indicated a potential for conducting oxidation and intramolecular cyclization steps in one-pot. Although several protocols were reported for desymmetrization of 4-subtituted 2,5-dienones,[3b,8] the Brønsted acid catalyzed intramolecular oxo-Michael addition

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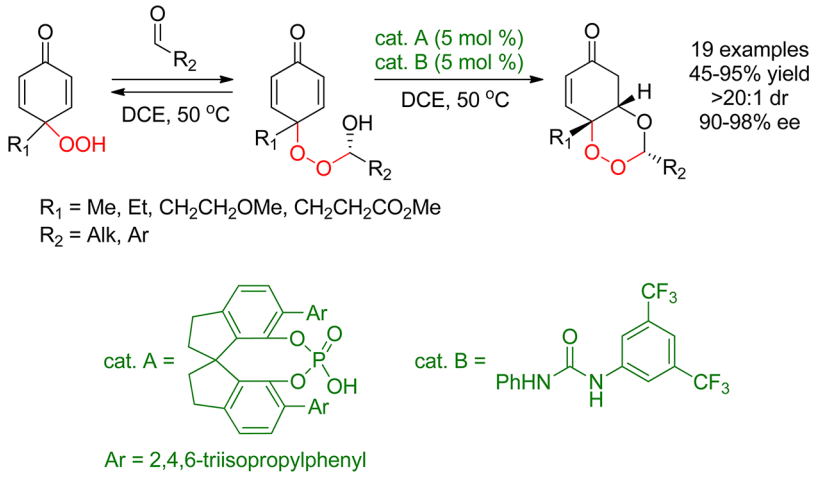
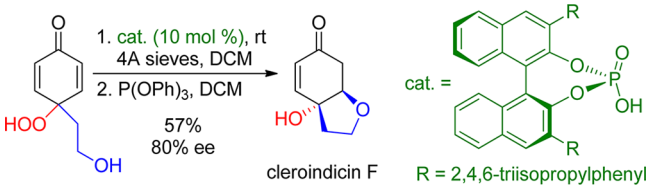
Scheme 1. Asymmetric Synthesis of 1,2,4-Trioxanes from 4-(Hydroperoxy)cyclohexa-2,5-dienones



is the most attractive.[2,9] Carreno prepared a series of *cis*-furan and *cis*-pyran-fused cyclohexenones in 47−91% yield from correspoding 4-substituted 2,5-dienones using *p*-toluenesulfonic acid (TsOH) to promote the intramolecular oxo-Michael addition.[9] A chiral version of the intramolecular oxo-Michael addition of 4-substituted 2,5-dieones was developed by You.[2] The method forms *cis*-fused 1-oxo- and 1,4-dioxo-heterocycles in 71−92% yield and 61−95% ee in the presence of BINOL-derived chiral phosphoric acids (Scheme 2). Moreover, activation of the 2,5-dienone fragment by a Brønsted acid was expected to be general not only for alcohols but also for carboxylates and aza-nucleophiles.

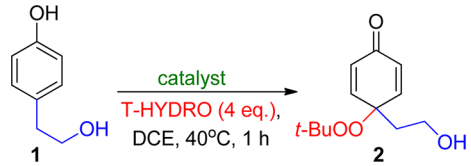
Scheme 2. The Asymmetric Intramolecular Oxo-Michael Addition Catalyzed by BINOL-Derived Chiral Phosphoric Acid



RESULTS AND DISCUSSION

Development of the phenol oxidation−Michael addition tandem transformation was begun with tyrosol **1**, the precursor to cleroindicin F[2] which is a component of *Clerodendrum indicum* plant extracts used to treat malaria and rheumatism.[10] Initial phenol oxidation experiments were conducted under conditions previously developed for the $Rh_2(cap)_4$ oxidation of 4-substituted phenols [4 equiv of T-HYDRO in 1,2-dichloroethane (DCE) at 40 °C].[1] The evaluation of the most active catalysts for 4-substituted phenol oxidation with T-HYDRO [$RuCl_3$, $RuCl_2(PPh_3)_3$, and $Rh_2(cap)_4$][1] at 1.0 mol % loading revealed that dirhodium caprolactamate provided the best yield in the conversion of **1** to **2** (Table 1, entries 1−3). The use of 2.0 mol % of $Rh_2(cap)_4$ eroded the yield of 2,5-dienone **2** (entry 4) while 0.5 mol % of $Rh_2(cap)_4$ gave incomplete conversion. Thus, 4 equiv of T-HYDRO in 1,2-dichloroethane (DCE) at 40 °C using 1.0 mol % of $Rh_2(cap)_4$ was selected as the first approximation of optimal conditions.

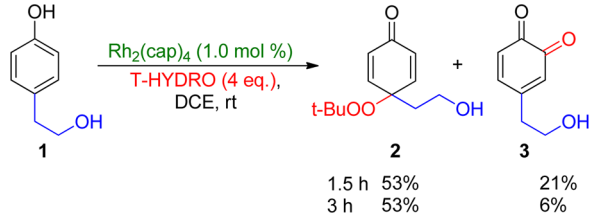
Table 1. Catalyst Optimization for Phenol Oxidation by T-HYDRO



entry	catalyst	catalyst loading, mole %	yield, %[a]
1	$RuCl_3$	1	23
2	$RuCl_2(PPh_3)_3$	1	48
3	**$Rh_2(cap)_4$**	**1**	**66**
4	$Rh_2(cap)_4$	2	48

[a]Determined by ^1H NMR spectroscopy from the ratio of the absorption (6.32 ppm, d, J = 10.2 Hz, 2H) corresponding to **2** and that for the biphenyl internal standard (7.60 ppm, d, J = 7.2 Hz, 4H).

Although ^1H NMR spectroscopic and TLC analyses showed that the sample contained only 2,5-dienone **2** after 1.5 h in the reaction mixture from $Rh_2(cap)_4$ catalyzed phenol oxidation by T-HYDRO, the isolated yield was not quantitative. The reaction temperature was lowered to room temperature in an attempt to improve product yield, and ^1H NMR spectroscopy revealed the formation of transient *o*-quinone **3** along with a 53% yield of 2,5-dienone **2** (eq 3). However, *o*-quinone **3** was



(3)

unstable under the reaction conditions, and its decomposition products were insoluble in the reaction mixture after 1.5 h at 40 °C. The evaluation of solvents, concentrations, anhydrous TBHP, and different modes of reactant addition gave no improvement of 2,5-dienone **2** yield (Supporting Information).

The versatility of $Rh_2(cap)_4$ catalyzed phenol oxidation by T-HYDRO was examined for 4-substituted phenols bearing alcohol groups, carboxylic acids, methyl ketone, and the Boc-protected amine. The corresponding 2,5-dienones were isolated

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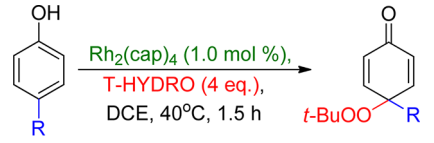
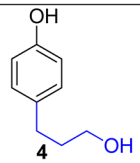
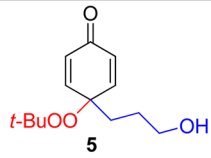
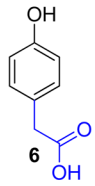
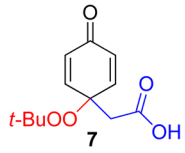
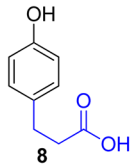
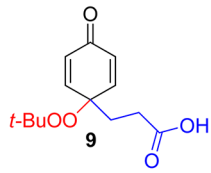
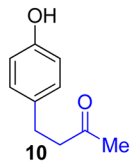
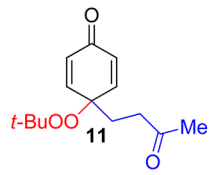
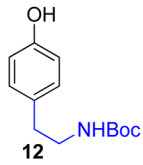
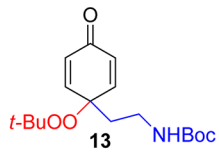
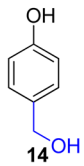
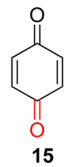
Table 2. Dirhodium Caprolactamate Oxidation of Phenols Bearing Tethered Nucleophiles by T-HYDRO



entry	phenol	product	isolated yield,[a] %
1			65
2			45[b]
3			46[b]
4			62
5			59
6			55[c]

[a]Yield after the silica gel plug. [b]A total of 2.0 mol % of [Rh_2(cap)$_4$] were used. [c]The yield of volatile *p*-quinone (6.70 ppm, s, 4H) was determined by ^{1}H NMR spectroscopy from the ratio of the absorption for **15** to that for the biphenyl internal standard (7.60 ppm, d, J = 7.2 Hz, 4H).

in 45−65% yields (Table 2). Similar to the oxidation of **1**, phenol oxidations presented in Table 2 contained only 2,5-dienone products in their reaction mixtures. Pure 2,5-dienone products can be rapidly isolated by filtration of the reaction mixture through a silica gel plug. Although product yields vary, phenol oxidation by T-HYDRO, catalyzed by Rh_2(cap)$_4$, is not restricted by carboxylic acid, alcohol, and ketone substituents that could serve as potential nucleophiles in subsequent reactions. Likewise, the presence of the *N*-Boc group in tyramine **12** did not alter the oxidation pathway and furnished 2,5-dienone **13** in 59% yield (entry 5). The oxidation of *p*-hydroxybenzyl alcohol **14**, however, produced *p*-quinone presumably due to fragmentation of the initially formed mixed peroxide to the observed *p*-benzoquinone (entry 6).[1]

All prepared 2,5-dienones were rapidly isolated by filtration of the reaction mixture through a silica gel plug.

The development of a phenol oxidation−Michael addition tandem transformation was initiated with the combination of catalysts for phenolic oxidation by Rh_2(cap)$_4$ and oxo-Michael addition by BINOL-based phosphoric acid **17**. However, addition of **17** inhibited the oxidation step (Table 3, entries 1 and 2), but introduction of **17** after completion of the phenol oxidation furnished **16** with >20:1 diastereoselectivity after 16 h at room temperature (entry 3). The stereochemistry of the bicyclic ring junction was extrapolated by analogy with the Brønsted acid catalyzed intramolecular oxo-Michael addition of 4-hydroperoxy-2,5-dienones reported by Carreno.[9] Furthermore, the addition of drying reagents improves percent conversion in the oxo-Michael reaction (entries 4−6). Addition

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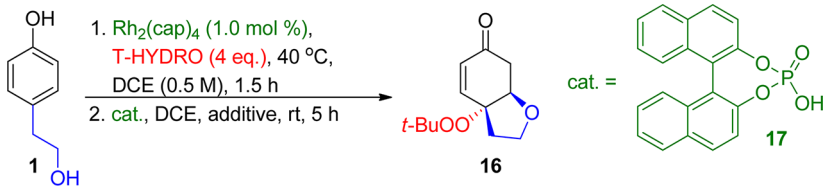
Table 3. Optimization of Conditions for Tandem Phenolic Oxidation−Michael Addition



entry	loading of acid **17**, %	mode of addition	additive	conversion of phenol oxidation, %[a,b]	conversion of Michael addition, %[c,d]
1	10	simultaneous	——	45	nd[e]
2	2	simultaneous	——	70	nd
3	10	stepwise	——	100	78
4	10	stepwise	4 Å sieves	100	85
5	2	stepwise	4 Å sieves	100	17
6	**10**	**stepwise**	**Na_2SO_4**	**100**	**91**

[a]Conversion of phenol oxidation step was determined from relative concentrations of **1** and **2**. [b]Relative concentrations of **1** and **2** were determined by ^{1}H NMR spectroscopy from the ratio of the absorptions (6.70 ppm, dd, J = 8.0, 2.1 Hz, 2H) corresponding to **1** and (6.32 ppm, d, J = 10.2 Hz, 2H) corresponding to **2**, and that for the biphenyl internal standard (7.60 ppm, d, J = 7.2 Hz, 4H). [c]Conversion of the Michael addition step was determined from relative concentrations of **2** and **16**. [d]Relative concentrations of **2** and **16** were determined by ^{1}H NMR spectroscopy from the ratio of the absorptions (6.32 ppm, d, J = 10.2 Hz, 2H) corresponding to **2**, (6.09 ppm, d, J = 10.3 Hz, 1H) corresponding to **16**, and that for the biphenyl internal standard (7.60 ppm, d, J = 7.2 Hz, 4H). [e]nd: not determined.

of anhydrous Na_2SO_4 was found to give optimal results for the stepwise $Rh_2(cap)_4$ phenol oxidation by T-HYDRO followed by Brønsted acid catalyzed oxo-Michael addition.

The isolated yields of cyclic products of the tandem $Rh_2(cap)_4$ catalyzed phenol oxidation and Brønsted acid catalyzed oxo-Michael addition were identical within experimental error to the yields for the two-pot tandem sequence. Hydrobenzofuran **16** and hydrobenzopyran **18** were prepared in 62% and 52% isolated yields, respectively, as single diastereomers (Table 4, entries 1 and 3). The oxo-Michael addition could also be catalyzed by TsOH with similar results (entry 2). Secondary alcohol **19** formed a mixture of only two out of four possible diastereomers (7.4:1) that were separated by column chromatography in 59% isolated yield (entry 4). The major diastereomer (**20**) was determined by a NOESY experiment that showed a cross-peak of two axial protons in the α-positions to the ether oxygen of **20** (Figure 1). The formation of lactone **22** showed that the developed tandem protocol could be applied to phenols with carboxylic acids tethered to the 4-position (entry 5). Factoring in the isolated yields of **2**, **5** and **7** for phenol oxidation (Table 1, entry 3, and Table 2, entries 1 and 2) into the isolated yields of **16**, **18**, and **22** for the tandem phenol oxidation−Michael addition (Table 4, entries 1, 2, 3, and 5) suggests that oxo-Michael addition occurs in yields above 80%.

To further elaborate the potential for generality of the tandem phenol oxidation−Michael addition, L-tyrosine derivatives were chosen as substrates due to their role in oxidative stress[11] and associated transformations.[5,11b] In agreement with the results from the phenol oxidations reported in Tables 2 and 4, L-tyrosine derivatives furnished single 2,5-dienone products along with polar unidentified materials that did not interfere with the subsequent Brønsted acid catalyzed cyclization. Carbamates **23** and **25** afforded dihydroindole derivatives **24** and **26** in 42% and 31% isolated yield, respectively (Table 5, entries 1 and 2). No cyclization was observed with acetyl-protected amine **27** (entry 3). The highest yield in the tandem reaction of L-tyrosine derivatives **23**, **25**, and **27** was achieved with **24** suggesting that the Boc-group is preferred for protection of the amine group in the phenol oxidation−aza-Michael addition process. The isolated yields of bicyclic products were improved if L-tyrosine derivatives lacked the carboxylic acid group (entry 4) or contained an ester functionality (entries 5 and 6). The lower product yield obtained in the absence of carboxylic acid is presumably caused by the lower yield in the phenol oxidation step (compare Table 5, entries 1 and 5 with Table 2, entries 1 and 2). Diastereomers formed from **31** and **32** were separable on silica gel and isolated as individual isomers. The diastereochemistry of the ester group was determined by NOE experiments for diastereomers **31** and **32** (Figure 2). The phenol oxidation−aza-Michael addition occurred in the presence of the amide group but required 1.5 equiv of Brønsted acid (entry 7). Furthermore, although the oxidation of dipeptide **37** could occur at the benzylic position of a phenylalanine residue as well as at the phenol group of a tyrosine residue, only the latter process was observed (entry 8).

The enantioselective version of the Brønsted acid catalyzed intramolecular Michael addition was also investigated. According to the mechanistic proposal by You, phosphoric acid **39** binds to the carbonyl and alcohol groups with the hydroperoxy group positioned away from the phosphoric acid (Figure 3).[2] Substitution of a *tert*-butyl group for a hydrogen atom of the hydroperoxide was expected to have no effect on the course of the reaction. However, the cyclization of **5** catalyzed by **39** afforded only moderate enantioselectivity (up to 59% ee) and took a considerably longer time (eq 4) than cyclization of 4-hydroperoxy-2,5-dienone (Figure 3).[2] A shorter alcohol linker gave a greater degree of enantiocontrol, reaching 70% ee for cyclization of **2** (eq 5). Unfortunately, phosphoric acid **39** showed no catalytic activity with 2,5-dienone **12**. The less sterically phosphoric acid **40** catalyzed the cyclization of **12**, albeit at the expense enantiomeric excess (eq 6).

Finally, the developed tandem phenol oxidation−oxo-Michael addition was employed for synthesis of cleroindicin F. To achieve this goal, selective reduction of the internal peroxide group was necessary. Several reagents and procedures applicable for reduction of internal peroxide **41** (eq 7)[12] were employed for the reduction of the *tert*-butylperoxy group of **16**. However, no desired product was isolated with any of these methods (Supporting Information). Surprisingly, dropwise addition of $TiCl_4$ solution in DCM to an anhydrous solution of pure peroxide **16** in DCM afforded **42** in 81% yield as a

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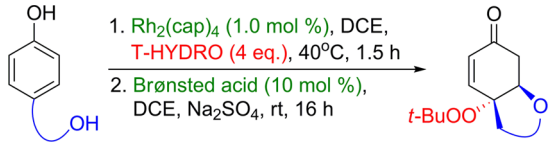
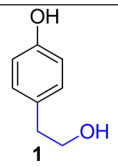
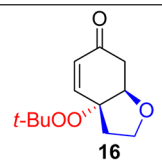
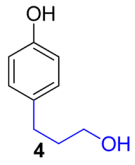
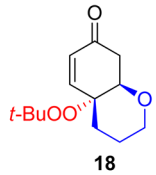
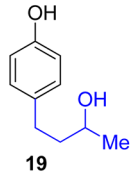
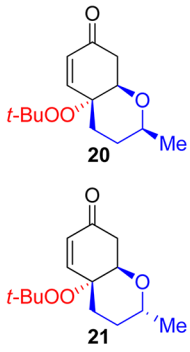
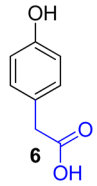
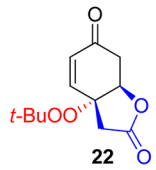
Table 4. Tandem Phenol Oxidation−Oxo-Michael Addition



entry	phenol	product[a]	Brønsted acid	diastereomer ratio	isolated yield, %[b]
1			**17**	> 20:1	62[c]
2	**1**	**16**	TsOH	> 20:1	60
3			**17**	> 20:1	52
	4	**18**			
4			**17**	> 20:1[d]	59[e]
	19	**20** + **21**			
5			**17**	> 20:1	40
	6	**22**			

[a]Major diastereomer is shown. [b]After flash chromatography through silica gel. [c]Phenolic oxidation forms 21% *o*-quinone that undergoes decomposition under reaction conditions. [d]The ratio of **20**/**21** is 7.4:1. [e]Each diastereomer is isolated as an individual compound.

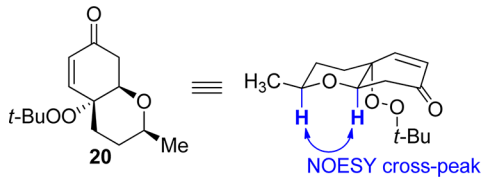


Figure 1. Determination of stereochemistry of hydrobenzopyrane **20**.

single product (eq 8). Thus, cleroindicin F was synthesized from tyrosol **1** in 50% overall yield over 3 steps, a process that is superior for cleroindicin F syntheses to those of You (3 steps, 22% overall yield),[2] of Pettus (10 steps, 18% overall yield),[10c] and of Hoveyda (9 steps, 17% overall yield).[13] Interestingly, the use of other Lewis acids in this protocol showed either no reactivity or led either to decomposition of **16** or reverse Michael reaction (Supporting Information). Treatment of peroxide **29** with $TiCl_4$ formed a complex mixture of products.

CONCLUSION

In conclusion, the scope of $Rh_2(cap)_4$ catalyzed phenol oxidations was expanded to phenols bearing carboxylic acids, alcohols, methyl ketone, and Boc-protected amine functional groups tethered to the 4-position. The one-pot stepwise tandem sequence of the phenol oxidation followed by the Brønsted acid catalyzed Michael addition was developed. This protocol improves the overall yield of cleroindicin F from phenol **1** from 22%[2] to 50%. The scope of Brønsted acid catalyzed intramolecular Michael addition to 2,5-dienones was expanded to include carboxylates and Boc-protected amine nucleophiles. The developed tandem protocol also includes multifunctional dipeptides. Finally, the selective cleavage of a hindered internal peroxide bond of **16** upon the treatment with $TiCl_4$ was discovered.

EXPERIMENTAL SECTION

General Information. All reactions were performed under atmospheric conditions unless the conditions are specified. ^{1}H NMR

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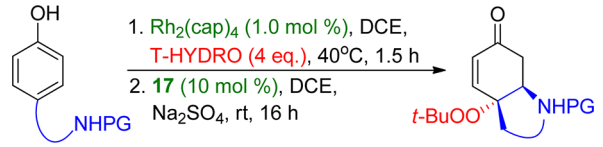
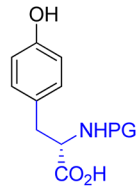
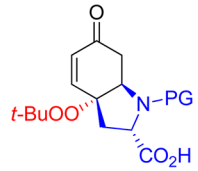
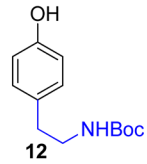
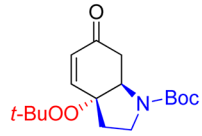
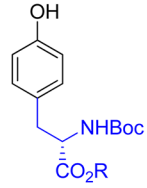
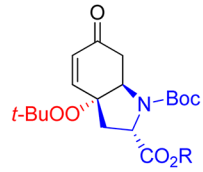
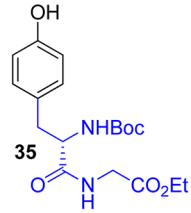
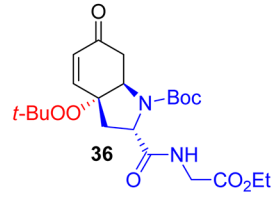
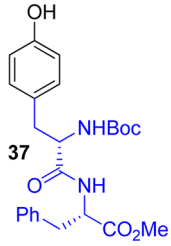
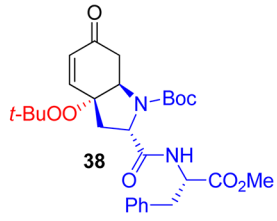
Table 5. Tandem Phenol Oxidation−Aza-Michael Addition



Entry	Phenol	Product[a,b]	Isolated Yield, % (dr)[c]
1	 PG = Boc **23**	 PG = Boc **24**	42 (2.8 : 1.0)
2	PG = Cbz **25**	PG = Cbz **26**	31[d]
3	PG = Ac **27**	PG = Ac **28**	N.R.[e]
4	 **12**	 **29**	55
5	 R = Me **30**	 R = Me **31**	53 (1.6 : 1.0)
6	R = *t*-Bu **33**	R = *t*-Bu **34**	62 (2.0 : 1.0)
7	 **35**	 **36**	43[f] (2.3 : 1.0)
8	 **37**	 **38**	39[f] (1.4 : 1.0)

[a]Major diastereomer is shown. [b]*cis*-Diastereomer of the bicyclic scaffold is formed in >20:1 ratio. [c]Each diastereomer is isolated as an individual compound. [d]Determined by ^{1}H NMR spectroscopy from the ratio of the absorption (6.09 ppm, d, J = 10.4 Hz, 1H) corresponding to **26** and that for the biphenyl internal standard (7.60 ppm, d, J = 7.2 Hz, 4H). [e]N.R.: no intramolecular aza-Michael addition. [f]Cyclization was achieved with TsOH (1.5 equiv).

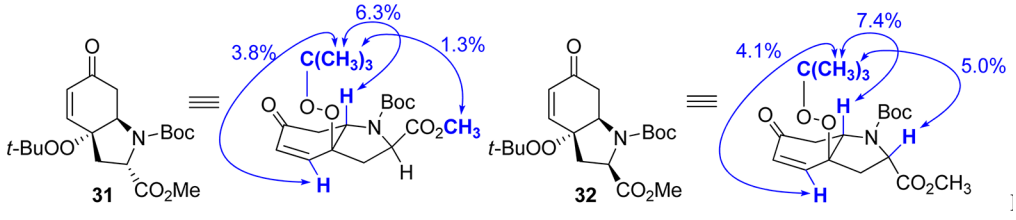


Figure 2. NOE analysis of dihydroindols **31** and **32**.

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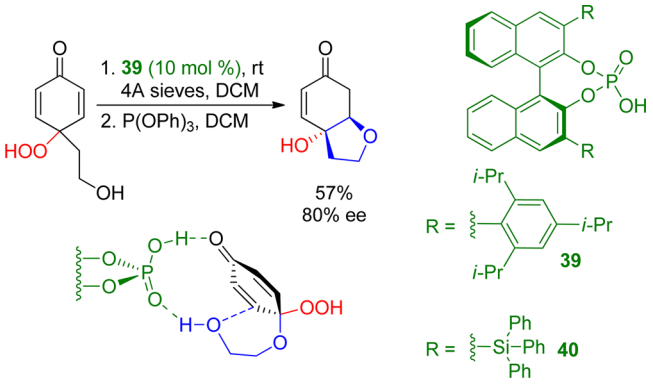
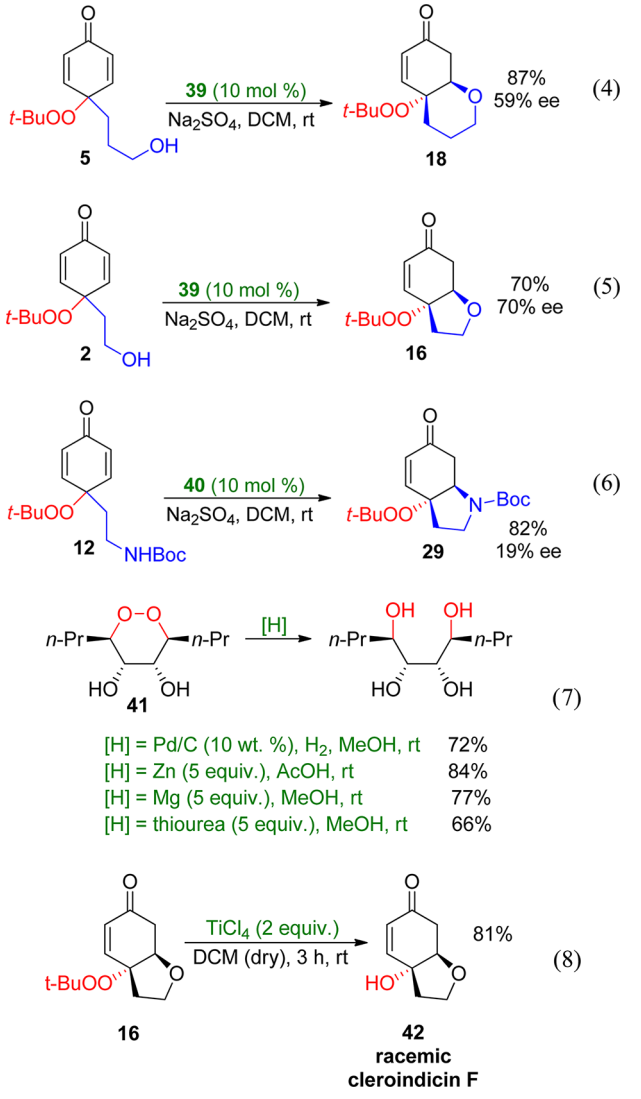


Figure 3. Mechanistic model of You for enantioselective desymmetrization of 2,5-dienones catalyzed by chiral phosphoric acid.[2].



spectra were recorded on 400 and 600 MHz spectrometers. Tetramethylsilane (TMS) was used as a reference (0.00 ppm) for all spectra. Data are reported as follows: chemical shift (in ppm, δ), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, br = broad, m = multiplet, comp = composite) and coupling constants (in Hz). ^{13}C NMR spectra were recorded on a 125 MHz spectrometer operated with complete proton decoupling. Chemical shifts are reported in ppm utilizing the central resonance of the $CDCl_3$ absorption as a reference (77.0 ppm). Thin layer chromatography was performed on silica gel coated glass plates (250 μm, F-254), and spots were visualized with either 254 nm ultraviolet light or a $KMnO_4$ stain. Flash chromatography used silica gel (32−63 μm). High-resolution mass spectra (HRMS) were acquired on a ESI-TOF spectrometer using CsI as a standard. $Rh_2(cap)_4$ was prepared according to the literature procedure.[14] Enantiomeric exesses were determined using a HPLC AD-H column and *i*-PrOH−hexane mixture as the eluting solvent. The concentration of TBHP in the commercial T-HYDRO reagent was determined by iodometric titration to be 70% by weight.

Spectra of peroxide **11** are in agreement with published information.[4b] Phosphoric acids **17**, **39**, **40** were prepared according to the published procedure.[15] Compounds **30**,[16] **33**,[16] **35**,[17] and **37**[17] were prepared according to published procedures. Compounds **24**, **29**, **31**, **32**, **34**, **36**, **38**, **43**, and **44** containing *N*-Boc group appeared as a pair of rotamers in ^{1}H and ^{13}C NMR spectra.

General Procedure for Transition Metal Complex Catalyzed Phenolic Oxidation. The phenol derivative (2.0 mmol), $Rh_2(cap)_4$ (0.02 mmol, 1 mol %), and DCE (4.0 mL) were placed in a 4-dram screw-cap vial containing a magnetic stirring bar. The suspension containing a small amount of undissolved phenol derivative and $Rh_2(cap)_4$ was heated to 40 °C at 250 rpm, and T-HYDRO (8.0 mmol, 4 equiv, 110 μL) was added all at once via syringe. The vial containing the suspension was loosely capped to allow release of pressure built-up, and its contents were stirred using a magnetic stirring bar at 40 °C. All solid materials dissolved within 10 min after T-HYDRO addition. After 1.5 h, the reaction mixture was transferred to a 100-mL round-bottom flask, concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel, DCM/AcOEt/hexane). Fractions containing the product were combined, and the solvent was evaporated under reduced pressure. The peroxide product was dried under high vacuum for 20 min (0.09 Torr, room temperature).

4-(tert-Butylperoxy)-4-(2-hydroxyethyl)cyclohexa-2,5-dien-1-one ***(2):*** 298 mg; 66%, R_f 0.30 (EtOAc/DCM/hexane (1:1:1)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (d, J = 10.2 Hz, 2H), 6.32 (d, J = 10.2 Hz, 2H), 3.77 (t, J = 6.2 Hz, 2H), 2.03 (t, J = 6.2 Hz, 2H), 1.22 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.0, 150.3, 129.5, 80.6, 78.2, 58.0, 39.3, 26.2; IR (neat, cm^{-1}): 3432, 3048, 2979, 2930, 1669, 1627, 1363, 1193, 1079, 1045, 984, 927, 857; EI-HRMS: calculated for $C_{12}H_{18}O_4$ (M + H), 227.12834; found, 227.12667.

4-(tert-Butylperoxy)-4-(3-hydroxypropyl)cyclohexa-2,5-dien-1-one ***(5):*** 312 mg, 65%, R_f 0.24 (EtOAc/DCM/hexane (1:1:1)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 (d, J = 10.2 Hz, 2H), 6.28 (d, J = 10.2 Hz, 2H), 3.63 (t, J = 6.3 Hz, 2H), 1.89−1.71 (comp, 2H), 1.66−1.44 (comp, 3H), 1.20 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.8, 150.4, 129.9, 80.2, 78.9, 62.4, 32.9, 26.6, 26.4; EI-HRMS: calculated for $C_{13}H_{20}O_4$ (M + H), 241.14399; found, 241.14334.

[1-(tert-Butylperoxy)-4-oxocyclohexa-2,5-dien-1-yl]acetic acid ***(7):*** 216 mg, 45%, R_f 0.20 (EtOAc/DCM/hexane (1:1:1)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (d, J = 10.0 Hz, 2H), 6.31 (d, J = 10.0 Hz, 2H), 2.79 (s, 2H), 1.21 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.0, 185.3, 147.5, 130.2, 80.9, 75.9, 31.2, 26.3; EI-HRMS: calculated for $C_{12}H_{16}O_5$ (M + H), 241.10760; found, 241.10911.

3-[1-(tert-Butylperoxy)-4-oxocyclohexa-2,5-dien-1-yl]propanoic acid ***(9):*** 234 mg, 46%, R_f 0.26 (EtOAc/DCM/hexane (1:1:1)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 (d, J = 10.2 Hz, 2H), 6.32 (d, J = 10.2 Hz, 2H), 2.39 (t, J = 7.9 Hz, 2H), 2.10 (t, J = 7.9 Hz, 2H), 1.22 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.5, 177.4, 149.3, 130.4, 80.4, 78.1, 31.0, 28.1, 26.3; EI-HRMS: calculated for $C_{13}H_{18}O_5$ (M + H), 255.12325; found, 255.12305.

4-(tert-Butylperoxy)-4-(3-oxobutyl)cyclohexa-2,5-dien-1-one ***(11):*** 312 mg, 62%, R_f 0.50 (EtOAc/DCM/hexane (1:1:1)); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (d, J = 10.2 Hz, 2H), 6.28 (d, J = 10.2 Hz, 2H), 2.39 (t, J = 7.7 Hz, 2H), 2.12 (s, 3H), 2.01 (t, J = 7.7 Hz, 2H), 1.20 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.9, 186.1, 150.3, 130.6, 80.7, 78.9, 37.7, 30.5, 29.8, 26.8; EI-HRMS: calculated for $C_{14}H_{20}O_4$ (M + H), 253.14399; found, 253.14494.

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*tert-Butyl [2-[1-(tert-Butylperoxy)-4-oxocyclohexa-2,5-dien-1-yl]-ethyl]carbamate (**13**):* 384 mg, 59%, R_f 0.30 (EtOAc/DCM/hexane (1:1:1)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.91 (d, J = 10.1 Hz, 2H), 6.28 (d, J = 10.1 Hz, 2H), 4.68 (s, 1H), 3.18 (br d, J = 6.3 Hz, 2H), 1.93 (t, J = 7.1 Hz, 2H), 1.43 (br s, 9H), 1.20 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.5, 149.5, 130.0, 80.8, 80.4, 79.5, 78.0, 36.9, 35.9, 28.4, 26.3; EI-HRMS: calculated for $C_{17}H_{27}O_5N$ (M + H), 326.19675; found, 326.19541.

General Procedure for Tandem Phenol Oxidation−Michael Addition Sequence. 4-(*tert*-Butyldioxy)cyclohexa-2,5-dienone (2.0 mmol), [Rh_2(cap)$_4$] (0.02 mmol, 0.01 equiv), and DCE (4.0 mL) were placed in a 4-dram screw-cap vial containing a magnetic stirring bar. The suspension containing a small amount of undissolved phenol derivative and Rh_2(cap)$_4$ was heated to 40 °C in an oil bath at 250 rpm, and T-HYDRO was added all at once via syringe. The vial containing the reaction mixture was loosely capped to allow release of pressure built-up, and its contents were stirred using a magnetic stirring bar at 40 °C. All solid materials dissolved within 10 min of T-HYDRO addition. After 90 min, the reaction mixture was allowed to cool to room temperature, and anhydrous Na_2SO_4 (600 mg), followed by TsOH or (*rac*)-BINOL-PO$_2$H (0.20 mmol, 0.1 equiv), was added to the mixture. The suspension was stirred overnight at room temperature, then transferred to a 100-mL round-bottom flask and concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel, DCM/AcOEt/hexane). Fractions containing the product were combined, and the solvent was evaporated under reduced pressure. The peroxide product was dried under high vacuum for 20 min (0.09 Torr, room temperature).

*(3aR,7aR)-3a-(tert-Butylperoxy)-3,3a,7,7a-tetrahydro-1-benzofuran-6(2H)-one (**16**):* 280 mg, 62%, R_f 0.14 (EtOAc/DCM/hexane (1:1:8)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77 (dd, J = 10.3, 1.6 Hz, 1H), 6.09 (d, J = 10.3 Hz, 1H), 4.46 (td, J = 5.0, 1.6 Hz, 1H), 3.96 (dd, J = 7.8, 6.7 Hz, 2H), 2.87 (dd, J = 16.9, 5.0 Hz, 1H), 2.68 (dd, J = 16.9, 4.4 Hz, 1H), 2.32 (dt, J = 13.5, 6.7 Hz, 1H), 2.08 (dt, J = 13.5, 7.8 Hz, 1H), 1.23 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.7 (C), 147.4 (CH), 129.7 (CH), 84.2 (C), 80.2 (C), 79.2 (CH), 66.0 (CH_2), 41.3 (CH_2), 36.9 (CH_2), 26.4 (CH_3); IR (neat, cm^{-1}): 3034, 2877, 2932, 2881, 1688, 1386, 1363, 1190, 1067, 1017, 877; ESI-HRMS: calculated for $C_{12}H_{18}O_4$ (M + H), 227.12841; found, 227.12817. The enantiomeric excess was determined by HPLC on an AD-H column (80:20 hexanes/*i*-PrOH, 1.0 mL/min): t_R (major) = 4.13 min; t_R (minor) = 4.75 min.

*(4aR,8aR)-4a-(tert-Butylperoxy)-2,3,4,4a,8,8a-hexahydro-7H-chromen-7-one (**18**):* 250 mg, 52%, R_f 0.08 (EtOAc/DCM/hexane (1:1:4)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.53 (dd, J = 10.2, 2.0 Hz, 1H), 6.15 (d, J = 10.2 Hz, 1H), 4.06 (td, J = 3.9, 2.0 Hz, 1H), 3.92 − 3.80 (m, 1H), 3.44 (td, J = 11.1, 2.7 Hz, 1H), 3.00 (dd, J = 16.8, 3.5 Hz, 1H), 2.57 (dd, J = 16.8, 4.2 Hz, 1H), 2.10 − 1.93 (comp, 2H), 1.79−1.67 (m, 1H), 1.68−1.54 (m, 1H), 1.21 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.6 (C), 147.1 (CH), 132.5 (CH), 79.9 (C), 75.7 (C), 75.3 (CH), 66.3 (CH_2), 41.1 (CH_2), 31.9 (CH_2), 26.5 (CH_3), 22.9 (CH_2); EI-HRMS: calculated for $C_{13}H_{20}O_4$ (M + H), 241.14394; found, 241.14362. The enantiomeric excess was determined by separation on a HPLC on an AD-H column (90:10 hexanes/*i*-PrOH, 1.0 mL/min): t_R (major) = 4.51 min; t_R (minor) = 5.35 min.

*(2S,4aR,8aR)-4a-(tert-Butylperoxy)-2-methyl-2,3,4,4a,8,8a-hexahydro-7H-chromen-7-one (**20**):* 254 mg, 52%, R_f 0.26 (EtOAc/DCM/hexane (1:1:16)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.46 (dd, J = 10.1, 2.4 Hz, 1H), 6.16 (d, J = 10.1 Hz, 1H), 4.01 (dd, J = 5.5, 2.4 Hz, 1H), 3.50 (dtd, J = 12.1, 6.1, 4.2 Hz, 1H), 3.03 (dd, J = 16.9, 3.3 Hz, 1H), 2.50 (dd, J = 16.9, 2.5 Hz, 1H), 2.13−1.92 (comp, 2H), 1.69 (dt, J = 13.6, 4.6 Hz, 1H), 1.38−1.24 (m, 1H), 1.20 (s, 9H), 1.12 (d, J = 6.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.7 (C), 146.1 (CH), 133.0 (CH), 79.9 (C), 75.8 (CH), 75.1 (C), 73.2 (CH), 41.5 (CH_2), 32.8 (CH_2), 30.6 (CH_2), 26.5 (CH_3), 21.3 (CH); EI-HRMS: calculated for $C_{14}H_{22}O_4$ (M + H), 255.15972; found, 255.15941.

*(2R,4aR,8aR)-4a-(tert-Butylperoxy)-2-methyl-2,3,4,4a,8,8a-hexahydro-7H-chromen-7-one (**21**):* 36 mg, 7%, R_f 0.09 (EtOAc/DCM/hexane (1:1:16)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.91 (d, J = 10.3 Hz, 1H), 5.99 (d, J = 10.3 Hz, 1H), 4.60 (dd, J = 12.2, 5.1 Hz, 1H), 3.90−3.72 (m, 1H), 2.94 (dd, J = 16.1, 12.2 Hz, 1H), 2.70 (dd, J = 16.2, 5.1 Hz, 1H), 2.14−1.99 (m, 1H), 1.83−1.70 (m, 1H), 1.67−1.53 (m, 1H), 1.49 (dd, J = 13.2, 3.3 Hz, 1H), 1.23 (s, 9H), 1.21 (t, J = 6.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.3, 153.5, 129.2, 80.0, 77.3, 70.1, 65.3, 40.1, 27.9, 27.2, 26.5, 21.1; EI-HRMS: calculated for $C_{14}H_{22}O_4$ (M + H), 255.15972; found 255.15974.

*(3aR,7aR)-3a-(tert-Butylperoxy)-3,3a,7,7a-tetrahydro-1-benzofuran-2,6-dione (**22**):* 192 mg, 40%, R_f 0.30 (EtOAc/DCM/hexane (1:1:4)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.75 (dd, J = 10.3, 1.2 Hz, 1H), 6.24 (d, J = 10.3 Hz, 1H), 5.11 (dd, J = 8.2, 1.2 Hz, 1H), 3.24−2.97 (comp, 2H), 2.89−2.65 (comp, 2H), 1.24 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.5, 171.4, 144.0, 131.5, 81.4, 80.4, 78.7, 40.4, 38.7, 26.3; EI-HRMS: calculated for $C_{12}H_{16}O_5$ (M + H), 241.10760; found, 241.10701.

*(2S,3aR,7aR)-1-(tert-Butoxycarbonyl)-3a-(tert-butylperoxy)-6-oxo-2,3,3a,6,7,7a-hexahydro-1H-indole-2-carboxylic acid (**24**):* 310 mg, 42%, R_f 0.36 (DCM/MeOH (9:1)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.14 (br s, 1H), 6.98−6.81 (m, 1H), 6.09 (d, J = 10.4 Hz, 1H), 4.82−4.63 (m, 1H), 4.63−4.43 (m, 1H), 3.43−3.14 (m, 1H), 2.85−2.56 (m, 1H), 2.55−2.26 (comp, 2H), 1.54−1.40 (comp, 9H), 1.23−1.18 (comp, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.0, 195.8, 175.8, 172.9, 155.6, 153.0, 148.2, 146.7, 130.5, 130.3, 85.2, 84.4, 82.6, 81.0, 80.8, 80.7, 59.6, 59.2, 58.5, 58.1, 42.2, 41.5, 37.5, 35.8, 28.4, 28.1, 26.7, 26.3; EI-HRMS: calculated for $C_{18}H_{27}NO_7$ (M + H), 370.18668; found, 370.18606.

*tert-Butyl (3aR,7aR)-3a-(tert-Butylperoxy)-6-oxo-2,3,3a,6,7,7a-hexahydro-1H-indole-1-carboxylate (**29**):* 358 mg, 55%, R_f 0.34 (EtOAc/DCM/hexane (1:1:4)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08−6.79 (m, 1H), 6.06 (d, J = 10.4 Hz, 1H), 4.77−4.50 (m, 1H), 3.70−3.41 (m, 2H), 3.24−2.96 (m, 1H), 2.51−2.31 (m, 1H), 2.31−2.19 (m, 1H), 2.19−2.02 (m, 1H), 1.46 (s, 9H), 1.21 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.0, 154.1, 148.9, 130.1, 86.1, 80.4, 80.1, 77.2, 58.7, 44.7, 42.7, 32.6, 28.4, 26.4; EI-HRMS: calculated for $C_{17}H_{27}NO_5$ (M + H), 326.19685; found, 326.19641. The enantiomeric excess was determined by HPLC on an AD-H column (97:3 hexanes/*i*-PrOH, 1.0 mL/min): t_R (major) = 7.04 min; t_R (minor) = 8.84 min.

*1-tert-Butyl 2-Methyl (2S,3aR,7aR)-3a-(tert-Butylperoxy)-6-oxo-2,3,3a,6,7,7a-hexahydro-1H-indole-1,2-dicarboxylate (**31**):* 132 mg, 35%, R_f 0.23 (EtOAc/DCM/hexane (1:1:4)); colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.94−6.85 (m, 1H), 6.09−6.03 (m, 1H), 4.85−4.61 (m, 1H), 4.55−4.39 (m, 1H), 3.81−3.71 (comp, 3H), 3.28−3.03 (m, 1H), 2.81−2.56 (comp, 2H), 2.27−2.11 (m, 1H), 1.47−1.39 (comp, 9H), 1.24−1.19 (comp, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.3, 196.1, 171.4, 170.5, 153.5, 153.0, 147.7, 146.9, 130.4, 130.1, 129.5, 125.7, 85.5, 84.3, 80.9, 80.8, 80.6, 80.5, 59.2, 58.2, 57.8, 52.1, 52.0, 42.7, 41.5, 37.6, 36.7, 28.4, 28.2, 26.3; EI-HRMS: calculated for $C_{19}H_{29}NO_7$ (M + H), 384.20222; found, 384.20319.

*1-tert-Butyl 2-Methyl (2S,3aS,7aS)-3a-(tert-Butylperoxy)-6-oxo-2,3,3a,6,7,7a-hexahydro-1H-indole-1,2-dicarboxylate (**32**):* 83 mg, 21%, R_f 0.31 (EtOAc/DCM/hexane (1:1:4)); colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.92−6.82 (m, 1H), 6.12−6.05 (m, 1H), 4.79−4.61 (m, 1H), 4.61−4.41 (m, 1H), 3.82−3.72 (comp, 3H), 3.40−3.14 (m, 1H), 2.67−2.51 (m, 1H), 2.51−2.42 (m, 1H), 2.41−2.27 (m, 1H), 1.53−1.40 (comp, 9H), 1.25−1.18 (comp, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.6, 196.2, 172.9, 172.8, 153.6, 153.0, 147.6, 146.9, 130.6, 130.4, 129.6, 125.8, 85.8, 85.0, 80.9, 80.6, 59.7, 59.6, 59.5, 59.0, 52.5, 52.3, 42.6, 42.2, 38.0, 37.3, 28.4, 28.2, 26.4, 26.3; EI-HRMS: calculated for $C_{19}H_{29}NO_7$ (M + H), 384.20222; found, 384.20352.

*Di-tert-butyl (2S,3aR,7aR)-3a-(tert-Butylperoxy)-6-oxo-2,3,3a,6,7,7a-hexahydro-1H-indole-1,2-dicarboxylate (**34**):* 176 mg, 41%, R_f 0.27 (EtOAc/hexane (1:5)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90−6.80 (m, 1H), 6.11−6.02 (m, 1H), 4.83−4.63 (m, 1H), 4.45−4.26 (m, 1H), 3.39−3.11 (m, 1H), 2.65−2.38 (comp, 2H), 2.39−2.28 (m, 1H), 1.52−1.40 (comp, 18H), 1.27−1.19 (comp, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.6, 196.4, 169.1, 168.8, 153.3, 153.3, 148.3, 147.7, 130.2, 130.0, 85.5, 84.4, 81.3, 81.0, 80.8, 80.7, 80.5, 80.3, 59.4, 59.3, 58.5, 58.4, 42.6, 41.7, 37.9, 37.0, 28.4, 28.2,

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28.1, 26.4, 26.4; EI-HRMS: calculated for $C_{22}H_{35}NO_7$ (M + H), 426.24896; found, 426.24793.

*Di-tert-butyl (2S,3aS,7aS)-3a-(tert-Butylperoxy)-6-oxo-2,3,3a,6,7,7a-hexahydro-1H-indole-1,2-dicarboxylate (**43**):* 88 mg, 21%, R_f 0.37 (EtOAc/hexane (1:5)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96−6.83 (m, 1H), 6.14−5.99 (m, 1H), 4.91−4.59 (m, 1H), 4.43−4.26 (m, 1H), 3.27−3.01 (m, 1H), 2.83−2.53 (comp, 2H), 2.25−2.07 (m, 1H), 1.53−1.40 (comp, 18H), 1.25−1.18 (comp, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.9, 196.5, 171.3, 171.2, 153.3, 153.2, 147.8, 147.3, 130.7, 130.4, 85.8, 84.9, 81.8, 81.7, 80.6, 80.5, 60.2, 60.1, 59.6, 42.5, 42.1, 38.2, 37.2, 28.3, 28.2, 27.9, 27.9, 26.3, 26.2; EI-HRMS: calculated for $C_{22}H_{35}NO_7$ (M + H), 426.24896; found, 426.24793.

*tert-Butyl (2S,3aR,7aR)-3a-(tert-Butylperoxy)-2-[(2-ethoxy-2-oxoethyl)amino]carbonyl-6-oxo-2,3,3a,6,7,7a-hexahydro-1H-indole-1-carboxylate (**36**):* 68 mg, 30%, R_f 0.16 (EtOAc/DCM/hexane (1:1:1)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (s, 1H), 7.01−6.82 (m, 1H), 6.76 (s, 1H), 6.07 (d, J = 10.4 Hz, 1H), 4.95−4.62 (m, 1H), 4.59−4.36 (m, 1H), 4.30−3.79 (comp, 4H), 3.53−3.16 (m, 1H), 2.88−2.13 (comp, 3H), 1.49 (comp, 9H), 1.28 (t, J = 7.1 Hz, 3H), 1.19 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.9, 195.5, 171.9, 170.8, 169.4, 168.4, 154.7, 153.2, 148.7, 147.5, 130.5, 130.0, 85.7, 85.2, 81.9, 81.5, 80.5, 61.4, 60.4, 59.9, 42.0, 41.7, 41.4, 40.7, 37.6, 35.9, 29.7, 28.3, 27.9, 26.4, 26.3, 14.1; EI-HRMS: calculated for $C_{22}H_{34}N_2O_8$ (M + H), 455.23947; found, 455.24020.

*(2S,3aR,7aR)-tert-Butyl 3a-(tert-Butylperoxy)-2-(((S)-1-methoxy-1-oxo-3-phenylpropan-2-yl)carbamoyl)-6-oxo-2,3,3a,6,7,7a-hexahydro-1H-indole-1-carboxylate (**38**):* 30 mg, 13%, R_f 0.35 (EtOAc/DCM/hexane (1:1:1)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69−6.64 (comp, 7H), 6.14−5.97 (m, 1H), 5.02−4.26 (comp, 3H), 3.76−3.59 (comp, 3H), 3.49−2.74 (comp, 4H), 2.59−2.13 (comp, 2H), 1.55−1.32 (comp, 9H), 1.30−1.06 (comp, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.9, 195.7, 171.7, 171.5, 170.9, 170.3, 155.0, 154.9, 148.9, 148.8, 147.8, 147.5, 136.3, 136.0, 85.7, 85.2, 81.8, 80.6, 80.5, 60.1, 60.0, 59.8, 56.1, 54.0, 53.8, 52.0, 51.8, 42.4, 41.9, 38.4, 38.3, 37.8, 37.7, 35.6, 35.3, 28.4, 28.3, 28.0, 26.7, 26.4, 26.3; EI-HRMS: calculated for $C_{28}H_{38}N_2O_8$ (M + H), 531.27079; found, 531.26927.

*(2S,3aS,7aS)-tert-Butyl 3a-(tert-Butylperoxy)-2-(((S)-1-methoxy-1-oxo-3-phenylpropan-2-yl)carbamoyl)-6-oxo-2,3,3a,6,7,7a-hexahydro-1H-indole-1-carboxylate (**44**):* 103 mg, 39%, R_f 0.46 (EtOAc/DCM/hexane (1:1:1)); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65−6.65 (comp, 5H), 6.17−6.03 (m, 1H), 4.94−4.29 (comp, 3H), 3.77−3.58 (comp, 3H), 3.48−3.25 (comp, 2H), 3.19−2.86 (comp, 2H), 2.62−2.25 (comp, 2H), 1.59−1.53 (m, 1H), 1.51−1.37 (comp, 9H), 1.29−1.20 (comp, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.0, 196.8, 168.6, 167.5, 153.7, 153.4, 147.4, 146.5, 130.6, 130.1, 129.3, 128.4, 84.8, 83.3, 80.9, 80.7, 80.6, 80.1, 60.1, 59.6, 58.9, 56.2, 52.0, 46.2, 43.5, 42.0, 40.0, 38.6, 38.2, 37.2, 28.4, 28.3, 26.4, 25.6, 24.6; EI-HRMS: calculated for $C_{28}H_{38}N_2O_8$ (M + H), 531.27079; found, 531.26875.

General Procedure for Asymmetric Intramolecular Michael Addition. 4-(*tert*-Butylperoxy)cyclohexa-2,5-dienones (0.10 mmol), chiral phosphoric acid (0.010 mmol, 0.1 equiv), and dry DCM (0.25 mL) were added under nitrogen to an oven-dried 1-dram screw-cap vial containing a magnetic stirring bar, and the reaction was stirred for 20 h at room temperature. The suspension was stirred overnight at room temperature and then transferred to a 100-mL round-bottom flask, concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel, DCM/AcOEt/hexane). Fractions containing the product were combined, and the solvent was evaporated under reduced pressure. The peroxide product was dried under high vacuum for 20 min (0.09 Torr, room temperature).

General Procedure for Dialkylperoxide 16 Cleavage by Lewis Acids. Peroxide **16** (0.30 mmol, 68 mg) and dry DCM (1.5 mL) were placed under nitrogen in an oven-dried 5-mL round-bottom flask capped with a septum. The Lewis acid (0.60 mmol) was slowly added to the solution at room temperature, and the reaction was stirred for 4 h at room temperature. A light brown precipitate formed after 30 s. The suspension was poured into an aqueous 5% solution of Na_2CO_3 (9 mL), the organic layer was separated, and the aqueous layer was washed with AcOEt (3 × 15 mL). The organic layers were combined, dried over Na_2SO_4, and the solvent was evaporated on rotary evaporator to yield cleroindicin F **42** as a colorless liquid (38 mg, 81%) that matched the previously reported ^{1}H NMR spectrum.[10c]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Optimization procedures and NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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