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Scandium Triflate Catalyzed Nazarov Cyclization of Arylvinyl Epoxides Derived from Alkoxides and Chloro(aryl)carbenes: A Facile Access to Resveratrol-Derived Natural Products

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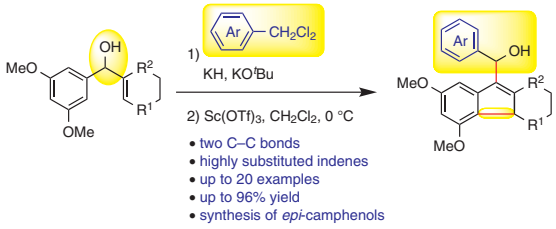

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Abstract The reaction of arylvinyl alkoxides with chloro(aryl)carbenes provided the corresponding arylvinyl epoxides that underwent Nazarov cyclization in a catalytic amount of scandium triflate, providing easy access to several highly substituted indenes, including some resveratrol-derived natural products.

Key words Nazarov cyclization, arylvinyl alcohol, arylvinyl epoxides, indenes, resveratrol-derived natural products, scandium triflate, chloro(aryl)carbenes

Resveratrol and its oligomers are a highly diverse and privileged class of natural products and are found to exhibit a wide range of biological activities[1] such as antioxidants,[2] anticancer,[3] antidiabetic,[4] cardioprotective,[5] and anti-aging properties.[6] Some Japanese and Chinese folk medicines, which are in a high concentration of resveratrol related compounds, are used to treat ailments related to the liver, skin, heart, and lipid metabolism.[7] The resveratrol monomer is oligomerized to form dimers, trimers, tetramers, and higher-order oligomers, generally up to 8 resveratrol units and these polyphenolic metabolites mainly act as biological defense agents similar to many other secondary metabolites in plants.[8] Pharmacological significance and dimeric skeletons to architecturally complex oligomers from simple resveratrol have been intriguing to the chemical community, thriving to isolate more than 300 resveratrol oligomers having dihydrobenzofuran and indane moieties and bicyclic [3.2.1] and [3.3.0] ring systems.[9] Out of all structural patterns, an indane skeleton containing resveratrol-based natural products (**I**–**XIV**, Figure 1), originated from dimers or substituted dimers of resveratrol, are given particular interest from a synthetic standpoint. Understanding biosynthetic pathways and developing general synthetic strategies that overcome these natural products' scarcity by isolation were initial aims to address. Synthetic attempts based on the proposed biosynthetic pathways were not satisfactory, often giving unselective and natural and unnatural compounds.[10] However, some synthetic strategies addressed these problems, and some managed to get a common intermediate, thereby accessing a reasonable number of natural products of this class.[11]

Given our ongoing interest in novel electrocyclization precursors,[12] we have reported converting arylvinyl ketones into arylvinyl oxiranes and utilizing them to synthesize various highly substituted indenes.[12e] Further, the synthesis of **3**, which was obtained from arylvinyl ketone **1** in 4 steps (Scheme 1A), served as an advanced intermediate for the total synthesis of resveratrol-based natural products, (±)-isoampelopsin D (**I**), and (±)-the proposed structure of caraphenol B (**V**).[12e] Nevertheless, in the present study, we have envisioned that compound **3** could be obtained from **1** via arylvinyl oxirane **2**, if successful affording **3** only in two steps, as illustrated in Scheme 1B. Herein we report a novel method to access indene derivatives, including resveratrol-based natural products, in a highly simplified manner.

Before we embark on precursors that yield resveratrol-derived natural products, we have prepared a model substrate **1a** in two steps to evaluate the anticipated outcome. First, reacting 3,5-dimethoxybezaldehyde (**7**) and (3-methylbut-2-en-2-yl)magnesium bromide followed by oxidation of the resulted **8a** afforded **1a** (Scheme 2). Compound **1a** was also achieved from compound **9** via compound **10** following our previous report.[12b]

At the outset, treating compound **1a** with benzal bromide in a trap solvent system (THF/diethyl ether/pentane, 4:1:1)[13] at –120 °C resulted in **2a** with a lower yield (Table 1, entry 1). Whereas temperatures at –110 °C and –78 °C provided little improved yields of **2a** (entries 2 and 3). THF or diethyl ether in place of trap solvent diminished the

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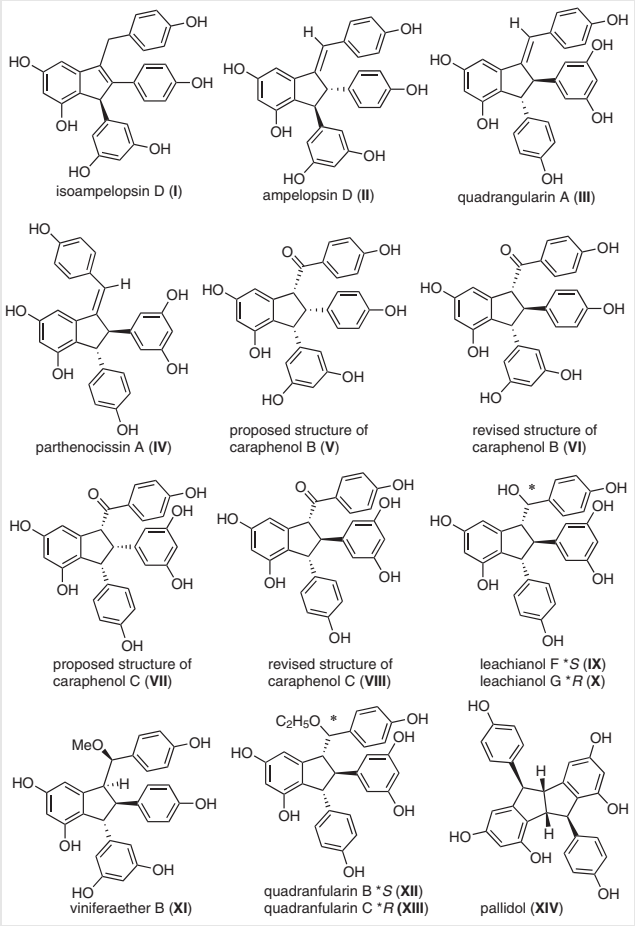
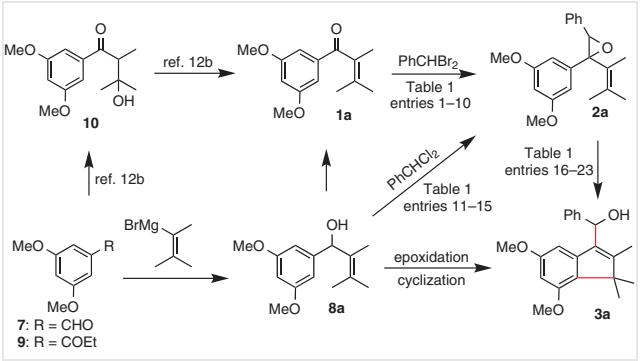


Figure 1 Resveratrol based natural products **I–XIV**

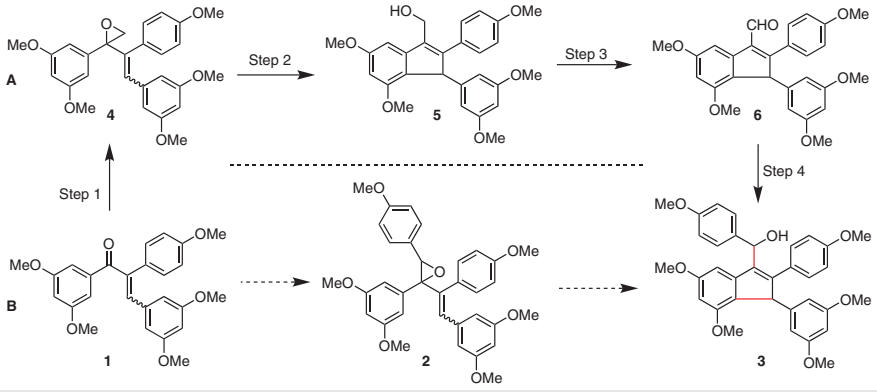


Scheme 2 Synthesis of **8a** and **1a** and converting them into **3a** via **2a**

product formation (entries 4 and 5). Conversely, the reaction in CH_2Cl_2 at –78 °C provided **2a** in moderate yield (entry 6). In order to further improve the yield in CH_2Cl_2, we have checked with raising the temperature (at 0 °C or 25 °C) and changing the base from *n*-BuLi to *s*-BuLi and *t*-BuLi, but observed only unsatisfactory yields (entries 7–10).

We found an interesting report in the literature at this stage, converting allylic or benzylic alcohols into an oxirane using dichlorocarbene and chlorophenylcarbene.[14] Inspired by this work, we have envisioned that under similar reaction conditions, **3a** could be obtained directly from **8a**. If successful, this would further simplify the synthesis of advanced intermediate **3a** or its analogues, allowing several indane moiety resveratrol-based natural products. Gratifyingly, the subjection of **8a** to benzal chloride ($PhCHCl_2$)[15] in the presence of KH and KO*t*-Bu in THF at 0 °C provided **2a** in 29% yield (Table 1, entry 11). Two equivalents of benzal chloride under the same conditions doubled the **2a** formation (entry 12) and obtained **2a** in a similar yield (entry 13), even doubling both benzal chloride and bases (KH and KO*t*-Bu). Pleasingly, the optimum yield (90%) of **2a** was obtained with 2.5 equivalents of benzal chloride, KH, and KO*t*-Bu (entry 14).[16] However, additional excess equivalents of benzal chloride and bases suppressed **2a** yield (62%, entry 15), likely the decomposition of formed product **2a** due to excess base.

With optimized reaction conditions for **2a** in hand, next, we turned our attention to the conversion of **2a** into **3a**, shown in Table 1 (entries 16–23). First, with Brønsted acid TFA, **2a** produced **3a** in a 27% yield (Table 1, entry 16). The



Scheme 1 (**A**) Our previous synthetic plan; (**B**) present plan

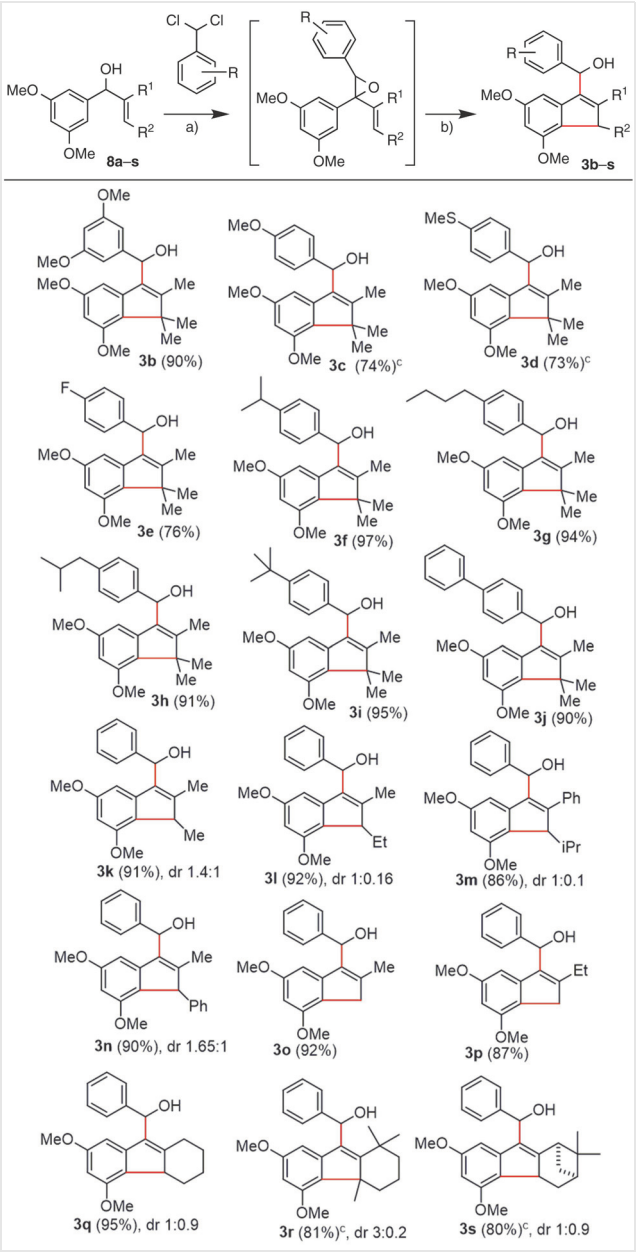
Table 1 Optimization of Reaction Conditions for **2a** and **3a**

Entry	Substrates	Reagent (equiv)	Solvent	Temp (°C)	Time (min)	Yield of **2a** and **3a** (%)
1	**1a** and $PhCHBr_2$ (1.2)	*n*-BuLi (1.2)	ts[a]	–120	5	**2a** (10)
2	**1a** and $PhCHBr_2$ (1.2)	*n*-BuLi (1.2)	ts[a]	–110	5	**2a** (20)
3	**1a** and $PhCHBr_2$ (1.2)	*n*-BuLi (1.2)	ts[a]	–78	5	**2a** (20)
4	**1a** and $PhCHBr_2$ (1.2)	*n*-BuLi (1.2)	THF	–78	60	**2a** (0)
5	**1a** and $PhCHBr_2$ (1.2)	*n*-BuLi (1.2)	Et_2O	–78	60	**2a** (0)
6	**1a** and $PhCHBr_2$ (1.2)	*n*-BuLi (1.2)	CH_2Cl_2	–78	5	**2a** (40)
7	**1a** and $PhCHBr_2$ (1.2)	*n*-BuLi (1.2)	CH_2Cl_2	0	5	**2a** (20)
8	**1a** and $PhCHBr_2$ (1.2)	*n*-BuLi (1.2)	CH_2Cl_2	25	5	**2a** (15)
9	**1a** and $PhCHBr_2$ (1.2)	*s*-BuLi (1.2)	CH_2Cl_2	–78	5	**2a** (15)
10	**1a** and $PhCHBr_2$ (1.2)	*t*-BuLi (1.2)	CH_2Cl_2	–78	5	**2a** (10)
11	**8a** and $PhCHCl_2$ (1.0)	KH/KO*t*-Bu (1:1)	THF	0	10	**2a** (29)[b]
12	**8a** and $PhCHCl_2$ (2.0)	KH/KO*t*-Bu (1:1)	THF	0	10	**2a** (58)[b]
13	**8a** and $PhCHCl_2$ (2.0)	KH/KO*t*-Bu (2:2)	THF	0	10	**2a** (59)[b]
14	**8a** and $PhCHCl_2$(2.5)	KH/KO*t*-Bu (2.5:2.5)	THF	0	10	**2a** (90)
15	**8a** and $PhCHCl_2$(3.0)	KH/KO*t*-Bu (3.0:3.0)	THF	0	10	**2a** (62)
16	**2a**	TFA (0.1)	CH_2Cl_2	0	10	**3a** (27)[b]
17	**2a**	$TiCl_4$ (0.1)	CH_2Cl_2	0	10	**3a** (50)
18	**2a**	$BF_3{\cdot}OEt_2$ (0.1)	CH_2Cl_2	0	10	**3a** (20)
19	**2a**	$Cu(OTf)_2$ (0.1)	CH_2Cl_2	0	50	**3a** (45)[b]
20	**2a**	$AlCl_3$ (0.1)	CH_2Cl_2	0	10	**3a** (32)[b]
21	**2a**	$Sc(OTf)_3$ (0.1)	CH_2Cl_2	0	45	**3a** (96)
22	**2a**	$Sc(OTf)_3$ (0.3)	CH_2Cl_2	0	45	**3a** (92)
23	**2a**	$Sc(OTf)_3$ (0.5)	CH_2Cl_2	0	45	**3a** (90)

[a] Compounds **1a**, **8a**, and **2a** were used in 1 equiv each in appropriate solvents: trap solvent (ts) THF/diethyl ether/pentane (4:1:1), CH_2Cl_2, and THF in 0.3 M concentration.
[b] Based on recovery of the starting material.

reaction of **2a** with Lewis acids, $TiCl_4$, and $BF_3{\cdot}OEt_2$ provided **3a** in 50% and 20% yields, respectively (entry 17 and 18). Treatment of **2a** with other Lewis acids, $Cu(OTf)_2$ or $AlCl_3$, also provided similar yields (entries 19 and 20). However, the subjection of **2a** to $Sc(OTf)_3$ dramatically improved yield, affording **3a** in 96% (entry 21).[16] Increasing $Sc(OTf)_3$ quantity slightly lowered the yields (entries 22 and 23).

Having had optimum reaction conditions for both key reactions in hand, we have surveyed the substrate scope with various benzal chlorides and different substitutions on arylvinyl alcohols (R^1 and R^2), as depicted in Scheme 3. First, reacting 3,5-dimethoxybenzal chloride with **8a** under standard reaction conditions furnished the corresponding product **3b** in a 90% yield. Benzal chloride with electron-donating groups/atoms such as –OMe, -SMe, and -F at *para* position lowered the yields, obtaining **3c–e** in 74–76% yield based on the recovery of the starting material (brsm). This implies that chlorophenyl carbenes having electron-donating groups at the *para* position are less effective than the simple phenyl in this reaction. Furthermore, under standard reaction conditions, electron-withdrawing groups such as $–NO_2$, –CN on benzal chloride failed to provide the corresponding product **3**, it appears that electron-withdrawing groups are detrimental to this reaction. Nonetheless, various alkyl substitutions such as *i*-Pr, *n*-Bu, *i*-Bu, and *t*-Bu at the *para* position delivered **3f–i** in excellent yields (91–97%). A phenyl substitution containing biphenyl derivative is also equally competitive in providing **3j** in 90% yield. Then, the substrate scope with substitutions on the R^2 position of arylvinyl alcohols **8** was verified. Either alkyl substitutions (Me, Et, and *i*-Pr) or aryl (Ph) substitution delivered the corresponding indene derivatives **3k–n** in good yields. Additionally, substrates without any substitution at R^2 position were also competitive to deliver expected indene derivatives, affording **3o** and **3p** in comparable yields. Moreover, tricyclic frameworks **3q** and **3r**, which are more complex indene derivatives in this series and structurally similar to taiwaniaquinoids,[17] were also achieved from this method. Interestingly, tetracyclic framework compound **3s** was also accessed from the corresponding arylvinyl alcohol in good yields (Scheme 3).



Scheme 3 Substrate scope (synthesis of **3b–s**). *Reagents and conditions*: $RPhCHCl_2$, KH, KO*t*-Bu, THF, 0 °C; b) $Sc(OTf)_3$, CH_2Cl_2, 0 °C; c) based on recovery of the starting materials (brsm).

Then, applying this method to synthesize resveratrol-based natural products is planned (Scheme 4). Accordingly, the advanced intermediates (**3t** and **3u**) were envisioned with the expectation of achieving this class of natural products from a divergent synthetic approach. First, **2t** was prepared in 73% yield from reacting **8t** under optimized reaction conditions, and the subsequent indene-formation step under optimized conditions resulted in low yields of **3t**. Changing the Lewis acid from $Sc(OTf)_3$ to $TiCl_4$ surmounted this problem, furnishing **3t** in 89% yield. Spectral data of **3t** has well resembled with data reported previously,[12e] which is becoming a formal synthesis for (±)-isoampelopsin D (**I**), and the proposed structure of (±)-caraphenol B (**V**)/*epi*-caraphenol B.[11d]

Afterwards, similarly, **3u** was prepared in 69% yield from **8u**. This advanced intermediate **3u** was subjected to DMP to give the corresponding enone **11** in 87% yield. Subsequently, hydrogenation on compound **11** resulted in permethylated *epi*-caraphenol C **12** in 91% yield. The data of **12** is in good agreement with the data reported in the literature,[11d] which turns into a formal synthesis of the proposed structure of (±)-caraphenol C (**VII**)/*epi*-caraphenol C.

In conclusion, we have developed a novel method to highly substituted indenes from arylvinyl alcohols via arylvinyl oxiranes. The method's scope was demonstrated by preparing several substrates including accessing some advanced intermediates of resveratrol-derived natural products in a highly efficient manner. Further application of this method in a variety of other natural products is in progress.

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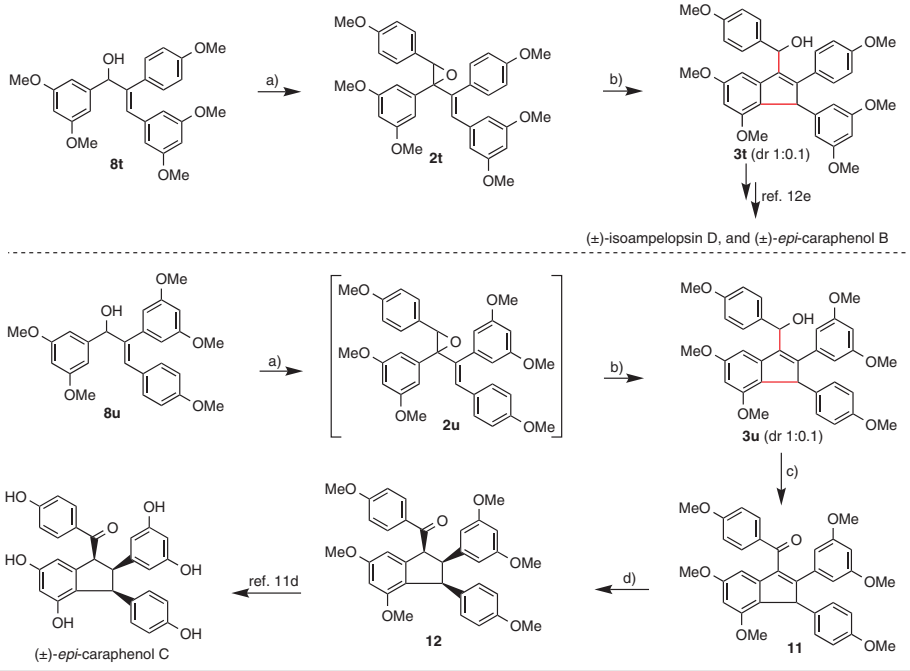
Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1705974.

References and Notes

(1) Keylor, M. H.; Matsuura, B. S.; Stephenson, R. *J. Chem. Rev.* **2015**, *115*, 8976.
(2) He, S.; Yan, X. *Curr. Med. Chem.* **2013**, *20*, 1005.
(3) (a) Jang, M.; Cai, L.; Udeani, G. O.; Slowing, K. V.; Thomas, C. F.; Beecher, C. W. W.; Fong, H. H. S.; Farnsworth, N. R.; Kinghorn, A. D.; Mehta, R. G.; Moon, R. C.; Pezzuto, J. M. *Science* **1997**, *275*, 218. (b) Xiao, Q.; Zhu, W.; Feng, W.; Lee, S. S.; Leung, A. W.; Shen, J.; Gao, L.; Xu, C. *Front. Pharmacol.* **2019**, *9*, 1534.
(4) (a) Banks, A. S.; Kon, N.; Knight, C.; Matsumoto, M.; Gutiérrez-Juárez, R.; Rossetti, L.; Gu, W.; Accili, D. *Cell Metab.* **2008**, *8*, 333. (b) Milne, J. C.; Lambert, P. D.; Schenk, S.; Carney, D. P.; Smith, J. J.; Gagne, D. J.; Jin, L.; Boss, O.; Perni, R. B.; Vu, C. B.; Bemis, J. E.; Xie, R.; Disch, J. S.; Ng, P. Y.; Nunes, J. J.; Lynch, A. V.; Yang, H.; Galonek, H.; Israelian, K.; Choy, W.; Iffland, A.; Lavu, S.; Medvedik, O.; Sinclair, D. A.; Olefsky, J. M.; Jirousek, M. R.; Elliott, P. J.; Westphal, C. H. *Nature* **2007**, *450*, 712.
(5) Frankel, E. N.; Waterhouse, A. L.; Kinsella, J. E. *Lancet* **1993**, *341*, 1103.
(6) Baur, J. A.; Pearson, K. J.; Price, N. L.; Jamieson, H. A.; Lerin, C.; Kalra, A.; Prabhu, V. V.; Allard, J. S.; Lopez-Lluch, G.; Lewis, K.; Pistell, P. J.; Poosala, S.; Becker, K. G.; Boss, O.; Gwinn, D.; Wang,



Scheme 4 Formal synthesis of *epi*-caraphenol B, isoampelopsine D, and *epi*-caraphenol C. *Reagents and conditions*: a) *p*-MeOPhCHCl$_2$, KH, KO*t*-Bu, THF, 0 °C, 73–79%; b) $TiCl_4$, CH_2Cl_2, –78 °C, 89%; c) DMP, CH_2Cl_2, 0 °C to rt, 2 h, 87%; d) H_2/Pd-C, MeOH, EtOAc, Et_3N, 1 h, 91%.

M.; Ramaswamy, S.; Fishbein, K. W.; Spencer, R. G.; Lakatta, E. G.; Le Couteur, D.; Shaw, R. J.; Navas, P.; Puigserver, P.; Ingram, D. K.; de Cabo, R.; Sinclair, D. A. *Nature* **2006**, *444*, 337.

(7) Nonomura, S.; Kanagawa, H.; Makimoto, A. *Yakugaku Zasshi* **1963**, *83*, 988.

(8) (a) Langcake, P.; Pryce, R. J. *Physiol. Plant Pathol.* **1976**, *9*, 77. (b) Langcake, P.; McCarthy, W. V. *Vitis* **1979**, *18*, 244.

(9) Xiao, K.; Zhang, H.-J.; Xuan, L.-J.; Zhang, J.; Xu, Y.-M.; Bai, D.-L. In *Studies in Natural Products Chemistry, Bioactive Natural Products, Part N, Vol. 34*; Atta-ur-Rahman, Ed.; Elsevier: New York, **2008**, 453–646.

(10) (a) Aguirre, J. M.; Alesso, E. N.; Iglesias, G. Y. M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1353. (b) Li, X.-C.; Ferreira, D. *Tetrahedron* **2003**, *59*, 1501. (c) Takaya, Y.; Terashima, K.; Ito, J.; He, Y.-H.; Takeoka, M.; Yamaguchi, N.; Niwa, M. *Tetrahedron* **2005**, *61*, 10285. (d) Langcake, P.; Pryce, R. J. *J. Chem. Soc., Chem. Commun.* **1977**, 208. (e) Sako, M.; Hosokawa, H.; Ito, T.; Iinuma, M. *J. Org. Chem.* **2004**, *69*, 2598. (f) Wenling, L.; Li, H.; Li, Y.; Hou, Z. *Angew. Chem. Int. Ed.* **2006**, *45*, 7609.

(11) (a) Klotter, F.; Studer, A. *Angew. Chem. Int. Ed.* **2014**, *53*, 2473. (b) Li, W.; Yang, S.; Lv, T.; Yang, Y. *Org. Biomol. Chem.* **2014**, *12*, 2273. (c) Zhong, C.; Zhu, J.; Chang, J.; Sun, X. *Tetrahedron Lett.* **2011**, *52*, 2815. (d) Snyder, S. A.; Brill, Z. G. *Org. Lett.* **2011**, *13*, 5524. (e) Keffrey, J. L.; Sarpong, R. *Org. Lett.* **2009**, *11*, 5450. (f) Snyder, S. A.; Breazzano, S. P.; Ross, A. G.; Lin, Y.; Zografos, A. L. *J. Am. Chem. Soc.* **2009**, *131*, 1753. (g) Jeffrey, J. L.; Sarpong, R. *Tetrahedron Lett.* **2009**, *50*, 1969. (h) Snyder, S. A.; Zografos, L.; Lin, Y. *Angew. Chem. Int. Ed.* **2007**, *46*, 8186.

(12) (a) Mahesh, S. K.; Nanubolu, J. B.; Sudhakar, G. *J. Org. Chem.* **2019**, *84*, 7815. (b) Sudhakar, G.; Mahesh, S. K.; Vemulapalli, S. P. B.; Nanubolu, J. B. *Org. Lett.* **2017**, *19*, 4500. (c) Sudhakar, G.; Raghavaiah, J.; Mahesh, G.; Singarapu, K. K. *Org. Biomol. Chem.* **2016**, *14*, 2866. (d) Sudhakar, G.; Reddy, K. J.; Nanubolu, J. B. *Org. Biomol. Chem.* **2015**, *13*, 8875. (e) Sudhakar, G.; Satish, K. *Chem. Eur. J.* **2015**, *21*, 6475.

(13) (a) Zhao, Y.; Kang, J.; Park, C.-M.; Bagdon, P. E.; Peng, B.; Xian, M. *Org. Lett.* **2014**, *16*, 4536. (b) Hoffmann, R. W.; Brumm, K.; Bewersdorf, M.; Mikolaiski, W.; Kusche, A. *Chem. Ber.* **1992**, *125*, 2741.

(14) Harada, T.; Akiba, E.; Oku, A. *J. Am. Chem. Soc.* **1983**, *105*, 2771.

(15) (a) Chen, J.; Lin, J.-H.; Xiao, J.-C. *Org. Lett.* **2018**, *20*, 3061. (b) Kaballa, G. W.; Wu, Z. *Tetrahedron Lett.* **2000**, *41*, 579. (c) Han, G. Y.; Han, P. F.; Perkins, J.; McBay, H. C. *J. Org. Chem.* **1981**, *46*, 4695.

(16) **Typical Procedure for the Synthesis of 2**

To a mixed suspension of potassium hydride (2.5 equiv) and potassium *tert*-butoxide (2.5 equiv) in THF was added a THF (2.5 mL) solution of **8** (1.0 equiv), and the mixture was stirred at 0 °C under an argon atmosphere for 5 min after that was added a THF (2.5 mL) solution of benzal chloride (2.5 equiv). After completing the starting material, the reaction was quenched with aq NH_4Cl and extracted with EtOAc. The organic layer was washed with aq NaCl, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by using basic Al_2O_3 column chromatography to isolate **2**.

Characterization Data of 2a

123.5 mg, 90% yield, *dr* 1:1 based on ^{1}H NMR spectroscopy. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.25–7.14 (m, 5 H), 6.41 (d, *J* = 2.3 Hz, 2 H), 6.22 (t, *J* = 2.3 Hz, 1 H), 4.37 (s, 1 H), 3.66 (s, 6 H), 2.08 (s, 3 H), 1.76 (s, 3 H), 1.74 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 139.1, 135.3, 128.9, 128.7, 127.8, 127.5, 126.7, 105.8, 99.2, 69.6, 68.3, 55.2, 22.5, 20.3, 15.0. IR (neat): ν_{max} = 2927, 1594, 1454, 1425, 1345, 1202, 1152, 1063, 842, 737, 697. HRMS (ESI): *m/z* calcd for $C_{21}H_{25}O_3$ [M + H]: 325.1798; found: 325.1791.

Typical Procedure for the Synthesis of 3

To a stirred solution of above-obtained **2** (1.0 equiv) in dry CH_2Cl_2 (3.7 mL) was added $Sc(OTf)_3$ (0.1 equiv) at 0 °C, and stirring was continued at the same temperature. After completing the starting material, the reaction was quenched with water or saturated aq $NaHCO_3$ solution and extracted with CH_2Cl_2. The organic layer was washed with aq NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by using silica gel column chromatography (EtOAc/hexanes) to give **3**.

Characterization Data of 3a

118 mg, 96% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 7.6 Hz, 2 H), 7.3 (t, *J* = 7.6 Hz, 2 H), 7.2 (t, *J* = 7.6 Hz, 1 H), 6.34 (d, *J* = 2.0 Hz, 1 H), 6.15 (d, *J* = 2.0 Hz, 1 H), 5.93 (s, 1 H), 3.73 (s, 3 H), 3.58 (s, 3 H), 2.1 (br s, 1 H), 1.92 (s, 3 H), 1.32 (s, 3 H), 1.30 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.9, 155.7, 153.2, 143.2, 142.4, 134.2, 131.5, 128.3, 126.9, 125.7, 98.5, 95.2, 69.4, 55.4, 55.1, 50.3, 21.8, 21.2, 9.9. IR (neat): ν_{max} = 3395, 2956, 2925, 2855, 1595, 1454, 1349, 1203, 1152, 1090, 699. HRMS (ESI): *m/z* calcd for $C_{21}H_{23}O_2$ [M – OH]: 307.1698; found: 307.1692.

(17) Majetich, G.; Shimkus, J. M. *J. Nat. Prod.* **2010**, *73*, 284.