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BF2OBn·OEt2: A Novel Lewis Acid and its use in a Regio- and Stereo-selective Opening of Trisubstituted Epoxides and its Application Towards Amphidinolide C

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$BF_2OBn{\cdot}OEt_2$: A Novel Lewis Acid and its use in a Regio- and Stereo-selective Opening of Trisubstituted Epoxides and its Application Towards Amphidinolide C and F

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Keywords: Lewis Acid / Epoxide Opening / Shi Epoxidation / $BF_2OBn{\cdot}OEt_2$ / amphidinolide

The generation of a novel Lewis acid ($BF_2OBn{\cdot}OEt_2$) has been reported and its usefulness has been demonstrated in the regio- and stereo- selective opening of trisubstituted epoxides. This Lewis acid is one in a series of novel Lewis acids generated from $BF_3{\cdot}OEt_2$ displaying varying levels of Lewis acidity. When paired with a modified Shi epoxidation protocol highly functionalized propionate units such as those found in a wide variety of natural products can be accessed. This procedure, in conjunction with the Mukaiyama oxidative cyclization employing our second generation catalyst, $Co(nmp)_2$, ultimately culminated in the shortest and highest yielding route towards the methyl substituted *trans*-THF fragment present in amphidinolide C, C2, and F.

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Introduction

The synthesis of amphidinolide C (**1**, Figure 1) has been approached by many groups, resulting in the completion of several fragments, but no total synthesis has been reported to date.[1,2] In particular, the C(1)-C(9) fragment has attracted considerable synthetic attention due to its stereochemical complexity. It contains a methyl substituted *trans*-THF ring, an *anti*-diol and an exocyclic olefin that is part of an unusual diene system. An efficient and concise synthesis of the methyl substituted *trans*-THF ring will be central to the total synthesis of amphidinolide C. Herein we describe a short synthesis of the C(1)-C(7) fragment of amphidinolide C featuring a novel Lewis acid and an aerobic oxidative cyclization to form the *trans*-THF ring.

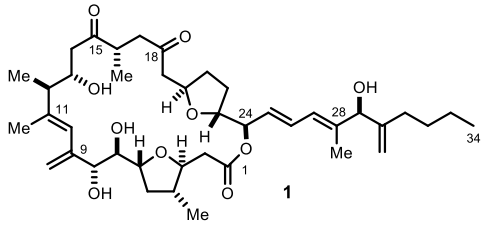
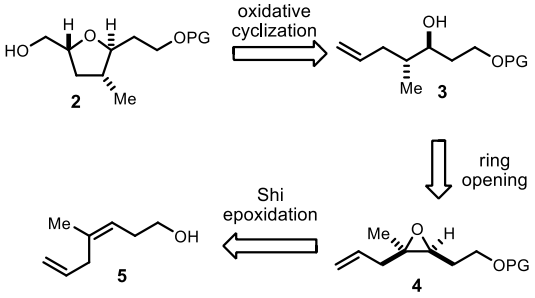


Figure 1. Amphidinolide C

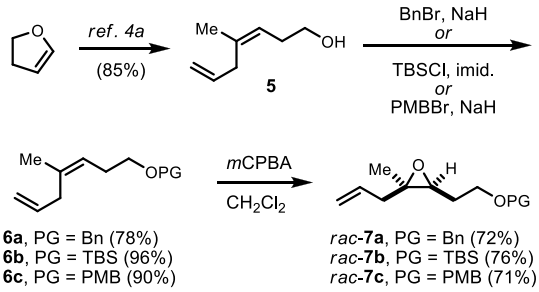
Our recent work on the Mukaiyama oxidative cyclization and development of a second generation catalyst, $Co(nmp)_2$, has resulted in a general and high yielding synthesis of *trans*-THF rings from their corresponding 4-pentenols.[3] With that in mind, the initial retrosynthetic disconnection was the formation of the *trans*-THF ring **2** via cyclization of the methyl substituted pentenol **3** (Scheme 1). This key synthetic intermediate was proposed to be secured by a regio- and stereo- selective ring opening of epoxide **4**, which would be accessed using a Shi epoxidation of diene **5**.



Scheme 1. Retrosynthetic analysis

Results and Discussion

The synthesis began with unsaturated alcohol **5**, which was prepared via a 1,2-metallate rearrangement of dihydrofuran in a one pot procedure (Scheme 2).[4] The resulting alcohol (**5**) was functionalized with a variety of protecting groups, followed by epoxidation using *m*CPBA, generating a set of racemic epoxides to evaluate the subsequent ring opening.



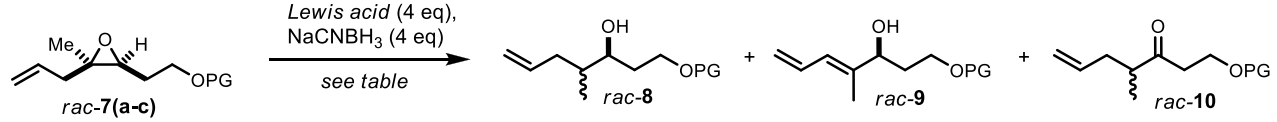
6a, PG = Bn (78%)
6b, PG = TBS (96%)
6c, PG = PMB (90%)

rac-**7a**, PG = Bn (72%)
rac-**7b**, PG = TBS (76%)
rac-**7c**, PG = PMB (71%)

Scheme 2. Synthesis of trisubstituted epoxides *rac*-**7a**, *rac*-**7b**, and *rac*-**7c**

The conversion of the mono-epoxides (**7a**-**7c)** to the desired alcohols required a regioselective hydride delivery at the more hindered carbon. Initially, the Hutchins protocol, which has been reported to proceed via apparent S_N2 reaction with inversion of

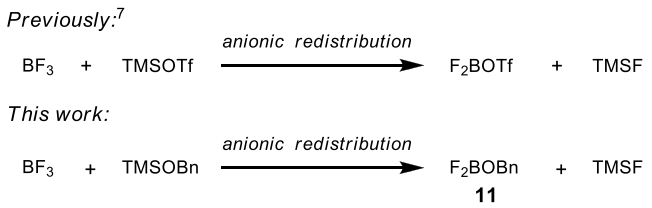
Table 1. Epoxide opening results



Entry	Epoxide	Lewis Acid (4 eq)	Solvent	Addition Time (h)	Yield of **8** (%)	Yield of **9** (%)	Yield of **10** (%)	d.r of **8** (*anti*:*syn*)
1	**7a**	$BF_3{\cdot}OEt_2$	THF	-	20	-	-	2:1
2	**7b**	$BF_3{\cdot}OEt_2$	CH_2Cl_2	3	-	99	-	-
3	**7a**	$BF_3{\cdot}OEt_2$	THF	0.5	50	-	25	2:1
4	**7a**	$BF_3{\cdot}OEt_2$	THF	3	65	-	15	2:1
5	**7c**	$BF_3{\cdot}OEt_2$	Et_2O	-	23	-	-	2:1
6	**7c**	$BF_3{\cdot}OEt_2$	Et_2O	0.5	51	-	-	2:1
7	**7c**	$BF_3{\cdot}OEt_2$	Et_2O	3	66	-	-	2:1
8	**7c**	$BF_3{\cdot}OEt_2$	Et_2O	4	90	-	-	2:1
9	**7c**	$InBr_3$	Et_2O	-	0[a]	-	-	-
10	**7c**	BEt_3	Et_2O	4	0[a]	-	-	-
11	**7c**	$BF_2OBn{\cdot}OEt_2$ (**11**)	Et_2O	4	91	-	-	>20:1

a) starting material recovered

stereochemistry, was explore.[5] Unfortunately, treatment of epoxide **7a** under the standard conditions ($BF_3{\cdot}OEt_2$, $NaCNBH_3$) gave results consistent with premature epoxide opening, with reactions of the presumed carbocation intermediate giving rise to an unfavorable mixture of diastereomers from S_N1 hydride delivery (*rac*-**8**, Table 1, entry 1), elimination (*rac*-**9**, Table 1, entry 2) or a pinacol-like hydride shift (*rac*-**10**, Table 1, entries 3-4). Reactions run in diethyl ether with slow addition of the Lewis acid resulted in an increase in yield but no further improvement in the diastereomeric ratio (Table 1, entries 5-8). A variety of Lewis acids were screened to achieve the desired transformation, without success (Table 1, entries 9-10).[6] Ultimately, it was decided to modify $BF_3{\cdot}OEt_2$ by attenuating its Lewis acidity through anionic redistribution wherein one of the fluorines would be replaced with a less electronegative group. We had previously seen success with this strategy with the more Lewis acidic species $BF_2OTf{\cdot}OEt_2$ and $BF_2OMs{\cdot}OEt_2$ (Scheme 3), which were used in the direct reduction of esters to ethers.[7] Thus, treatment of $BF_3{\cdot}OEt_2$ with TMSOBn generated the modified Lewis acid $BF_2OBn{\cdot}OEt_2$ (**11**) that displayed a ^{19}F NMR signal at −151.5 ppm that is indicative of decreased Lewis acidity compared to the $BF_3{\cdot}OEt_2$ (Scheme 3).[8]

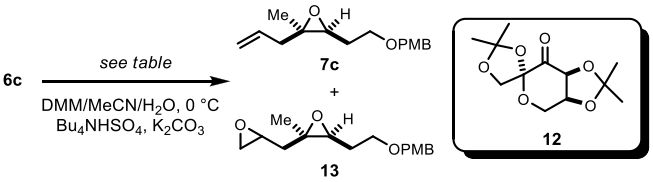


Scheme 3. Generation of two novel Lewis acids by anionic redistribution of $BF_3{\cdot}OEt_2$

Gratifyingly, **11** displayed sufficient Lewis acidity to efficiently facilitate the desired S_N2 conversion of racemic epoxide *rac*-**7c** to alcohol *rac*-**8**, without promoting the troublesome side reactions encountered with the use of $BF_3{\cdot}OEt_2$ (Table 1, entry 11). The PMB protected epoxide *rac*-**7c** gave the most consistent results during the epoxide opening reaction.

The Shi epoxidation protocol appeared to be an ideal candidate for securing an enantioselective route to epoxide **7c**, as it generally shows excellent preference for unactivated tri-substituted over mono-substituted olefins.[9] While the enantiomer of the Shi catalyst (**12**) derived from L-fructose would be required for this application, it is accessible from inexpensive L-sorbose in 5 steps.[10] Unfortunately, initial reactions resulted in a disappointing yield (61%) and selectivity (3:1 ratio) of the monoepoxide **7c** to the bis-epoxide **13** (Table 2, entry 1).

Table 2. Synthesis of epoxide **7c**



Entry	Addition Time (h)	**12** (mol%)	Recovered **6c** (%)	**7c** (%)	**13** (%)
1	2	20	14	61	20
2	4	20	32	50	11
3	6	20	45	40	7
4[a]	4	20	62	23	8
5[b]	4	35	0	75	13
6[b]	4	25	0	74	11
7[b]	4	20	11	60	8

a) reaction run at −10 °C [b] catalyst added in 4 portions over 4 hours

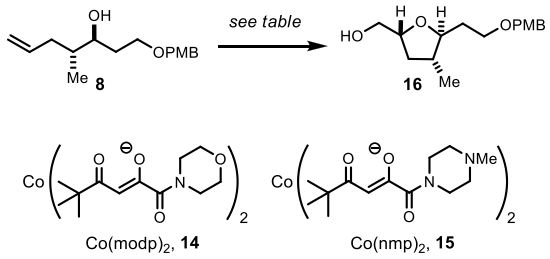
Attempts were made to improve selectivity by increasing the addition time of the base and Oxone® to 4 or 6 hours, which led to increases in selectivity but a decrease in overall yield (Table 2, entries 2-3), while a lower reaction temperature resulted in a decrease in both yield and selectivity (Table 2, entry 4). It is known that the Shi catalyst decomposes during the course of the reaction,[11] therefore the catalyst was added portion-wise. At higher catalyst loadings, complete conversion was finally achieved (Table 2, entries 5-6) with selectivities of approximately 7:1 of the desired product **7c** to the bis-epoxide **13**. Further attempts to decrease the amount of catalyst used resulted in incomplete conversions (Table 2, entry 7).

With a concise route towards pentenol **8** secured, attention was focused on the oxidative cyclization to form the *trans*-THF ring (Table 3). The first generation catalyst $Co(modp)_2$ (**14**) has been previously shown to be incompatible with the easily oxidized PMB group,[3] and attempts to cyclize **8** were unsuccessful (Table 3, entry 1). Using the standard oxidation conditions, the second generation $Co(nmp)_2$ (**15**) also afforded little success in forming *trans*-THF

ring **16** (Table 3, entry 2). In an attempt to reduce the amount of over-oxidation byproducts formed during the course of the reaction, lower reaction temperatures were examined and an optimal yield of 81% was obtained at 35 °C (Table 3, entries 3-5). It is noteworthy that even at room temperature a comparable yield of 85% BORSM was observed. Upon scale-up of the lower temperature cyclizations, yields were found to be uncharacteristically erratic (Table 3, entry 6) and it was speculated that the peroxide used during catalyst activation could be contributing to the over-oxidation byproducts.

Thus, an alternative protocol was performed whereby the catalyst was activated prior to introduction of the pentenol to ensure no peroxides were present. Initial reactions using this pre-activated $Co(nmp)_2$ (**15**) provided significant advantages in terms of yield reproducibility (Table 3, entry 7), but over-oxidation remained problematic. Eventually, careful monitoring of the reaction by TLC resulted in a surprising finding: the reaction was complete after just 1 h (Table 3, entry 8), whereas similar reactions typically require more than 12 h. Further optimization showed that a catalyst loading of 10 mol % resulted in the highest yield of **16** (94%) and the cleanest reactions, while lower catalyst loadings led to incomplete conversions (Table 3, entries 9-10). These optimized conditions proved reproducible on multi-gram scale.

Table 3. Optimization of oxidative cyclization



Entry	Catalyst	Loading (mol %)	Temp (°C)	Time (h)	Yield of **16** (%)
1	**14**	15	55	16	0
2	**15**	15	55	16	10
3	**15**	15	45	16	55
4	**15**	15	35	16	81
5	**15**	15	22	16	67 (85[a])
6	**15**	15	35	16	65[c]
7	**15**	15[b]	35	16	80[c]
8	**15**	15[b]	55	1	91
9	**15**	10[b]	55	1	94[c]
10	**15**	5[b]	55	16	77 (92[a])

a) yields based on recovered starting material b) catalyst was pre-activated c) reaction performed on a 15 mmol scale

Conclusions

In summary, we have reported a highly selective Shi epoxidation of a skipped diene followed by a reductive epoxide opening mediated by the novel Lewis acid $BF_2OBn{\cdot}OEt_2$ that can provide compounds containing useful propionate units. Implementation of these procedures for the synthesis of the C(1)-C(9) fragment of amphidinolide C and F and will be disclosed elsewhere.

Experimental Section

(*Z*)-1-Methoxy-4-((4-methylhepta-3,6-dienyloxy)methyl)benzene (**6c**)
To a suspension of NaH (780 mg, 32.5 mmol, 1.3 eq) in THF (150 mL) at 0 °C was added freshly prepared PMBBr (6.53 g, 32.5 mmol, 1.3 eq), followed by alcohol **5** (2.15 g, 25 mmol, 1.0 eq). The ice-bath was removed and after ca. 16 h the reaction was poured into a half-saturated solution of NH_4Cl (100 mL) in water ice (200 mL) and stirred for 5 min, after which the aqueous layer was extracted with EtOAc (150 mL x 3). The combined organics were washed with brine, dried over $MgSO_4$, and filtered through a thin pad of packed celite. Solvent was removed under reduced pressure and the crude oil was purified by flash chromatography (10% EtOAc/Hex) to yield the PMB ether (**6c**) as a colorless oil (5.54 g, 22.5 mmol, 90%). R_f 0.42 (10% EtOAc/Hex); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.72 (ddt, *J* = 16.7, 10.1, 6.4 Hz, 1H), 5.22 (t, *J* = 6.7 Hz, 1H), 5.03-4.96 (m, 1H), 4.44 (s, 2H), 3.78 (s, 3H), 3.42 (t, *J* = 7.0 Hz, 2H), 2.76 (d, *J* = 6.4 Hz, 2H), 2.31 (q, *J* = 7.0 Hz, 2H), 1.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 135.9, 135.1, 130.6, 129.2, 121.8, 115.2, 113.7, 72.5, 69.8, 55.3, 36.5, 28.5, 23.4. HRMS *m/z* 246.1615 (calcd for $C_{16}H_{22}O_2$, 246.1619).

(2*R*,3*S*)-2-Allyl-3-(2-(4-methoxybenzyloxy)ethyl)-2-methyloxirane (**7c**)
To a flask charged with diene **6c** (2.46 g, 10 mmol, 1.0 eq) was added dimethoxymethane (100 mL), acetonitrile (50 mL), buffer[12] (100 mL), **12** (157 mg), and $Bu_4N{\cdot}HSO_4$ (50 mg, catalytic) and the flask was cooled to 0 °C. A syringe pump was fitted with two 60 mL syringes, one charged with K_2CO_3 (6.90 g) in water (60 mL), the second charged with Oxone® (6.90 g) in water (60 mL). The K_2CO_3 and Oxone® solutions were added to the vigorously stirred solution over 4 h, and **12** was added portion-wise at the 1 h, 2 h and 3 h time mark (157 mg per addition, 630 mg total, 2.50 mmol, 0.25 eq). The reaction was stirred for 15 min after additions of the base and Oxone® were complete, at which point hexanes (200 mL) was added. The solution was transferred to a separatory funnel and the aqueous layer was extracted with hexanes (100 mL x 4). The combined organics were washed with brine, dried over $MgSO_4$, and filtered through a thin pad of packed celite. Solvent was removed under reduced pressure and the crude oil was purified by flash chromatography (20% EtOAc/Hex) to yield the mono-epoxide **7c** (1.93 g, 7.40 mmol, 74%) and the di-epoxide **13** (305 mg, 1.10 mmol, 11%) as yellow oils. R_f 0.17 (10% EtOAc/Hex); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.77 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.10-5.05 (m, 2H), 4.43 (ABd, *J* = 11.7 Hz, 2H), 3.59-3.56 (m, 2H), 2.86 (dd, *J* = 7.4, 4.7 Hz, 1H), 2.30 (dd, *J* = 7.0, 7.0 Hz, 1H), 2.18 (dd, *J* = 7.0, 7.0 Hz, 1H), 1.98-1.89 (m, 1H), 1.77-1.68 (m, 1H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 133.5, 130.4, 129.3, 117.8, 113.8, 72.8, 67.3, 61.9, 60.1, 55.3, 37.9, 29.4, 22.1. HRMS *m/z* 262.1576 (calcd for $C_{16}H_{22}O_3$, 262.1569).

Benzyloxydifluoroborane etherate (**11**)
To a round-bottomed flask charged with TMSOBn (1.90 g, 10.5 mmol, 1.05 eq) in diethyl ether (100 mL) and fitted with a rubber septum and an argon filled balloon (20.5 gauge needle) was added $BF_3{\cdot}OEt_2$ (1.26 mL, 10 mmol, 1.0 eq). To facilitate the evaporation of the TMSF the septa was pierced with another 20.5 gauge needle. The argon balloon was replaced as necessary, and the solution evaporates to a viscous oil in about 1 h, and argon flow was maintained for an additional 10 min.[13] To the residue was added an additional portion of diethyl ether (8 mL) to give an approximately 1.0 M solution of $BF_2OBn{\cdot}OEt_2$ (**11**).[14] It may be necessary to repeat the evaporation process,[14]. If well sealed the $BF_2OBn{\cdot}OEt_2$ solution is stable for several weeks at rt or refrigerated. Solvents other than diethyl ether caused decomposition; therefore it was used for characterization and reactions. ^{19}F NMR (375 MHz, Et_2O) δ -151.5 ppm. Trifluorotoluene (-63.9 ppm) was used as an internal standard.

(3*S*,4*R*)-1-(4-Methoxybenzyloxy)-4-methylhept-6-en-3-ol (**8**)
To a flask charged with $NaCNBH_3$ (255 mg, 4.0 mmol, 4.0 eq) in diethyl ether (15 mL) was added epoxide **7c** (262 mg, 1.0 mmol, 1.0 eq). A solution of $BF_2OBn{\cdot}OEt_2$ (~1.0 M, 4.0 mL, 4.0 mmol, 4.0 eq) was added to the vigorously stirred solution via syringe pump over 4 h. After the addition was complete, the reaction was stirred for 15 min before being poured into a half-saturated aqueous sodium bicarbonate (100 mL). The mixture was transferred to a separatory funnel and the aqueous layer was extracted with

EtOAc (50 mL x 3). The combined organics were washed with brine, dried over $MgSO_4$, and filtered through a thin pad of packed celite. Solvent was removed under reduced pressure and the crude oil was purified by flash chromatography (30% EtOAc/Hex) to yield alcohol **8** (240 mg, 0.91 mmol, 91%) as a yellow oil. R_f 0.50 (40% EtOAc/Hex); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.79 (ddt, *J* = 17.3, 10.0, 7.1 Hz, 1H), 5.04-4.97 (m, 2H), 4.45 (m, 2H), 4.45 (s, 2H), 3.79 (s, 3H), 3.71 (dt, *J* = 9.5, 4.9 Hz, 1H), 3.61 (q, *J* = 6.4 Hz, 2H), 3.00 (d, *J* = 2.3 Hz, 1H), 2.30-2.26 (m, 1H), 1.90 (dt, *J* = 13.9, 8.3 Hz, 1H), 1.73-1.70 (m, 2H), 1.64-1.59 (m, 1H), 0.86 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.3, 137.6, 130.0, 129.3, 115.8, 113.8, 75.2, 73.0, 69.4, 55.3, 38.6, 36.9, 32.8, 15.1. HRMS *m/z* 264.1725 (calcd for $C_{16}H_{24}O_3$, 264.1725). $[\alpha]^{20}_D$ = +1.73° (*c* 1.0, $CHCl_3$). The *ee* was determined to be 85% by (*R*)-Mosher's analysis.

((2*R*,4*R*,5*S*)-5-(2-(4-Methoxybenzyloxy)ethyl)-4-methyltetrahydrofuran-2-yl)methanol (**16**)

Procedure to pre-activate Co(nmp)$_2$: To a flask charged with Co(nmp)$_2$ (**15**) (452 mg, 0.8 mmol, 0.1 eq) and *i*PrOH (100 mL) was added *t*BuOOH (5.33 M, 0.2 mL, 1.08 mmol, 0.14 eq). The reaction was heated to 55 °C under an oxygen atmosphere for 1 h, and solvent was removed under reduced pressure. The activated Co(nmp)$_2$ was dried under high vacuum (0.1 mmHg) for 5 min to ensure that any remaining peroxide was removed.

Cyclization: The pre-activated Co(nmp)$_2$ (**15**) (prepared above, 0.8 mmol, 0.1 eq) was diluted with 100 mL *i*PrOH, and alcohol (**8**) was added (2.06 g, 7.8 mmol, 1 eq). The reaction was heated to 55 °C under an oxygen atmosphere for exactly 1 h, and allowed to cool to rt. Solvent was removed under reduced pressure, followed by high vacuum (0.1 mmHg) to remove all traces of *i*PrOH. The crude mixture was diluted with EtOAc (40 mL) and filtered through a thin pad of silica (<1 cm) over packed celite to remove the catalyst. The pad was washed with EtOAc (400 mL) and the filtrate was concentrated under reduced pressure to give THF-alcohol (**16**) (2.05 g, 7.34 mmol, 94%) as a yellow oil, which was used without further purification. The product rapidly decomposes, and the decomposition product characteristically results in broad peaks at 3.65 and 3.45 ppm. The presence of the decomposition product leads to the loss of fine splitting and peaks are reported as multiplets. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.43 (d, *J* = 2.0 Hz, 2H), 4.06 (ddt, *J* = 9.4, 6.2, 3.1 Hz, 1H), 3.79 (s, 3H), 3.62 – 3.48 (m, 4H), 2.09-2.03 (m, 1H), 1.94-1.85 (m, 2H), 1.73-1.65 (m, 1H), 1.37-1.29 (m, 1H), 1.01 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.1, 130.6, 129.2, 113.7, 82.4, 78.3, 72.6, 67.4, 65.2, 55.3, 40.1, 36.6, 34.3, 16.4. HRMS *m/z* 280.1667 (calcd for $C_{16}H_{24}O_4$, 280.1675).

Supporting Information (see footnote on the first page of this article):

Acknowledgments

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6 Other Lewis acids screened: $MgBr_2$, $ZnCl_2$, $TiCl_4$, $SnCl_4$, $Yb(OTf)_3$, $Sc(OTf)_3$.

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8 The ^{19}F NMR peak shift can be correlated to the strength of the Lewis acid. In order of strongest to weakest: $BF_2OTf{\cdot}OEt_2$ (-146.9 ppm), $BF_2OMs{\cdot}OEt_2$ (-148.3 ppm), $BF_2OBn{\cdot}OEt_2$ (-151.5 ppm). Trifluorotoluene (-63.9 ppm) was used as an internal standard.

9 Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224-11235.

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11 The catalyst can be deactivated by a competing Baeyer-Villiger oxidation which is disfavoured at higher pH.

12 Buffer is a 0.05 M solution of $Na_2B_2O_7{\cdot}H_2O$ in 1 x 10^{-4} M aqueous Na_2EDTA.

13 This setup was found to be optimal for production of $BF_2OBn{\cdot}OEt_2$ without formation of $BFOBn_2{\cdot}OEt_2$. Alternative procedures including heating, reduced pressure and Schlenk line nitrogen flow were examined but were less effective.

14 If the solution contains significant amounts of $BF_3{\cdot}OEt_2$, the evaporation procedure can be repeated as needed until the ^{19}F NMR shows only product. The concentration of the solution can be more accurately determined by adding an internal standard (e.g., trifluorotoluene) and comparing peak integration using no D ^{19}F NMR. See: Hoye, T. R.; Eklov, B. M.; Voloshin, M. *J. Am. Chem. Soc.* **2004**, *126*, 2567-2570.

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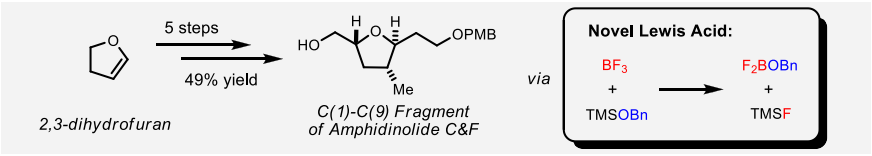

The novel Lewis acid $BF_2OBn{\cdot}OEt_2$ has been developed via anionic distribution between $BF_3{\cdot}OEt_2$ and TMSOBn. This compound demonstrates slightly lower Lewis acidity when compared to the parent Lewis acid, and was used in a regio- and stereo-selective reductive epoxide opening. The utility of this reaction was demonstrated by the conversion of commercially available and inexpensive 2,3-dihydrofuran to the C(1)-C(9) fragment of Amphidinolie C and F in 5 steps and 49% overall yield.

Studies Toward Amphidinolides

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$BF_2OBn{\cdot}OEt_2$: A Novel Lewis Acid and its use in a Regio- and Stereo- Selective Opening of Trisubstituted Epoxides and its Application Towards Amphidinolide C and F

Keywords: : Lewis Acid / Epoxide Opening / Shi Epoxidation / $BF_2OBn{\cdot}OEt_2$/ amphidinolide

Supporting Information