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Type 2 Ring-Opening Reactions of Cyclopropanated 7-Oxabenzonorbornadienes with Carboxylic Acid Nucleophiles

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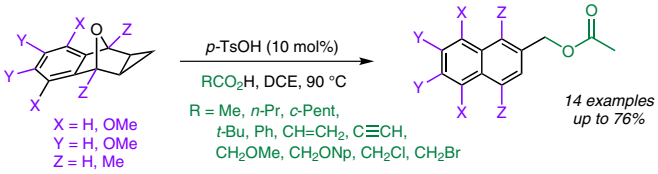

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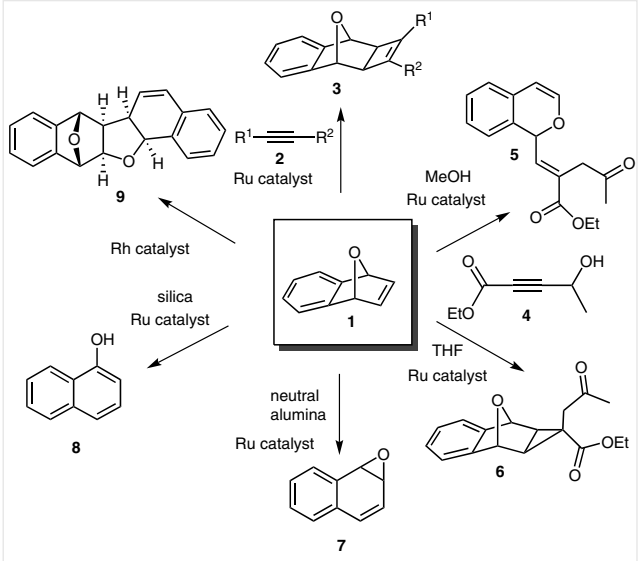
Abstract Ring-opening reactions of strained heterocyclic compounds provide efficient routes to various organic frameworks. In this work, the ability of carboxylic acid nucleophiles to promote ring-opening of cyclopropanated 7-oxabenzonorbornadienes was investigated. Reactions proceeded smoothly to yield 2-naphthylmethyl esters in moderate yields, and optimal conditions were found with the use of 10 mol% *p*-toluenesulfonic acid monohydrate in dichloroethane heated to 90 °C. The amount of nucleophile could be decreased from a large excess to 8 equivalents without diminishing the yield. When varying the structure of the acid catalyst or carboxylic acid nucleophile, reaction rates showed a marked dependence on acidity of these species. Ring-opening was well tolerated by functionalized substrates, with substitution on the bridgehead or aromatic portions of the molecule. The present work is the second account of this type of reaction, and provides a new route to 2-naphthylmethyl esters. The transformations observed in this work should be useful in predicting the reactivity of similar fused-ring systems.

Key words 7-oxabenzonorbornadiene, cyclopropane, ring-opening, fused-ring systems, acid catalysis

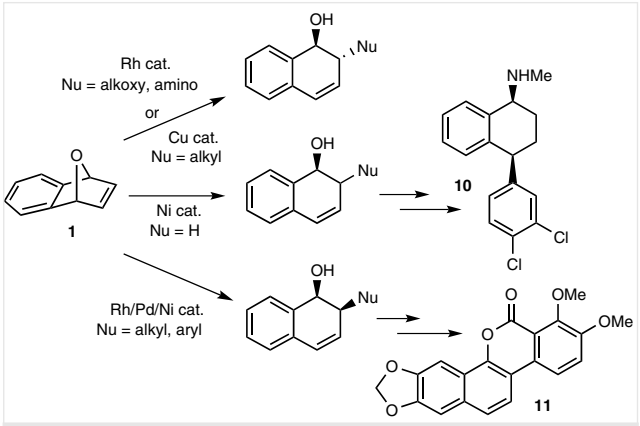
Bridged or fused-ring compounds have been popular systems of study in many areas of chemical research. Due to their innate strain, bridged heterocyclic compounds in particular are valued as synthetic tools to prepare more complex structures.[1] One such example is the use of 7-oxabenzonorbornadiene (**1**) to arrive at various highly substituted organic frameworks (Scheme 1).[2,3] In the presence of alkyne **2** and Cp*Ru(COD)Cl, we have found that [2+2] cycloaddition with **1** proceeds to form cyclobutene **3**,[4,5] which is also observed when using alkynyl halides[6] or ynamides.[7] Reaction of **1** with secondary propargylic alcohol **4** in MeOH leads to production of isochromene **5**, which is also observed when using a cationic Ru catalyst [Cp-Ru($CH_3CN)_3$]$^+PF_6^-$.[8,9] The same reagents in THF, however, afford cyclopropane **6** instead.[10] We have also observed that in the absence of an alkyne, Cp*Ru(COD)Cl promotes isomerization of **1** to its naphthalene oxide **7** or naphthol **8**.[11,12] Furthermore, asymmetric cyclodimerization of **1** can produce the polycyclic system **9** in excellent enantioselectivity (up to 99% ee) with the use of a cationic Rh(I) catalyst.[13]



Scheme 1 Transition-metal-catalyzed transformations of 7-oxabenzonorbornadiene (**1**)

7-Oxabenzonorbornadiene (**1**) is known to undergo several stereoselective ring-opening reactions depending on the transition metal catalyst and nucleophile of choice. For instance, dihydronaphthalenols with *trans* substitution are obtained when using rhodium catalysts with heteroatomic nucleophiles, or copper catalysts with alkyl nucleophiles, while *cis* substitution is obtained using rhodium, palladium, or nickel catalysts with carbon-based nucleo-

philes.[2,14] The resulting frameworks allow for facile preparations of biologically active compounds, such as sertraline (**10**) or arnottin I (**11**) (Scheme 2).[15,16]



Scheme 2 Ring-opening reactions of 7-oxabenzonorbornadiene (**1**) in natural product synthesis

Our group has recently been expanding this area of research through the creation of cyclopropanated analogues **12**,[17–19] in order to examine their involvement in ring-opening reactions (Figure 1). Since these compounds have only been developed in the last couple of years, not much is known yet about their chemical behavior. It is, however, projected that derivatives **12** should show similar reactivity to their uncyclopropanated parent alkenes **1**.[20] To date, we have discovered 'type 1' ring-opening reactions of cyclopropanated oxa- and azabenzonorbornadienes **12** and **13** with organocuprates, which were found to produce *cis*-1,2-dihydro-2-methylnaphthalenols **14** from oxacyclic precursors,[21] as well as polycyclic γ-lactams **15** in the case of the aza compounds (Scheme 3).[22] Thus far, 'type 2' ring-opening reactions have only been observed as acid-catalyzed opening of **12** using alcohol nucleophiles, to produce 2-(alkoxymethyl)naphthalenes (**16**).[23] It was felt that the participation of other heteroatom nucleophiles in the ring-opening of these novel substrates should be pursued and as such, in this work we decided to explore the reactivity of weaker carboxylic acid nucleophiles with cyclopropanated oxabenzonorbornadienes. We began by investigating the formerly successful acid-mediated conditions.[23]

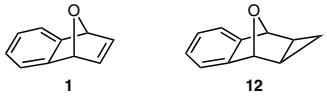
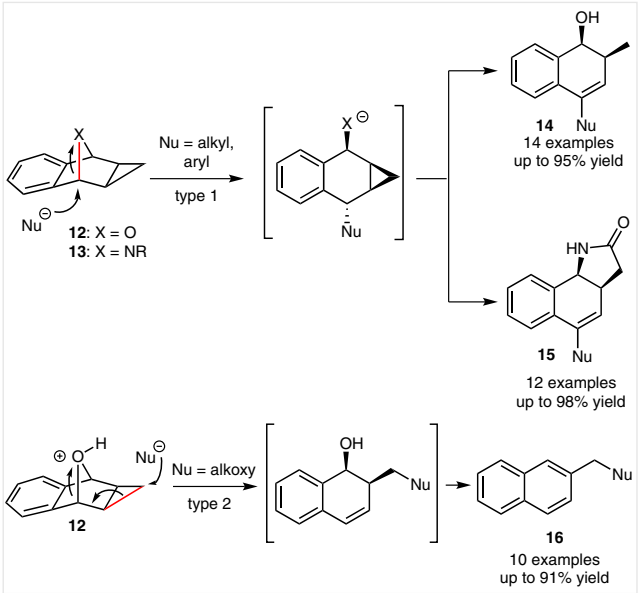


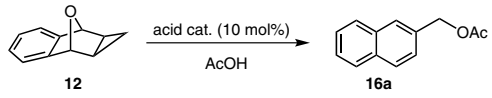
Figure 1 Structural comparison between conventional alkene **1** and novel cyclopropane system **12**



Scheme 3 Currently known ring-opening reactions of cyclopropanated heterobenzonorbornadienes

The effects of external acid catalyst and temperature on type 2 ring-opening reactions of **12** using acetic acid as both nucleophile and solvent are summarized in Table 1. In the absence of an acid catalyst and at room temperature, the reaction did not proceed (Table 1, entry 1). In fact, even after 10 days at 90 °C it was found that no reaction took place when an acid catalyst was not supplied (entry 2). Some inorganic acid catalysts were then investigated, of which sulfuric acid showed the fastest effect at room temperature, where moderate yields of **16a** were obtained after only 1 hour (entry 3). When nitric acid was used as the catalyst, the reaction took a much longer time to proceed, and yields were slightly worse (entry 4). At the expense of time, tetrafluoroboric acid gave improved yield of 65% at room temperature (entry 5), although no appreciable improvement in yield could be made by increasing the reaction temperature (entry 6). With the organic acid catalysts screened, camphorsulfonic acid showed slow conversion when the reaction was heated to 40 °C (entry 7), while pyridinium *p*-toluenesulfonate required heating to 90 °C to obtain similar results (entry 8). Finally, use of *p*-toluenesulfonic acid monohydrate showed decent conversion at room temperature (entry 9), which was enhanced at higher temperatures (entries 10–12). The best conditions among these optimizations was thus found to be with the use of catalytic *p*-toluenesulfonic acid at 90 °C for 20 hours, giving 70% yield (entry 12).

Table 1 Effect of Acid Catalyst and Reaction Temperature on Type 2 Ring-Opening Reactions of **12**



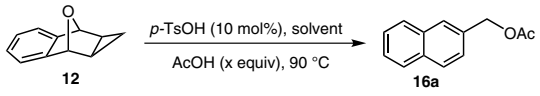
12 **16a**

Entry	Acid source (0.1 equiv)	Temp (°C)[a]	Time (h)	Yield (%)[b] of recovered **12**	Yield (%)[b] of product **16a**
1	none	r.t.	48	88	0
2	none	90	240	64	0
3	H_2SO_4	r.t.	1	0	59
4	HNO_3	r.t.	120	12	48
5	HBF_4	r.t.	168	0	65
6[c]	HBF_4	90	20	0	69
7	CSA	40	168	44	36
8	PPTS	90	168	27	33
9	*p*-TsOH·H_2O	r.t.	168	36	41
10	*p*-TsOH·H_2O	40	30	5	55
11	*p*-TsOH·H_2O	60	24	0	66
12	*p*-TsOH·H_2O	90	20	0	70

[a] Room temperature; r.t. = 19–24 °C.
[b] Isolated yield after column chromatography.
[c] Aqueous solution of 48 wt% HBF_4.

Next, the effect of solvent and equivalency of acetic acid were screened (Table 2). It was found that relative to when acetic acid was the sole reaction medium (Table 2, entry 1), addition of acetonitrile led to a reduction in yield (entry 2), which was also suggested with the use of toluene (entry 3). This reduction in yield was even more pronounced with the use of dimethyl sulfoxide (entry 4), which only gave moderate yields after one week. Although the use of 1,4-dioxane resulted in reasonable yields, the reaction took two days to complete (entry 5), whereas similar results were seen with the use of 1,2-dichloroethane (DCE, entry 6), which gave 74% of product after only 28 hours. When the amount of acetic acid was reduced to 8 equivalents (entry 7), the reaction showed comparable results as to when acetic acid was used in large excess (entry 6). However, when smaller equivalents of acetic acid were used, the yield of **16a** was seen to suffer (entries 8 and 9).

Table 2 Effect of Solvent and Nucleophile Equivalency on Type 2 Ring-Opening Reactions of **12**



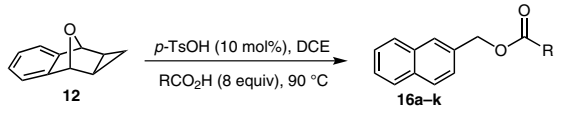
12 **16a**

Entry	Solvent	AcOH (× equiv)	Time (h)	Yield (%)[a] of recovered **12**	Yield (%)[a] of product **16a**
1	none	>50	20	0	70
2	MeCN	>50	20	0	54
3	toluene	>50	28	0	67
4	DMSO	>50	168	11	44
5	1,4-dioxane	>50	48	7	68
6	DCE	>50	28	0	74
7	DCE	8	18	0	73
8	DCE	4	24	0	63
9	DCE	2	24	0	48

[a] Isolated yield after column chromatography.

Using the optimized conditions of 8 equivalents of nucleophile in DCE with catalytic *p*-toluenesulfonic acid at 90 °C, several different carboxylic acid nucleophiles were then subjected to type 2 ring-opening reaction (Table 3). This resulted in a large collection of diverse products with decent yields. Relative to acetic acid (entry 1), the primary *n*-butyric acid nucleophile (*n*-PrCO_2H) produced comparable yield of corresponding ring-opened product **16b** after 24 hours (Table 3, entry 2). Use of cyclopentanecarboxylic acid resulted in similar yield of **16c** after an additional day (entry 3), and pivalic acid gave comparable yield of **16d** after a further day of reaction (entry 4). When benzoic acid was used as the nucleophile, once again a very similar yield of **16e** could be attained (entry 5), although the reaction was much faster. Use of 2-propenoic acid resulted in a similar reaction rate and yield, as well (entry 6). When 2-propynoic acid was used, the reaction was complete after only 1 hour, with no starting material observed by NMR, although product could only be isolated in 29% yield (entry 7). These fast-

Table 3 Effect of Nucleophile on Type 2 Ring-Opening Reactions of **12**



12 **16a–k**

Entry	R	pK_a of RCO_2H[a]	Time (h)	Product	Yield (%)[b]
1	Me	4.76[24]	18	**16a**	73
2	*n*-Pr	4.81[25]	22	**16b**	72
3	*c*-C_5H_9	4.98[26]	48	**16c**	76
4	*t*-Bu	5.05[24]	68	**16d**	70
5	Ph	4.17[24]	24	**16e**	70
6	H_2C=CH	4.25[24]	32	**16f**	63
7	HC≡C	1.84[27]	1	**16g**	29
8	$MeOCH_2$	3.53[24]	6	**16h**	75
9[c]	$NpOCH_2$	3.2[28]	6	**16i**	16
10	$ClCH_2$	2.86[24]	2	**16j**	37
11	$BrCH_2$	2.86[24]	2	**16k**	51

[a] Values according to literature references.
[b] Isolated yield after column chromatography.
[c] Calculated pK_a value, as reported in reference.

er reaction times were found to correlate with the pK_a values of each carboxylic acid. When methoxyacetic acid ($MeOCH_2CO_2H$) and 2-naphthoxyacetic acid ($NpOCH_2CO_2H$) were subjected to reaction, both transformations were complete after 6 hours (entries 8 and 9), and a similar correlation in reaction rate with pK_a value of the nucleophile was also noted for chloro- and bromoacetic acid (entries 10 and 11). All reactions were left to react until complete consumption of starting material **12** was confirmed by NMR analysis. Thus, in trials where lower isolated yields were obtained, it appeared that decomposition of **12** had occurred under the reaction conditions.

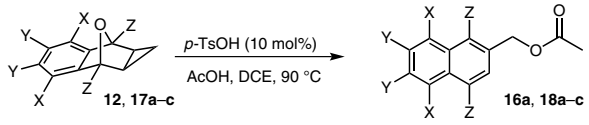
The type 2 ring-opening reactions were then applied to transformations using more diversely substituted variants of cyclopropanated oxabenzonorbornadiene (Table 4). As with the parent compound **12** (Table 4, entry 1), substrate **17a** bearing bridgehead methyl groups underwent ring-opening smoothly, furnishing expected product **18a** in 60% yield after 20 hours (entry 2). Substrate **17b** with *p*-dimethoxy substitution was found to undergo a more rapid transformation (entry 3), while the same substituents in the *ortho* orientation (**17c**) resulted in an even faster reaction (entry 4).

The transformation at hand is explained by the following mechanism (Scheme 4): the oxygen of **12** becomes protonated (presumably by the acid catalyst, when pK_a of catalyst << pK_a of carboxylic acid nucleophile). Following electrophilic opening of the ether bridge in **19**, an equivalent of carboxylic acid then attacks at the external cyclopropane carbon of **20**, and subsequent dehydration produces naphthalene **16**. Since the increased nucleophilicities of the carboxylic acids (having higher pK_a values) do not show an enhancement in reaction rate, the data do not lend support to the nucleophilic attack being the slow step in the reaction. Thus, it is likely that the electrophilic ring-opening and formation of carbocation **19** is the slow step, although the mechanism of these conversions may be more complicated than what is currently understood. The present study, however, does show that the pK_a of the carboxylic acid has some effect on the rate of reaction.

In addition, it was found that 2-propynoic acid (which had the lowest pK_a of all the acids tested in this work, Table 3), could promote ring-opening of **12** even in the absence of an added catalyst. Relative to the reaction with added *p*-toluenesulfonic acid (which took only 1 hour to complete), the same reaction without any catalyst took 3 days to reach completion (Scheme 5). Since these conditions only utilized 8 equivalents of carboxylic acid diluted in DCE, the reaction was then repeated in the absence of acid catalyst, but using a large excess of carboxylic acid as both solvent and nucleophile. In this case, the reaction was much faster, with full consumption of starting material after 2 hours. This is in stark contrast to the reaction using pure acetic acid in the absence of catalyst, whose reaction did not proceed even after a full week.

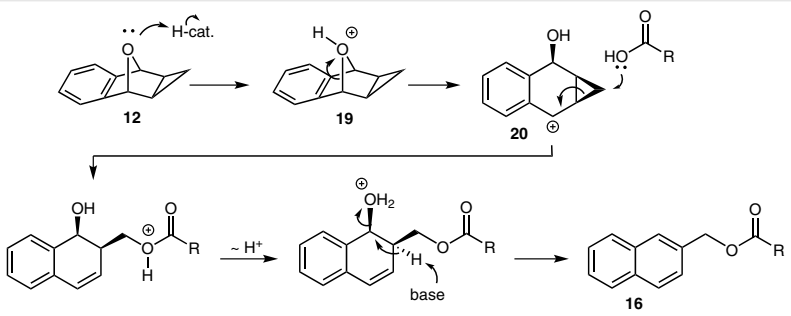
In conclusion, the present work demonstrates the ability of carboxylic acid nucleophiles to cleave cyclopropanated oxabenzonorbornadienes in a type 2 fashion, under acid mediation. The strength and source of the acid catalyst was seen to affect the rate of ring-opening, and the conversion took place most efficiently when *p*-toluenesulfonic acid monohydrate was used in conjunction with DCE at 90 °C. The amount of nucleophile could be reduced to 8 equivalents without hampering the reaction yield. This mode of ring-opening showed successful conversion with diverse nucleophile and substrate combinations. The benzylic esters produced in this way could be useful in the preparation

Table 4 Effect of Substrate Functionalization on Type 2 Ring-Opening Reactions of Cyclopropanated 7-Oxabenzonorbornadiene

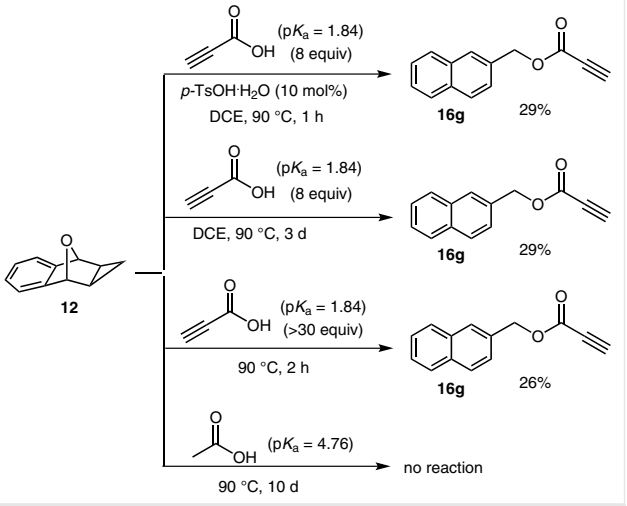


Entry	X	Y	Z	Time (h)	Product	Yield (%)[a]
1	H	H	H	18	**16a**	73
2	H	H	Me	20	**18a**	60
3	OMe	H	H	7	**18b**	45
4	H	OMe	H	1	**18c**	40

[a] Isolated yield after column chromatography.



Scheme 4 Proposed mechanism for type 2 ring-opening of **12**



Scheme 5 Ability of 2-propynoic acid to react in the absence of added catalyst

of biologically active frameworks, through transformations such as cross-coupling reactions.[29] The chemistry introduced in this work may show appeal in further transformations of similarly strained fused-ring systems.

All commercial reagents were used without further purification. Cyclopropanated oxabenzonorbornadiene was prepared as previously reported.[17,18] Dichloroethane was obtained from an LC-SPS solvent purification system supplied with dry packed columns containing 3Å molecular sieves. Standard column chromatography was performed on 230–400 mesh silica gel using flash column chromatography techniques.[30] Analytical TLC was performed on precoated silica gel 60 F254 plates. Melting points were measured using a Mel-Temp apparatus. IR spectra were acquired as solids or as neat oils on a Bruker ALPHA platinum single reflection diamond ATR spectrophotometer and are reported in wave numbers (cm^{-1}). ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 600 MHz or 400 MHz spectrometer equipped with a Cryoplatform® Prodigy cryoprobe, and reported as chemical shift (δ) values in parts per million (ppm) from TMS with the solvent resonance as the internal standard ($CDCl_3$ ^1H: 7.24 ppm; ^{13}C: 77.0 ppm).

Acid-Catalyzed Ring-Opening Reaction of Cyclopropanated 7-Oxabenzonorbornadiene; General Procedure

In a small screw-cap vial equipped with a stir bar, cyclopropanated oxabenzonorbornadiene **12** (0.19 mmol, 1.0 equiv) was dissolved in dichloroethane (0.25 mL). *p*-TsOH·H_2O (0.1 equiv) was added as a solid, and carboxylic acid nucleophile (8.0 equiv) was introduced, rinsing with dichloroethane (0.25 mL). The vial was sealed tightly and heated to 90 °C with continuous stirring for 1–168 h. The crude product was quenched with sat. aq $NaHCO_3$, extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic layers were dried ($MgSO_4$): The solvent was removed by rotary evaporation, and the crude mixture was purified by column chromatography (EtOAc–hexanes, 2:98 to 5:95) to give the corresponding ring-opened product (Tables 3, 4).

Acetic Acid 2-Naphthalenylmethyl Ester (16a)

Yield: 23.8 mg (73%); white solid; mp 50–53 °C (Lit.[31,32] mp 53–55 °C); R_f = 0.22 (EtOAc–hexanes, 2:98).

IR (ATR): 3056, 2952, 1732 (C=O), 1223, 1022, 821, 743, 479 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.86 (m, 4 H), 7.55–7.48 (m, 3 H), 5.30 (s, 2 H), 2.16 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 133.2, 133.1, 133.0, 128.3, 128.0, 127.6, 127.3, 126.2, 1261, 125.8, 66.3, 21.0.

Spectral data are consistent with those previously reported.[31,32]

Butanoic Acid 2-Naphthalenylmethyl Ester (16b)

Yield: 39.0 mg (72%); yellow oil; R_f = 0.32 (EtOAc–hexanes, 5:95).

IR (ATR): 3056, 2964, 2875, 1731 (C=O), 1169, 814, 473 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.83–7.80 (m, 4 H), 7.48–7.43 (m, 3 H), 5.26 (s, 2 H), 2.35 (t, *J* = 7.5 Hz, 2 H), 1.70–1.66 (m, 2 H), 0.94 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.6, 133.6, 133.2, 133.1, 128.4, 128.0, 127.7, 127.3, 126.3, 126.2, 125.9, 66.2, 36.3, 18.5, 13.7.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{15}H_{16}O_2$: 228.1150; found: 228.1155.

Cyclopentanecarboxylic Acid 2-Naphthalenylmethyl Ester (16c)

Yield: 38.0 mg (76%); clear oil; R_f = 0.27 (EtOAc–hexanes, 5:95).

IR (ATR): 3055, 2955, 2870, 1726 (C=O), 1601, 1508, 1451, 1173, 1145, 815, 472 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.88–7.84 (m, 4 H), 7.53–7.49 (m, 3 H), 5.30 (s, 2 H), 2.84 (pent, *J* = 8.0 Hz, 1 H), 1.96–1.85 (m, 4 H), 1.78–1.72 (m, 2 H), 1.63–1.60 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.7, 133.7, 133.2, 133.1, 128.4, 128.0, 127.7, 127.2, 126.3, 126.2, 125.8, 66.2, 43.9, 30.1 (2 C), 25.8 (2 C).

HRMS: *m*/*z* $[M]^+$ calcd for $C_{17}H_{18}O_2$: 254.1307; found: 254.1301.

2,2-Dimethylpropanoic Acid 2-Naphthalenylmethyl Ester (16d)

Yield: 30.3 mg (70%); clear oil; R_f = 0.23 (EtOAc–hexanes, 5:95).

IR (ATR): 3056, 2971, 2872, 1725 (C=O), 1478, 1279, 1141, 814, 733, 472 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.83–7.78 (m, 4 H), 7.48–7.41 (m, 3 H), 5.24 (s, 2 H), 1.22 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.4, 133.9, 133.2, 133.0, 128.3, 128.0, 127.7, 126.9, 126.3, 126.2, 125.6, 66.2, 38.9, 27.2 (3 C).

Spectral data are consistent with those previously reported.[33]

Benzoic Acid 2-Naphthalenylmethyl Ester (16e)

Yield: 41.5 mg (70%); white solid; mp 45–47 °C; R_f = 0.21 (EtOAc–hexanes, 5:95).

IR (ATR): 3403, 3058, 2975, 1706, 1599, 1506, 1450, 1311, 1274, 1261, 819, 699, 679 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.12 (m, 2 H), 7.94 (s, 1 H), 7.89 (m, 3 H), 7.60–7.47 (m, 6 H), 5.56 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5, 133.4, 133.2, 133.14, 133.10, 130.1, 129.8 (2 C), 128.5, 128.4 (2 C), 128.0, 127.8, 127.4, 126.4, 126.3, 125.9, 66.9.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{18}H_{14}O_2$: 262.0994; found: 262.0999.

2-Propenoic Acid 2-Naphthalenylmethyl Ester (16f)

Yield: 28.8 mg (63%); clear oil; R_f = 0.30 (EtOAc–hexanes, 1:9).

IR (ATR): 3055, 2954, 2108, 1719 (C=O), 1405, 1176, 967, 809 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.83 (m, 4 H), 7.51–7.47 (m, 3 H), 6.47 (dd, *J* = 17.3 Hz, 1.4 Hz, 1 H), 6.19 (dd, *J* = 17.3 Hz, 10.4 Hz, 1 H), 5.87 (dd, *J* = 10.4 Hz, 1.4 Hz, 1 H), 5.36 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.1, 133.3, 133.2, 133.1, 131.3, 128.4, 128.3, 128.0, 127.7, 127.4, 126.4, 126.3, 125.9, 66.5.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{14}H_{12}O_2$: 212.0837; found: 212.0842.

2-Propynoic Acid 2-Naphthalenylmethyl Ester (16g)

Yield: 17.9 mg (29%); white solid; mp 89–92 °C; R_f = 0.18 (EtOAc–hexanes, 5:95).

IR (ATR): 3402, 3246, 3061, 2940, 2112, 1703 (C=O), 1227, 822, 749, 716 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.87 (m, 4 H), 7.54–7.49 (m, 3 H), 5.41 (s, 2 H), 2.93 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.6, 133.3, 133.1, 131.9, 128.6, 128.1, 128.0, 127.8, 126.6, 126.5, 125.9, 75.2, 74.5, 68.1.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{14}H_{10}O_2$: 210.0681; found: 210.0688.

Methoxyacetic Acid 2-Naphthalenylmethyl Ester (16h)

Yield: 32.4 mg (75%); white solid; mp 30–32 °C; R_f = 0.14 (EtOAc–hexanes, 5:95).

IR (ATR): 3467, 3053, 2994, 2927, 2889, 2869, 2827, 1737 (C=O), 1449, 1212, 1192, 1124, 829, 740 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.87 (m, 4 H), 7.54 (m, 3 H), 5.40 (s, 2 H), 4.13 (s, 2 H), 3.49 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.2, 133.19, 133.15, 132.8, 128.5, 128.0, 127.8, 127.7, 126.5, 126.4, 126.0, 69.9, 66.8, 59.5.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{14}H_{14}O_3$: 230.0943; found: 230.0949.

Naphthoxyacetic Acid 2-Naphthalenylmethyl Ester (16i)

Yield: 13.2 mg (16%); white solid; mp 98–100 °C; R_f = 0.10 (EtOAc–hexanes, 5:95).

IR (ATR): 3054, 2971, 2116, 1738 (C=O), 1597, 1272, 1215, 1190, 1170, 1061, 841 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.84–7.79 (m, 6 H), 7.64 (d, *J* = 8.1 Hz, 1 H), 7.52 (m, 2 H), 7.44 (m, 3 H), 7.28 (m, 1 H), 7.07 (d, *J* = 2.5 Hz, 1 H), 5.46 (s, 2 H), 4.85 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 155.7, 134.2, 133.2, 133.1, 132.5, 129.8, 129.4, 128.5, 129.1, 127.8, 127.73, 127.68, 126.9, 126.54, 126.47, 126.4, 125.9, 124.2, 118.6, 107.1, 67.2, 65.4.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{23}H_{18}O_3$: 342.1256; found: 342.1263.

Chloroacetic Acid 2-Naphthalenylmethyl Ester (16j)

Yield: 16.2 mg (37%); white solid; mp 50–51 °C; R_f = 0.44 (EtOAc–hexanes, 25:75).

IR (ATR): 3479, 3059, 3026, 2955, 1747 (C=O), 1310, 1185, 962, 828 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.84 (m, 4 H), 7.51–7.49 (m, 2 H), 7.46–7.45 (m, 1 H), 5.37 (s, 2 H), 4.11 (s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.3, 133.3, 133.2, 132.3, 128.6, 128.1, 127.9, 127.8, 126.6, 126.5, 125.9, 68.1, 41.0.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{13}H_{11}ClO_2$: 234.0448; found: 234.0441.

Bromoacetic Acid 2-Naphthalenylmethyl Ester (16k)

Yield: 22.6 mg (51%); white solid; mp 48–49 °C; R_f = 0.48 (EtOAc–hexanes, 25:75).

IR (ATR): 3024, 2964, 2108, 1916, 1750, 1718 (C=O), 1270, 1230, 966, 816 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.87–7.84 (m, 4 H), 7.51–7.50 (m, 2 H), 7.47–7.46 (m, 1 H), 5.37 (s, 2 H), 3.90 (s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.1, 133.3, 133.2, 132.4, 128.6, 128.1, 127.8 (2 C), 126.52, 126.46, 125.9, 68.1, 25.9.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{13}H_{11}BrO_2$: 277.9942; found: 277.9948.

Acetic Acid 1,4-Dimethyl-2-naphthalenylmethyl Ester (18a)

Yield: 24.1 mg (60%); yellow oil; R_f = 0.19 (EtOAc–hexanes, 5:95).

IR (ATR): 3072, 2942, 2254, 1732 (C=O), 1224, 1021, 729 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.15–8.12 (m, 1 H), 8.04–8.01 (m, 1 H), 7.59–7.56 (m, 2 H), 7.33 (s, 1 H), 5.33 (s, 2 H), 2.71 (s, 3 H), 2.70 (s, 3 H), 2.14 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 132.9, 132.7, 132.4, 131.6, 130.2, 128.3, 125.81, 125.78, 124.8, 124.6, 65.3, 21.1, 19.4, 14.2.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{15}H_{16}O_2$: 228.1150; found: 228.1156.

Acetic Acid 5,8-Dimethoxy-2-naphthalenylmethyl Ester (18b)

Yield: 13.5 mg (45%); yellow oil; R_f = 0.38 (EtOAc–hexanes, 1:4).

IR (ATR): 3000, 2938, 2835, 1733 (C=O), 1603, 1462, 1365, 1270, 1214, 1086, 801 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, *J* = 8.8 Hz, 1 H), 8.19 (s, 1 H), 7.48 (dd, *J* = 8.6 Hz, 1.8 Hz, 1 H), 6.71 (s, 2 H), 5.27 (s, 2 H), 3.96 (s, 3 H), 3.95 (s, 3 H), 2.13 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 149.42, 149.40, 133.3, 126.1, 126.0, 125.9, 122.4, 121.5, 103.62, 103.60, 66.7, 55.8, 55.7, 21.1.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{15}H_{16}O_4$: 260.1049; found: 260.1055.

Acetic Acid 6,7-Dimethoxy-2-naphthalenylmethyl Ester (18c)

Yield: 8.6 mg (40%); white solid; mp 66–68 °C; R_f = 0.24 (EtOAc–hexanes, 1:9).

IR (ATR): 3004, 2955, 2831, 1736, 1492, 1254, 1227, 1163 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 7.9 Hz, 1 H), 7.68 (s, 1 H), 7.32 (dd, *J* = 8.4 Hz, 1.6 Hz, 1 H), 7.12 (s, 2 H), 5.23 (s, 2 H), 4.006 (s, 3 H), 4.003 (s, 3 H), 2.12 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 149.8, 131.6 (2 C), 128.9 (2 C), 126.8, 126.2, 124.5, 106.3, 106.1, 66.7, 55.9 (2 C), 21.2.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{15}H_{16}O_4$: 260.1049; found: 260.1053.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1560565.

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