Development of Electrophilic Addition Reactions to Carbonyl Compounds through the Photocatalytic Carbinol Cation/Anion Umpolung

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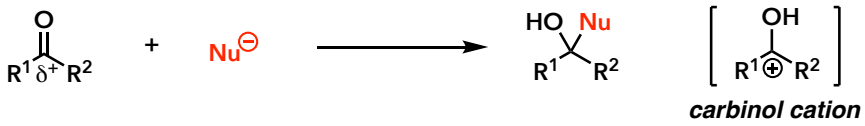
General Introduction

Original reactivity of carbonyl carbons

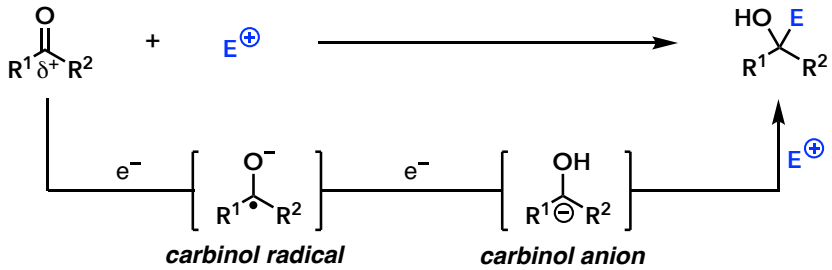
Transformation of carbonyl compounds is one of the most fundamental and essential organic reactions. Carbon atoms of the carbonyl group are positively polarized and hence serve as electrophiles in reactions with nucleophiles affording alcohols (Scheme 1). Consequently, nucleophilic addition reactions (e.g. Grignard reaction) are the mainstream of carbonyl chemistry, where carbonyl compounds such as aldehydes and ketones serve as cationic carbinol synthon.



Scheme 1. Conventional carbonyl chemistry.

Umpoled reactivity of carbonyl carbons

Symmetrization of chemical reactivity (umpolung) is a powerful strategy to develop the unconventional transformation in organic synthesis. However, carbinol cation/anion umpolung has not received much attention so far.[1] One-electron reduction of aldehydes and ketones is well-known process to generate carbinol radicals. Second one-electron reduction of the carbinol radicals should afford nucleophilic carbinol anions (Scheme 2). If a general approach for carbinol cation/anion umpolung could be developed, this would open the door to novel electrophilic addition reactions to carbonyl compounds.



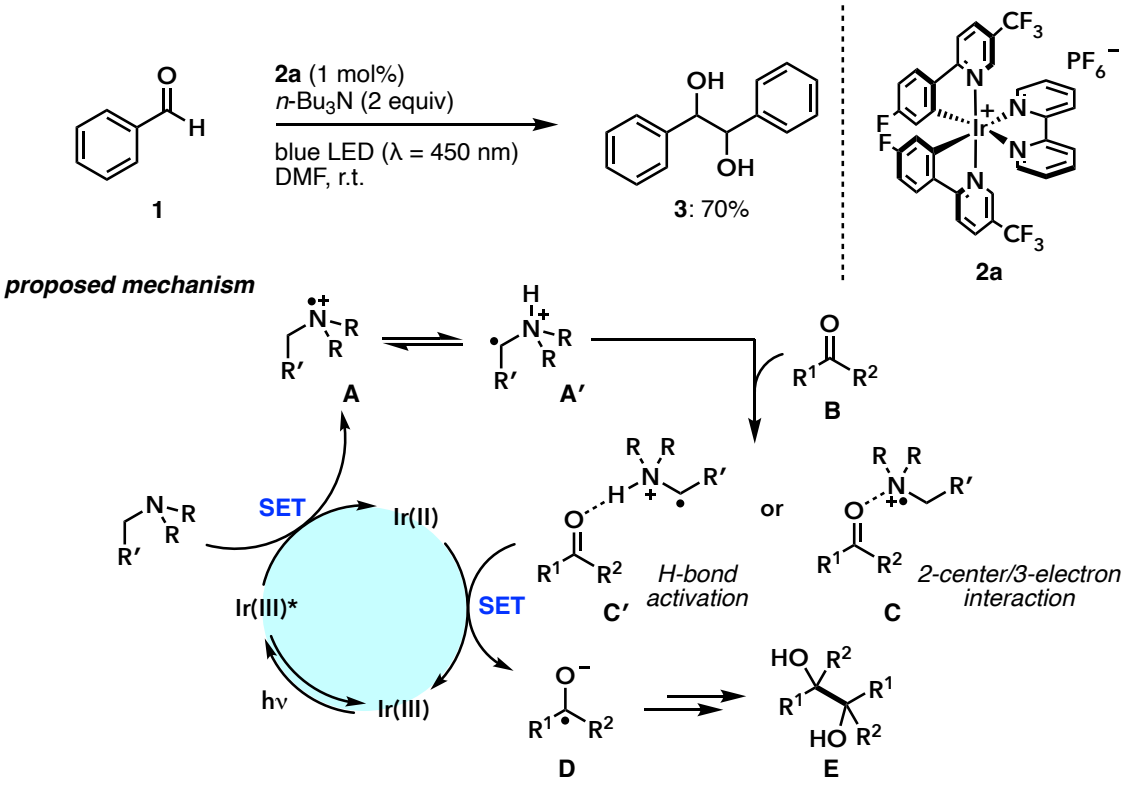
Scheme 2. Umpolung of carbonyl compounds.

Reductive transformation of carbonyl compounds under photocatalytic conditions

Visible-light-induced photoredox catalysis has received much attention as a fascinating strategy for reducing various organic compounds under mild conditions.[2] Although reductive photocatalytic transformations of carbonyl compounds have been well-investigated,[3–7] most of these are radical reactions involving carbinol radicals generated through one-electron reduction of aldehydes or

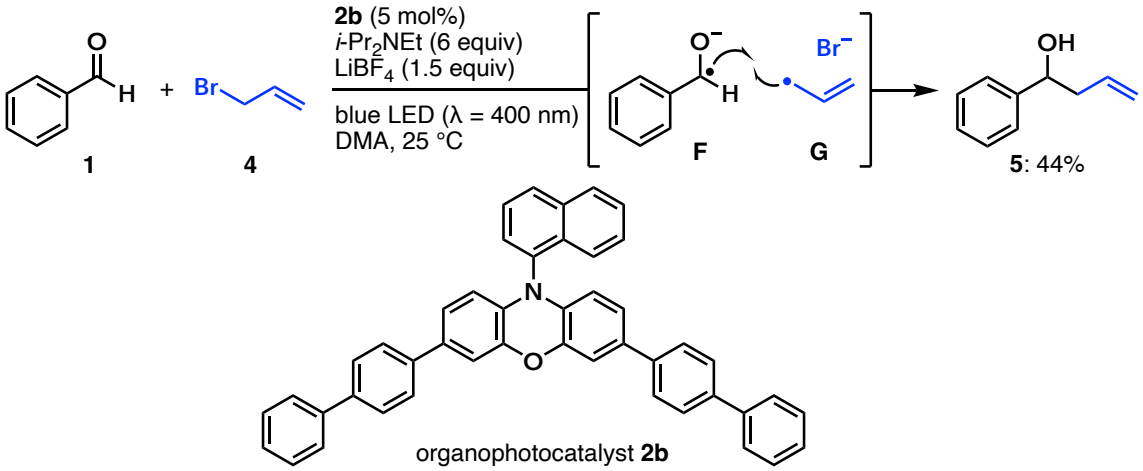
ketones.

For instance, Rueping and co-workers reported the photocatalytic reductive homo-coupling of aldehydes or ketones to give dimeric 1,2-diols (Scheme 3).[4b] Ir[F(CF_3)ppy]$_2$(bpy)PF_6 (ppy, 2-phenylpyridinato; bpy, 2,2'-bipyridine) (**2a**) catalyzed the reductive homo-coupling of aromatic aldehyde **1** in the presence of tributylamine (*n*-Bu_3N) under blue LED irradiation to give dimeric 1,2-diol **3** in 70% yield. This reaction was initiated by the photoexcitation of Ir(III) with blue LED irradiation, and then excited Ir(III)* was quenched by *n*-Bu_3N to generate Ir(II) species and *n*-$Bu_3N^{\bullet+}$ (**A** and **A'**). Carbonyl substrates **B** were activated by *n*-$Bu_3N^{\bullet+}$ and subsequently underwent the one-electron reduction by Ir(II) species to give the corresponding carbinol radicals **D** and regenerate Ir(III). Finally, radical–radical homo-coupling of **D** afforded dimeric 1,2-diols **E**.



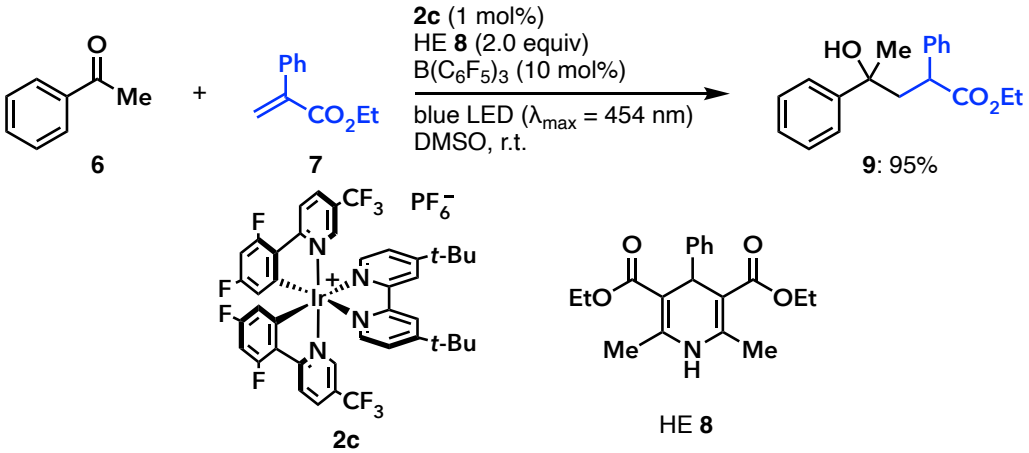
Scheme 3. Photocatalytic homo-coupling of carbinol radicals (Rueping, 2015).

In 2018, König and co-workers reported a photocatalytic Barbier reaction between aromatic aldehydes or ketones and allyl or benzyl bromides (Scheme 4).[5c] Phenoxazine **2b** promoted the coupling between aromatic aldehyde **1** and allyl bromide **4** in the presence of *i*-Pr_2NEt and $LiBF_4$ in *N*,*N*-dimethylacetamide (DMA) under blue LED irradiation to give the corresponding alcohol **5** in 44% yield. In this reaction, carbinol radical **F** and allyl radical **G** were generated through the one-electron reduction of substrates **1** and **4** followed by the radical–radical coupling to give alcohol **5**.



Scheme 4. Photocatalytic cross-coupling involving carbinol radicals (König, 2018).

The group of He and Guan reported the photocatalytic intermolecular 1,4-addition of aromatic aldehydes or ketones to electron-deficient olefins via carbinol radicals (Scheme 5).[7b] Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$ (**2c**) catalyzed the 1,4-addition of aromatic ketone **6** to acrylate **7** in the presence of Hantzsch ester (HE **8**) and tris(pentafluorophenyl)borane [B(C$_6$F$_5$)$_3$] under blue LED irradiation to give γ-hydroxy ester **9** in 95% yield. In this reaction, one-electron reduction of carbonyl substrates proceeded to give carbinol radicals, which reacted with electron-deficient olefins.

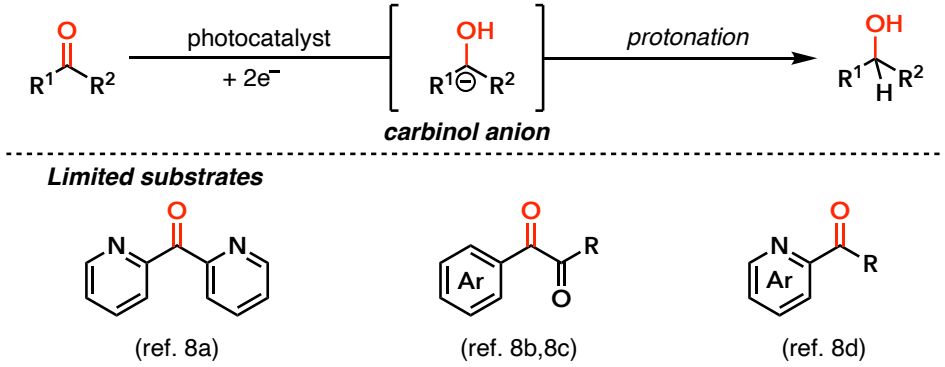


Scheme 5. Photocatalytic 1,4-addition of carbinol radicals to electron-deficient olefins (He & Guan, 2020).

As just described, carbinol radicals, generated through one-electron reduction of carbonyls, have so high reactivity that they undergo various radical reactions in preference to second one-electron reduction.

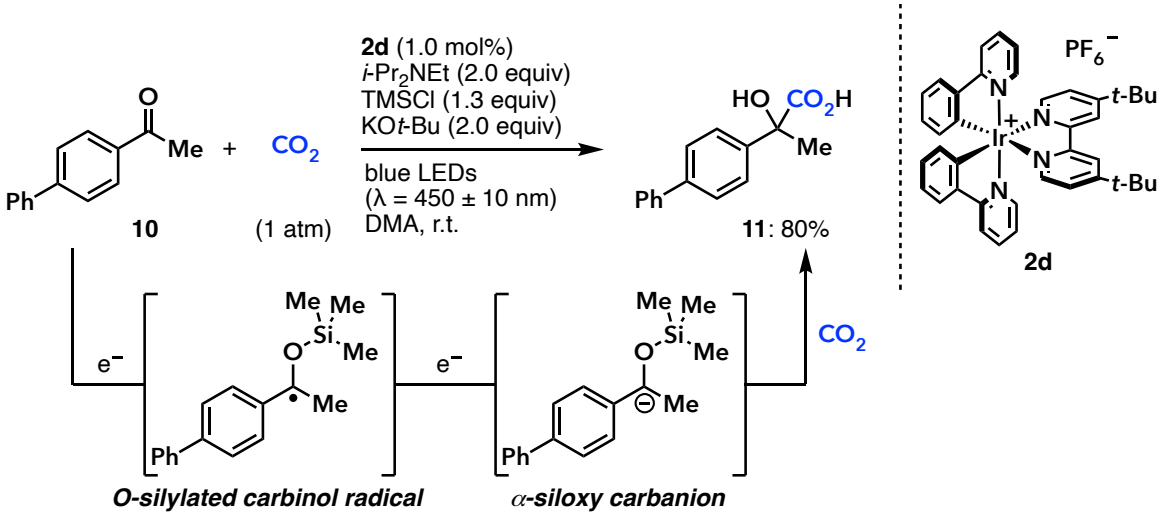
Photocatalytic carbinol cation/anion umpolung

If carbinol radicals can receive one more electron, carbinol anions should be generated. However, photocatalytic generation of carbinol anions through two successive one-electron reductions has been scarcely reported and limited to the protonation of specific substrates (Scheme 6).[8]



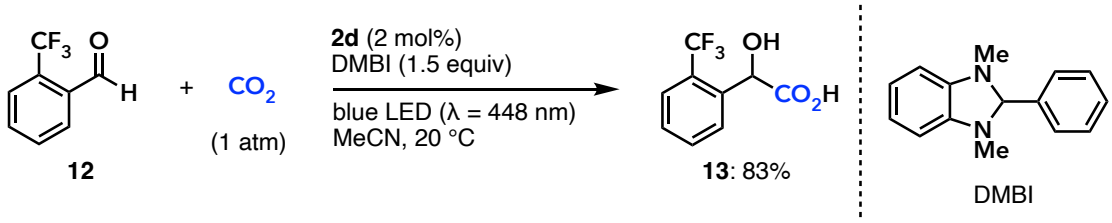
Scheme 6. Photocatalytic protonation of carbonyls via carbinol anion.

Nevertheless, two groups independently reported novel electrophilic addition reactions to carbonyl compounds via carbinol anions under photocatalytic conditions in 2021. Yu and co-workers reported the photocatalytic carboxylation of aldehydes and ketones to give α-hydroxycarboxylic acids (Scheme 7).[9] In this reaction, $Ir(ppy)_2(dtbbpy)PF_6$ (dtbbpy, 4,4'-di-*tert*-butyl-2,2'-bipyridine) (**2d**) catalyzed the one-electron reduction of carbonyl compound **10** in the presence of *i*-Pr_2NEt, trimethylsilyl chloride, and KO*t*-Bu to give the α-siloxy radical (i.e. *O*-silylated carbinol radical). The *O*-silyl group prevented the radical–radical homo-coupling pathway due to the steric hindrance of the silyl group. As a result, second one-electron reduction of the α-siloxy radical proceeded to give the α-siloxy carbanion. The resulting α-siloxy carbanion subsequently reacted with carbon dioxide to give α-hydroxycarboxylic acid **11** in 80% yield.



Scheme 7. Photocatalytic α-siloxy carbanions generation (Yu, 2021).

Okumura and Uozumi also reported the photocatalytic carboxylation of aromatic aldehydes and ketones using **2d** as a catalyst and 1,3-dimethyl-2-phenyl-2,3-dihydro-1*H*-benzimidazole (DMBI) as an electron source to afford α-hydroxycarboxylic acids (Scheme 8).[10] Aldehydes and ketones underwent two successive one-electron reductions to generate carbinol anions, which then reacted with carbon dioxide to give α-hydroxycarboxylic acids.



Scheme 8. Photocatalytic generation of carbinol anions using Ir catalyst and DMBI (Okumura & Uozumi, 2021).

There is good reason to believe that this carbinol cation/anion umpolung method should realize various electrophilic addition reactions to carbonyl compounds. Herein, the author describes the photocatalytic electrophilic carbonyl 1,2-addition of second carbonyl compounds, the so-called cross-pinacol coupling (Chapter 1), and the carbonyl 1,4-addition to electron-deficient olefins under photocatalytic conditions (Chapter 2). Finally, the author mentions General Conclusion of this thesis.

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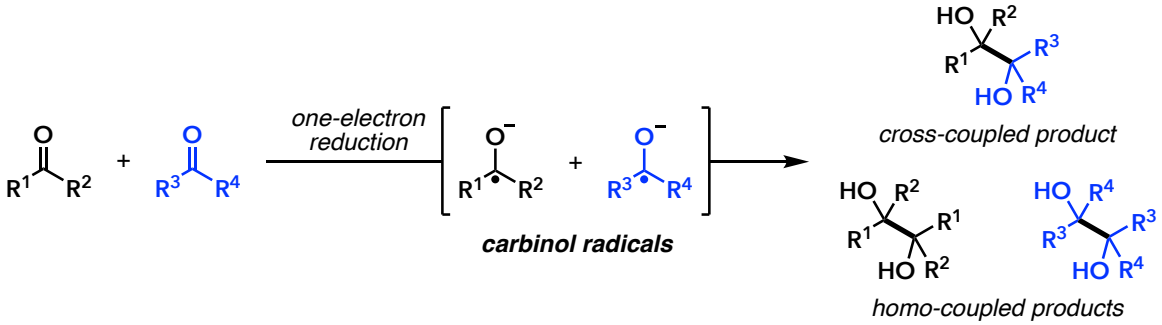
Chapter 1

Introduction

1,2-Diols have aroused considerable interest due to their presence in many therapeutically and biologically active compounds, as well as their significance in synthetic chemistry. Reductive coupling of carbonyl compounds, the so-called pinacol coupling, has been recognized as a fundamental and straightforward method for forming 1,2-diols.[1,2] Several investigations have shown that the pinacol coupling of carbonyls proceeds in the presence of strong metal reducing agents (e.g., Mg, Zn, Al, or Ti) via the corresponding carbinol radical species, which undergo the radical–radical couplings to form 1,2-diol units.[1] However, owing to the mechanism involved radical–radical coupling, conventional intermolecular pinacol coupling is limited to the homo-coupling of carbonyl compounds to give symmetric 1,2-diols. The cross-coupling of two different carbonyl compounds, i.e. cross-pinacol coupling, would offer an attractive alternative for forming unsymmetric 1,2-diols. However, carbinol radicals generated in situ are so reactive that one carbinol radical cannot selectively couple with a second carbonyl radical; this results in the formation of homo-coupled and cross-coupled 1,2-diols as products (Scheme 1).[2i,3,4c]



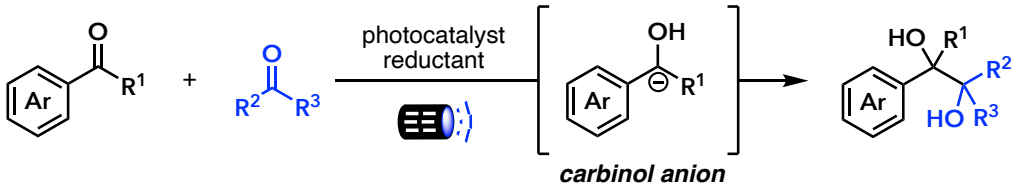
Scheme 1. Conventional cross-pinacol coupling via carbinol radicals.

Recently, the groups of Ohmiya,[4f] and Zhang[4g] independently developed an intermolecular cross-pinacol coupling of two different carbonyl compounds through copper-catalyzed or electrochemical generation of nucleophilic carbinol species, respectively. However, the cross-pinacol coupling reactions were controlled only when one of the carbonyl components was electronically activated or had a markedly different structure from that of the other carbonyl compound.[4,5] Therefore, cross-pinacol coupling between two carbonyl compounds bearing similar structures and comparable reactivities remains a major challenge.[3]

As mentioned in General Introduction, Okumura and Uozumi recently developed a novel photocatalytic carboxylation of aromatic aldehydes and ketones to give mandelic acid derivatives.[6] In this reaction, the carbonyl substrates underwent successive one-electron reduction under blue-

light irradiation in the presence of an iridium photoredox catalyst and a 1,3-dimethyl-2,3-dihydro-1*H*-benzimidazole-based reductant[7] to generate nucleophilic carbinol anion species that subsequently reacted with carbon dioxide to afford the corresponding carboxylation products.[8,9] If the inherent electrophilic nature of carbonyl groups is taken into account, the photocatalytic process brought about an umpolung of the carbonyls serving as nucleophilic carbinol synthons.

Based on this background, the author developed the first photocatalytic cross-pinacol coupling between two different carbonyl compounds to afford unsymmetric 1,2-diols (Scheme 2). The reaction proceeds by a novel umpolung pathway in which one carbonyl compound serves as a carbinol anion nucleophile through rapid two-electron reduction to react with a second relatively electron-rich carbonyl compound possessing inherent electrophilic reactivity. Various combinations of reactants, two aldehydes, two ketones, or an aldehyde and a ketone, have been coupled, including couplings of two carbonyl substrates with similar structures.

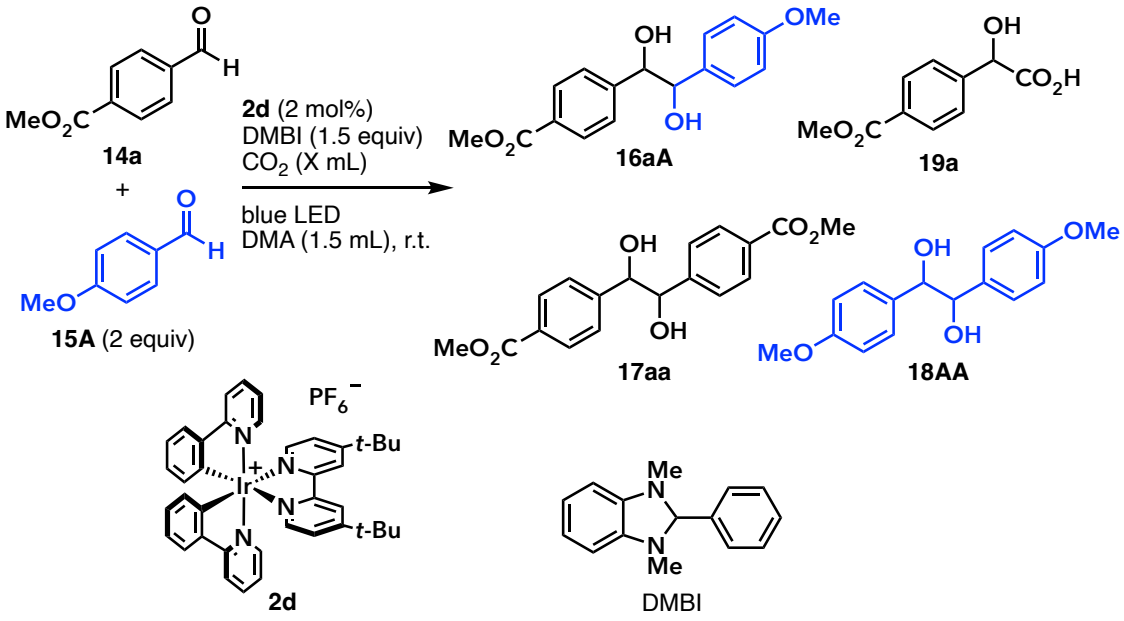


Scheme 2. Photocatalytic cross-pinacol coupling (this work).

Optimization of reaction conditions

First, the coupling reaction of two aromatic aldehydes was examined under photocatalytic conditions. Methyl 4-formylbenzoate (**14a**, 1 equiv) was added to a DMA solution containing *p*-anisaldehyde (**15A**, 2 equiv), $Ir(ppy)_2(dtbbpy)PF_6$ (**2d**, 2 mol%) as a photocatalyst, and DMBI (1.5 equiv) as a reductant under blue light irradiation (λ_{max} = 462 nm) at room temperature (r.t.) to afford the desired unsymmetric 1,2-diol **16aA** in 26% yield, together with the dimeric diol **17aa** in 52% yield as the major product (Table 1, entry 1). Surprisingly, when the reaction was carried out under a CO_2 atmosphere, the cross-pinacol selectivity markedly improved, and **16aA** was obtained in 77% NMR yield, along with a 7% yield of the homo-coupled dimer **17aa** and a 9% yield of the α-hydroxycarboxylic acid **19a** (entry 2).[6] The presence of a small amount of CO_2 (1 mL) was enough to promote cross-pinacol coupling, without the formation of the carboxylic acid **19a** as a by-product,

Table 1. Screening of CO_2 amount in the cross-pinacol coupling of methyl 4-formylbenzoate (**10a**) with *p*-anisaldehyde (**11A**).[a]



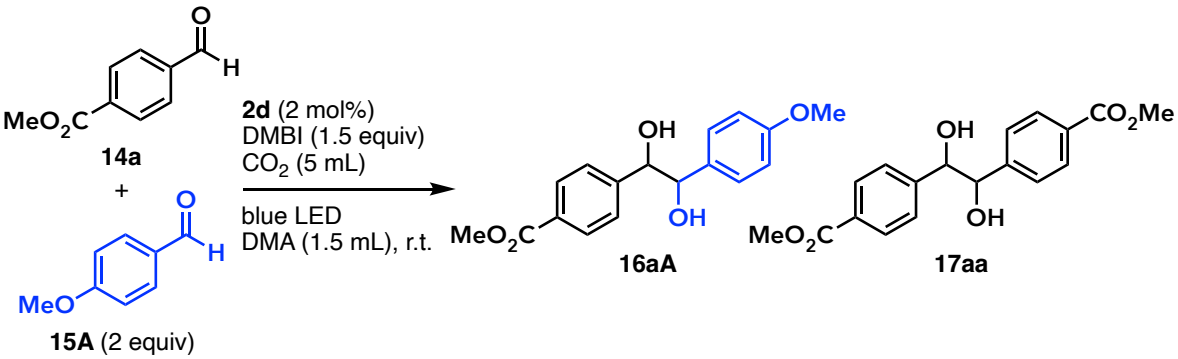
entry	CO_2 (mL)	yield (%)[b]			
		16aA	**17aa**	**18AA**	**19a**
1	none	26	52	0	0
2	balloon	77	7	0	9
3	1	67	13	0	0
4	2.2	75	7	0	1
5	5	82	5	0	0
6	10	82	7	0	0

[a] Reaction conditions: aldehyde **15A** (0.4 mmol, 2 equiv), **2d** (0.004 mmol, 2 mol %), DMBI (0.3 mmol, 1.5 equiv), DMA (1.5 mL); dropwise addition of aldehyde **14a** (0.2 mmol) over 20 min, then stirring for 40 min, blue LED irradiation (40 W, λ_{max} = 462 nm), r.t. [b] NMR yield.

giving **16aA** in 67% yield together with a 13% yield of the homo-coupled product **17aa** (entry 3). Bubbling of CO_2 (5 mL) through the solution for 30 seconds prior to the photoirradiation under a N_2 atmosphere was enough to promote the reaction effectively (entries 4–6). As a result, 82% of **16aA** was obtained along with 5% of **17aa**; none of the α-hydroxycarboxylic acid **19a** was formed (entry 5). The product of dimerization of **15A** (**18AA**) was also not obtained, indicating that the carbinol radical from **15A** was hardly generated under the photocatalytic conditions. This suggested that the cross-pinacol coupling proceeded via the carbinol anion of **14a**, which reacted with the electrophilic coupling partner **15A** to give the cross-pinacol product **16aA**.

The author also examined the loading of electrophile **15A** and a reductant, and necessity of dropwise addition of **14a** (Table 2). As the amount of **15A** was decreased to 1.0 equivalent, the yield of **16aA** was decreased to 70% (entries 2 and 3). Although the cross-pinacol coupling proceeded smoothly with 1.0 equivalent of DMBI, the homo-coupled product **17aa** slightly increased to 8% (entry 4). When a DMA solution of all reagents and **14a** was irradiated with blue light for 1 hour, the yield of **16aA** dramatically decreased to 16% and diol **17aa** was formed in 66% as the major product (entry 5). This result indicates that high-dilution technique is essential to proceed the cross-pinacol reaction with high selectivity.

Table 2. Screening of the amount of **15A** and DMBI.[a]

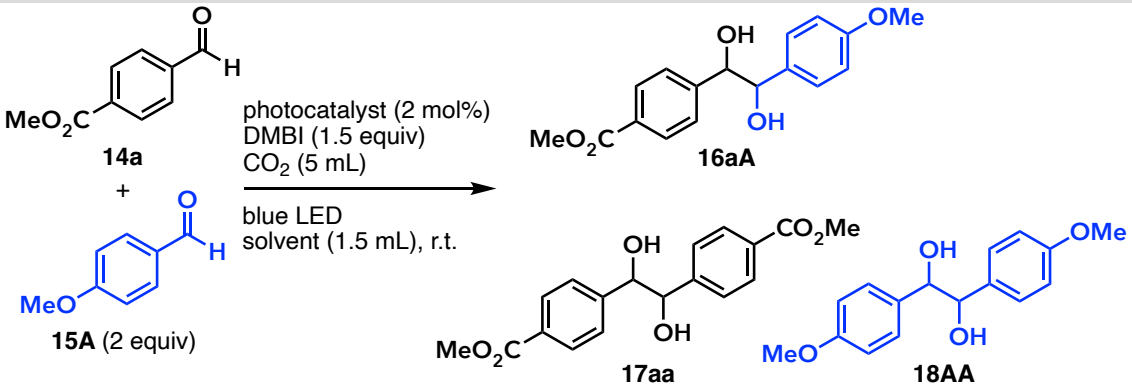


entry	variation	yield (%)[b]	
		16aA	**17aa**
1	none	82	5
2	1.5 equiv of **15A**	74	8
3	1.0 equiv of **15A**	70	9
4	1.0 equiv of DMBI	82	8
5	without dropwise addtion[c]	16	66

[a] Reaction conditions: aldehyde **15A** (0.4 mmol, 2 equiv), **2d** (0.004 mmol, 2 mol %), DMBI (0.3 mmol, 1.5 equiv), DMA (1.5 mL); dropwise addition of aldehyde **14a** (0.2 mmol) over 20 min, then stirring for 40 min, blue LED irradiation (40 W, λ_{max} = 462 nm), r.t. [b] NMR yield. [c] DMA solution of all reagents and **14a** irradiated with blue light for 1 h.

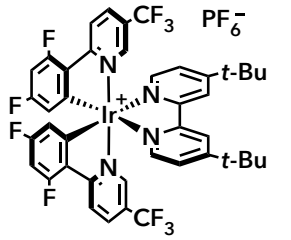
Next, suitable solvents and photocatalysts were investigated (Table 3). Polar aprotic solvents provided **16aA** in moderate to high yields (entries 1–4). When toluene and MeOH was used as the

Table 3. Screening of solvents and photocatalysts.[a]

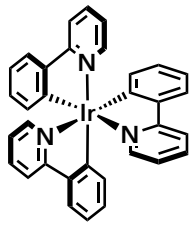


entry	solvent	photocatalyst	yield (%)[b]		
			16aA	**17aa**	**18AA**
1	DMA	**2d**	82	5	0
2	DMF	**2d**	76	9	0
3	MeCN	**2d**	82	9	0
4	THF	**2d**	54	30	0
5	toluene	**2d**	27	56	0
6	MeOH	**2d**	2	25	27
7[c]	DMA	**2c**	24	<60	1
8[c]	DMA	**2e**	68	15	7
9[c]	DMA	**2f**	69	18	0
10[c]	DMA	**2b**	74	17	5
11[c]	DMA	**2g**	7	<24	0
12[c]	DMA	**2h**	21	72	0

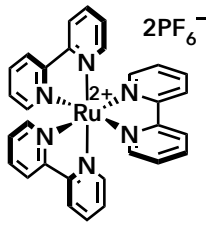
[a] Reaction conditions: aldehyde **15A** (0.4 mmol, 2 equiv), photocatalyst (0.004 mmol, 2 mol %), DMBI (0.3 mmol, 1.5 equiv), solvent (1.5 mL); dropwise addition of aldehyde **14a** (0.2 mmol) over 20 min, then stirring for 40 min, blue LED irradiation (40 W, λ_{max} = 462 nm), r.t. [b] NMR yield. [c] CO_2 (10 mL).



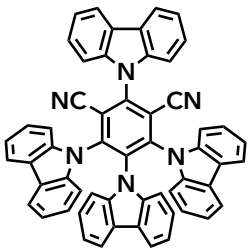
2c
$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$



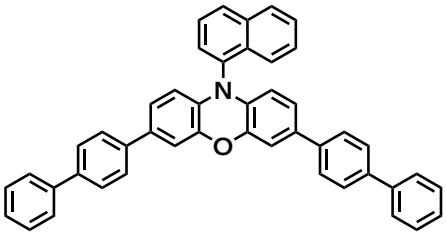
2e
$Ir(ppy)_3$



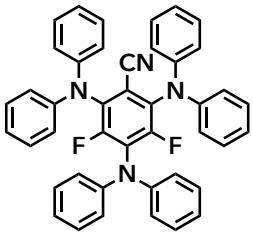
2f
$Ru(bpy)_3(PF_6)_2$



2g
4CzIPN



2b
Phenox O-PC

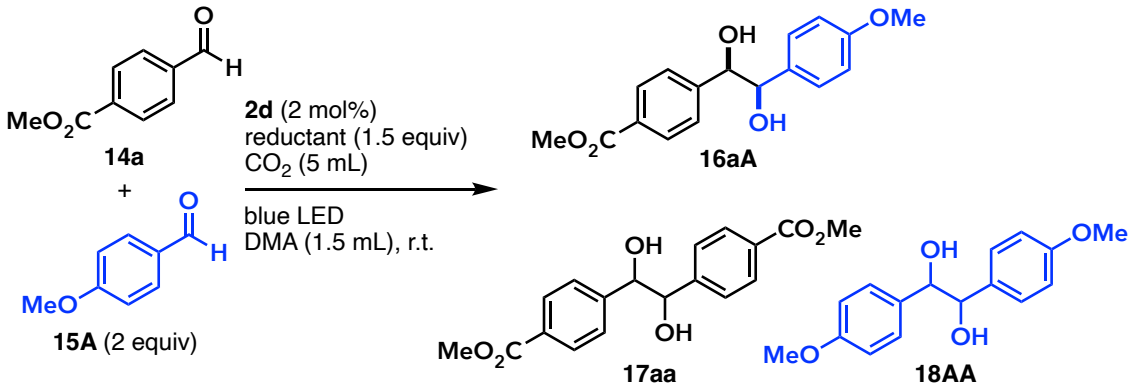


2h
3DPA2FBN

solvents, **16aA** was obtained in yields of only 27% and 2%, respectively (entries 5 and 6). DMA solvent provided the best result, 82% NMR yield of **16aA** (entry 1). A wide variety of photocatalysts, including iridium and ruthenium polypyridyl complexes, and organophotocatalyts, were examined in the cross-pinacol coupling reaction (entries 1 and 7–12), among which **2d** was identified as the best photocatalyst.

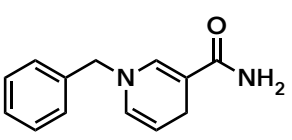
Various reductants were investigated (Table 4). When Et_3N and *i*-Pr_2NEt were used instead of DMBI, the yield of diol **16aA** was less than 32% and the dimeric diol **17aa** was obtained as the major product (entries 2 and 3). Other reductants such as 1-benzyl-1,4-dihydronicotinamide (BNAH) and Hantzsch

Table 4. Screening of reductants.[a]

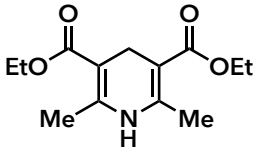


entry	reductant	yield (%)[b] 16aA	17aa	18AA
1	DMBI	82	5	0
2	Et_3N	26	52	0
3	*i*-Pr_2NEt	31	56	0
4	BNAH	25	40	3
5	HE **20**	43	27	76
6	DMBI-CF_3	84 (81)[c]	5	0
7	DMBI **21**	78	4	0
8	DMBI **22**	10	6	0

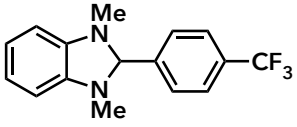
[a] Reaction conditions: aldehyde **15A** (0.4 mmol, 2 equiv), **2d** (0.004 mmol, 2 mol %), reductant (0.3 mmol, 1.5 equiv), DMA (1.5 mL); dropwise addition of aldehyde **14a** (0.2 mmol) over 20 min, then stirring for 40 min, blue LED irradiation (40 W, λ_{max} = 462 nm), r.t. [b] NMR yield. [c] Isolated yield; the diastereomeric *syn*/*anti* ratio for **16aA** was 80:20 (*syn*-**16aA** diastereomer is shown in the scheme).



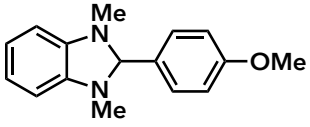
BNAH



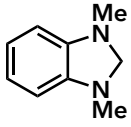
HE **20**



DMBI-CF_3



DMBI **21**

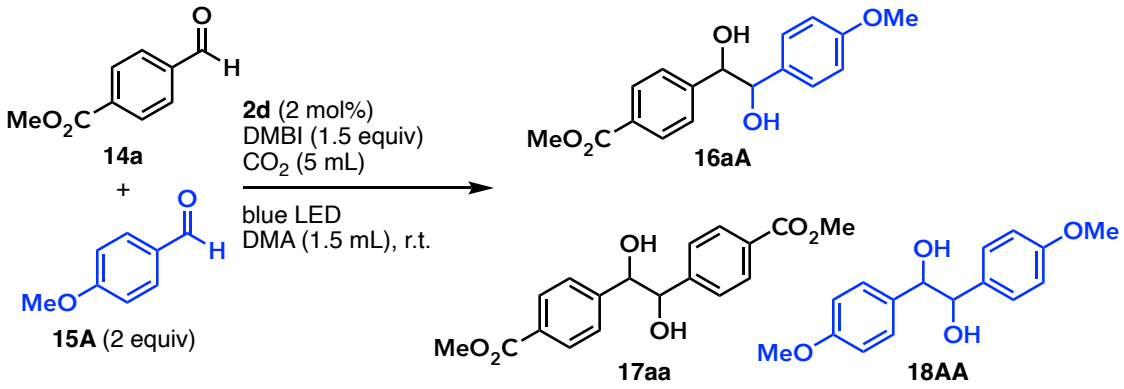


DMBI **22**

ester (HE **20**) resulted in forming **16aA** in yields of 25% and 43% (entries 4 and 5). These results suggested that the DMBI reductant was essential for achieving an effective cross-pinacol coupling. The best result was obtained when DMBI-CF_3 was used as a reductant instead of DMBI; this gave the desired cross-pinacol product **16aA** (*syn*/*anti* = 80:20) in 81% isolated yield (84% NMR yield) (entry 6).

Control experiments showed that all the reagents, as well as blue-light irradiation, were essential for the formation of cross-coupled 1,2-diol **16aA** (Table 5, entries 2–4).

Table 5. Control experiments.[a]



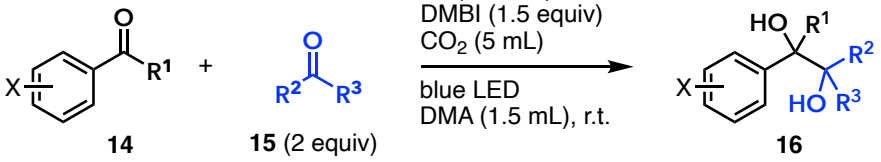
entry	variation	yield (%)[b]		
		16aA	**17aa**	**18AA**
1	none	82	5	0
2	no photocatalyst	0	5	0
3	no light	0	2	0
4	no DMBI	0	0	0

[a] Reaction conditions: aldehyde **15A** (0.4 mmol, 2 equiv), **2d** (0.004 mmol, 2 mol %), DMBI (0.3 mmol, 1.5 equiv), DMA (1.5 mL); dropwise addition of aldehyde **14a** (0.2 mmol) over 20 min, then stirring for 40 min, blue LED irradiation (40 W, λ_{max} = 462 nm), r.t. [b] NMR yield.

Substrate scope

Having identified an efficient cross-pinacol coupling system, the author next examined the scope of the reaction between two different aldehydes (Scheme 3). Aromatic aldehydes **15A**–**E** bearing electron-donating groups such as methoxy, methyl, or methylsulfanyl, when used as electrophilic substrates, coupled with the nucleophilic aldehyde **14a** under the photocatalytic conditions to afford the unsymmetric 1,2-diols **16aA**–**aE** in yields of 76–88%; aromatic C–F (**14aF**) and C–Cl (**14aG**) bonds were also well tolerated. Aliphatic aldehydes were also suitable electrophiles. The primary and secondary alkyl aldehydes **15H** and **15I**, respectively, gave the corresponding 1,2-diols **16aH** and

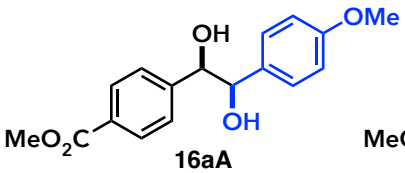
16aI in yields of 78% and 71%. Even the sterically hindered tertiary alkyl aldehyde **15J** reacted with **14a** to afford the coupled product **16aJ** in 53% yield. Paraformaldehyde (**15K**) was also tolerated as an electrophilic substrate to give the corresponding 1,2-diol **16aK** in 71% NMR (48% isolated) yield. A variety of aryl aldehydes **14b–f** were then tested as nucleophiles to react with *p*-anisaldehyde (**15A**) as an electrophile. Aryl aldehydes **14c** and **14b** bearing a *tert*-butoxycarbonyl group or a carboxylic acid group, gave the desired 1,2-diols **16cA** and **16bA** in yields of 51% and 91%, respectively. When 4-acetylbenzaldehyde (**14d**) was used, the aldehyde part coupled with **15A** to afford **16dA** in 61% NMR (46% isolated) yield. A 2-trifluoromethyl substituent, which has a high inductive effect, promoted the generation of the carbinol anion to afford the cross-coupled product **16eA** in 62% yield. The coupling reaction of biphenyl-4-carboxaldehyde (**14f**), which has a π-expanded aromatic moiety, gave the 1,2-diol **16fA** in 54% yield.[10] When the reaction of methyl 2-formylbenzoate (**14g**) with *p*-anisaldehyde (**15A**) was performed, the corresponding 1,2-diol was generated and smoothly converted to cyclized product **23gA** in 47% yield.



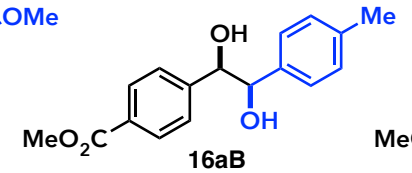
14 15 (2 equiv) 16

	X	R^1		X	R^1
14a	4-CO_2Me	H	**14d**	4-COMe	H
14b	4-COOH	H	**14e**	2-CF_3	H
14c	4-CO_2*t*-Bu	H	**14f**	4-C_6H_5	H
			14g	2-CO_2Me	H

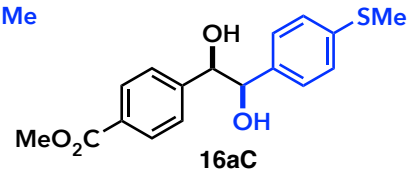
	R^2	R^3		R^2	R^3
15A	4-$MeOC_6H_4$	H	**15F**	4-FC_6H_4	H
15B	4-MeC_6H_4	H	**15G**	4-ClC_6H_4	H
15C	4-$MeSC_6H_4$	H	**15H**	*n*-$C_{10}H_{21}$	H
15D	2-$MeOC_6H_4$	H	**15I**	*c*-C_6H_{11}	H
15E	3-$MeOC_6H_4$	H	**15J**	*t*-Bu	H
			15K	H	H



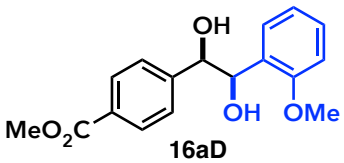
16aA
81%[a] (80:20)



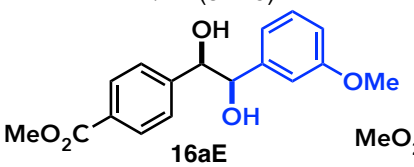
16aB
76% (81:19)
74%[b] (81:19)



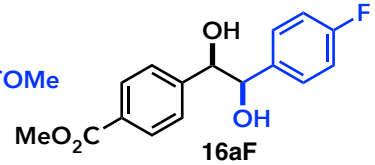
16aC
79% (77:23)



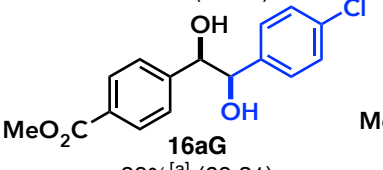
16aD
79%[a] (72:28)



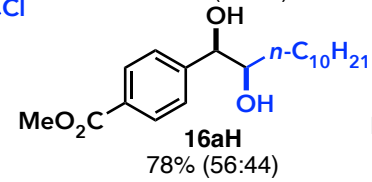
16aE
88%[a] (78:22)



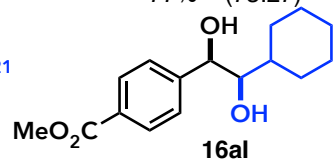
16aF
77%[a] (73:27)



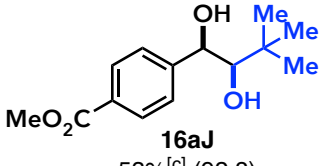
16aG
89%[a] (69:31)



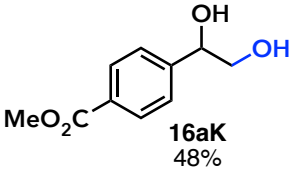
16aH
78% (56:44)



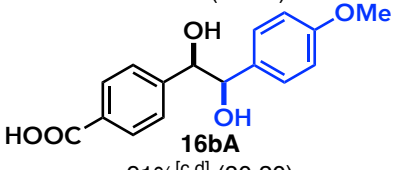
16aI
71%[a] (63:37)



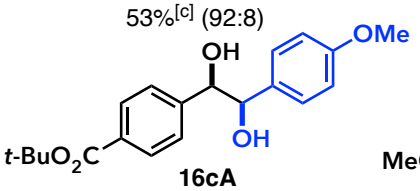
16aJ
53%[c] (92:8)



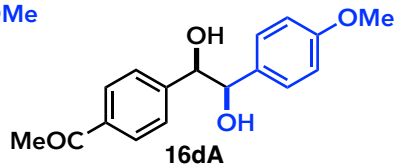
16aK
48%



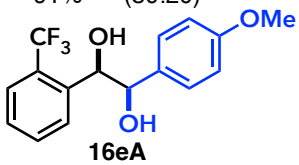
16bA
91%[c,d] (80:20)



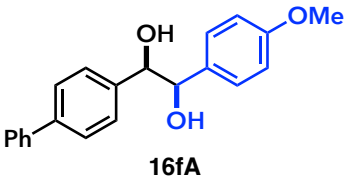
16cA
51% (77:23)



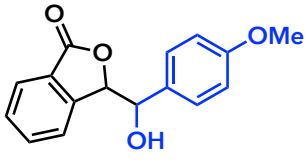
16dA
46%[e,f] (75:25)



16eA
62%[e] (67:33)



16fA
54%[e,g,h] (63:37)

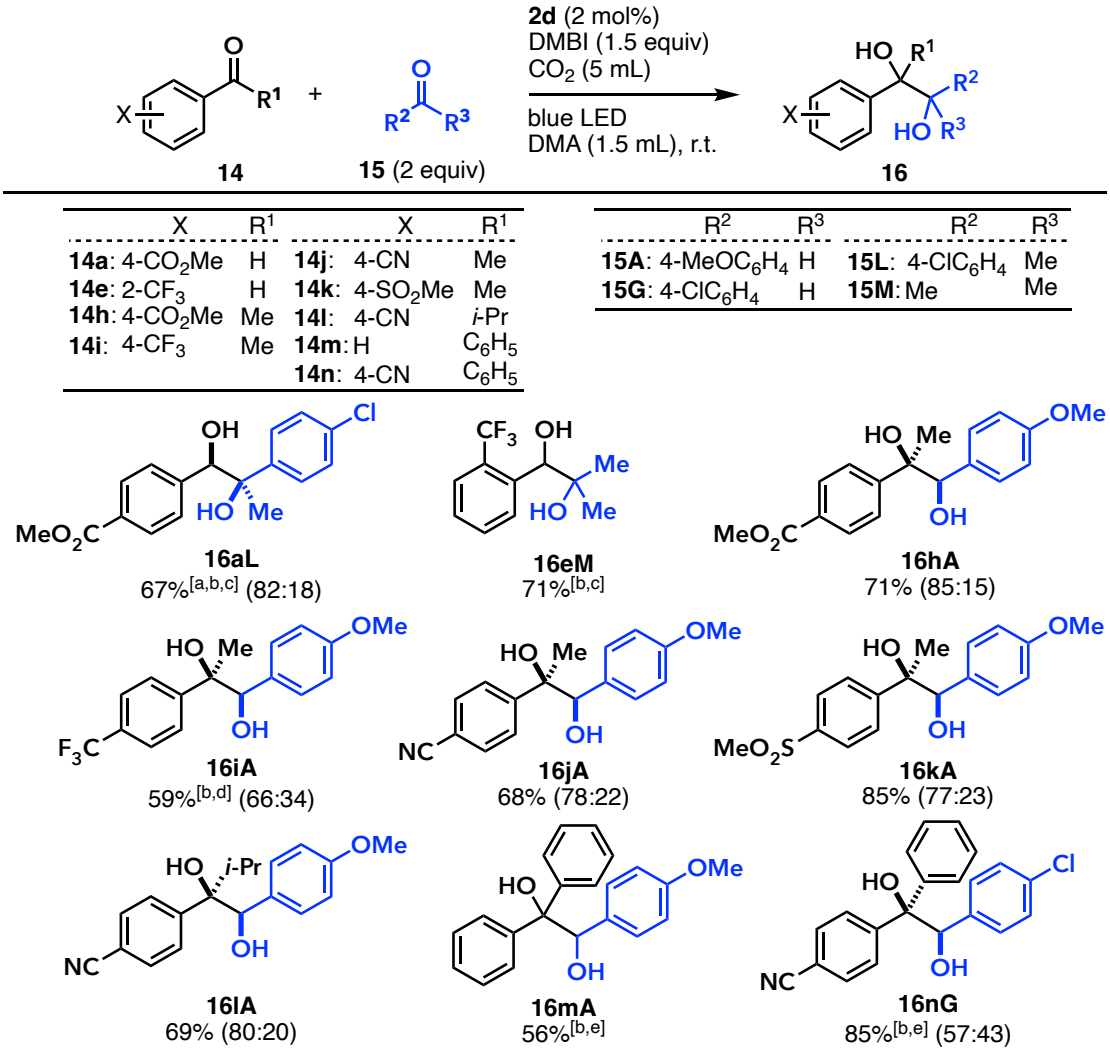


23gA
47%

Reaction conditions: carbonyl compound **15** (2 equiv), **2d** (2 mol%), DMBI (1.5 equiv), CO_2 (5 mL), DMA (0.13 M), r.t., dropwise addition of **14** (0.2 mmol) over 20 min followed by stirring for 40 min. [a] DMBI-CF_3 was used instead of DMBI. [b] 1.0 mmol scale. [c] dropwise addition of **14** over 50 min followed by stirring for 10 min. [d] CO_2 (10 mL). [e] CO_2 (20 mL), [f] **15** (5 equiv). [g] **15** (10 equiv), [h] dropwise addition of **14** over 50 min followed by stirring for 1 h.

Scheme 3. Scope of the reaction between aldehydes.

The author also examined the reactions between aldehydes with ketones (Scheme 4). The cross-pinacol coupling reactions of ketones afforded sterically hindered quaternary carbinol carbons. Carbinol anions derived from electron-deficient aromatic aldehydes attacked aromatic or aliphatic ketones. Methyl 4-formylbenzoate (**14a**) and 2-(trifluoromethyl)benzaldehyde (**14e**) coupled with 4-chloroacetophenone (**15L**) or acetone (**15M**), respectively, to give 1,2-diols **16aL** and **16eM** in yields of 67% and 71%.[11] Nucleophilic carbinol anions were successfully generated, not only from aromatic aldehydes, but also from aromatic ketones. Electron-deficient acetophenone derivatives **14h–k** bearing methyl ester, trifluoromethyl, cyano, or methyl sulfone groups reacted with *p*-anisaldehyde to give the corresponding products **16hA–kA** in yields of 59–85%. Alkyl aryl ketone **14l** bearing an isopropyl group as an alkyl moiety was an eligible reactant and gave the

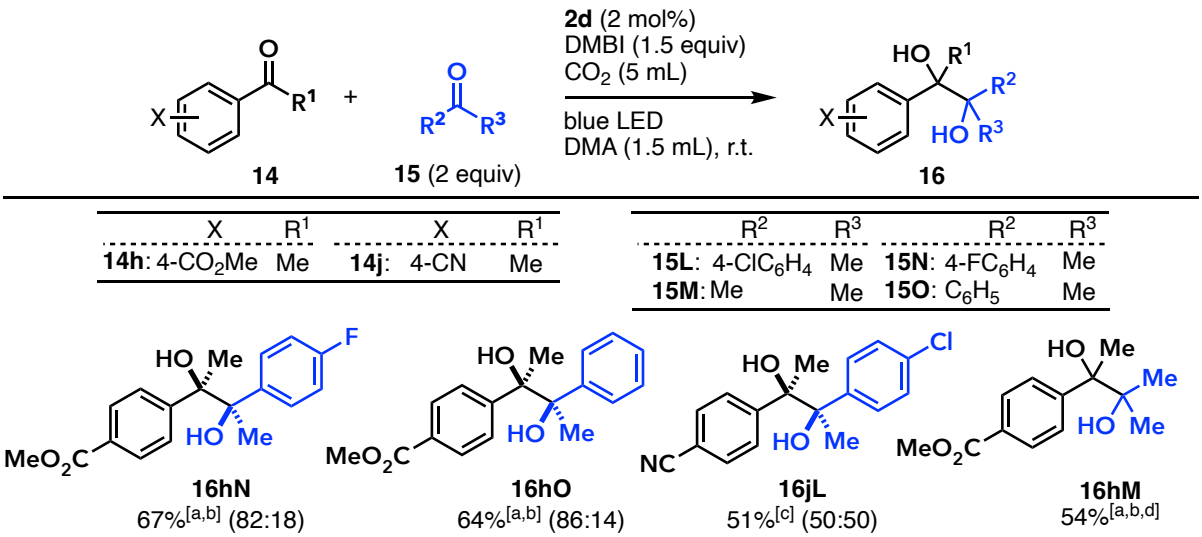


Reaction conditions: carbonyl compound **15** (2 equiv), **2d** (2 mol%), DMBI (1.5 equiv), CO_2 (5 mL), DMA (0.13 M), r.t., dropwise addition of **14** (0.2 mmol) over 20 min followed by stirring for 40 min. [a] DMBI-CF_3 was used instead of DMBI. [b] CO_2 (20 mL), [c] **15** (5 equiv). [d] dropwise addition of **14** over 50 min followed by stirring for 10 min. [e] DMA solution of all reagents and **14** irradiated with blue light for 1 h.

Scheme 4. Scope of the reaction between aldehydes with ketones.

corresponding diol **16lA** in 69% yield. Diaryl ketones such as benzophenone (**14m**) and 4-cyanobenzophenone (**14n**) selectively coupled with aromatic aldehydes **15A** and **15G**, respectively, to afford the corresponding diols **16mA** and **16nG** in yields of 56% (76% NMR)[12] and 85%. Note that the presence of two large aryl groups on the diaryl ketones prevented dimerization; consequently, these reactions could be carried out by mixing all the reagents without using a high-dilution protocol.

A cross-pinacol coupling between two different ketones was also achieved (Scheme 5); in these reactions, the tertiary carbinol anions that were generated underwent subsequent addition to other ketones to construct sterically hindered vicinal quaternary carbons. Methyl 4-acetylbenzoate (**14h**) reacted with 4-fluoroacetophenone (**15N**) or acetophenone (**15O**) to give 1,2-diols **16hN** and **16hO**, respectively, in yields of 67% and 64%. Cyano and chloro groups were well tolerated, and the unsymmetric 1,2-diol **16jL** was obtained in 51% yield. In the presence of an excess of acetone (**15M**), the tertiary carbinol anion also reacted with the aliphatic ketone to give **16hM** in 54% yield.

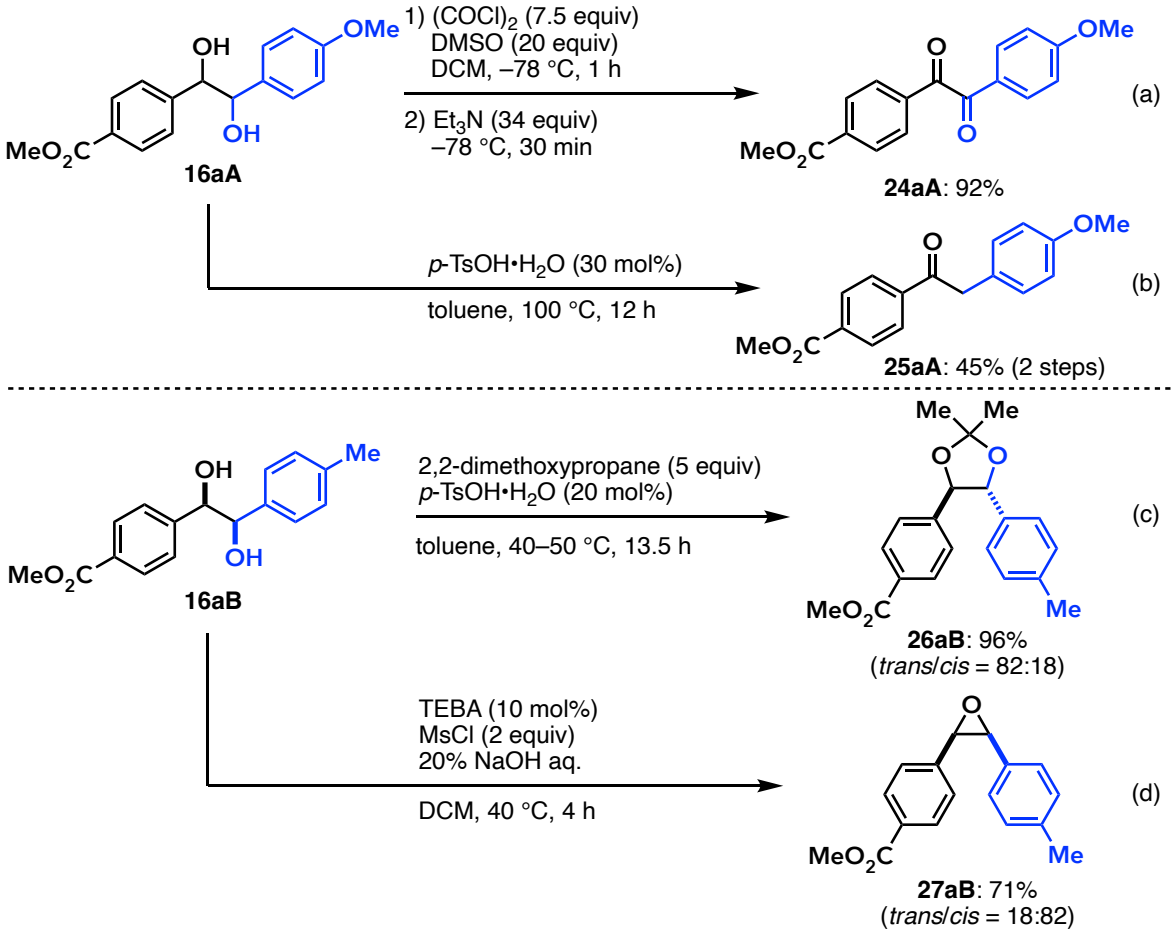


Reaction conditions: carbonyl compound **15** (2 equiv), **2d** (2 mol%), DMBI (1.5 equiv), CO_2 (5 mL), DMA (0.13 M), r.t., dropwise addition of **14** (0.2 mmol) over 20 min followed by stirring for 40 min. [a] dropwise addition of **14** over 50 min followed by stirring for 10 min [b] CO_2 (20 mL), [c] DMA solution of all reagents and **14** irradiated with blue light for 1 h. [d] **15** (50 equiv).

Scheme 5. Scope of the reaction between ketones.

Synthetic applications of unsymmetric 1,2-diols

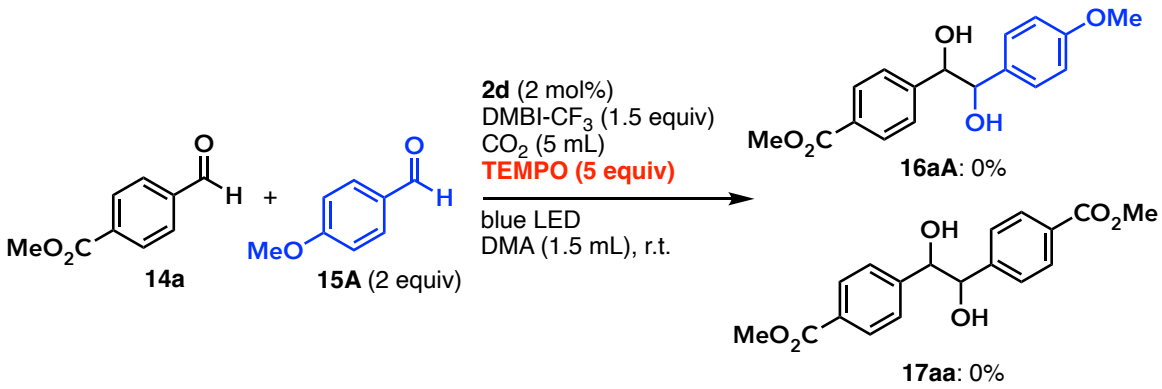
The resulting 1,2-diols are useful as building blocks for synthesizing various unsymmetric compounds (Scheme 6). The unsymmetric 1,2-diketone **24aA** was obtained in 92% yield by Swern oxidation of diol **16aA** (Scheme 6a).[13] A reaction involving a cross-pinacol coupling of **14a** and **15A** followed by treatment with TsOH afforded ketone **25aA** in 45% yield (two steps, Scheme 6b). The reaction of **16aB** with 2,2-dimethoxypropane in the presence of TsOH gave the cyclic acetal **26aB** in 96% yield (Scheme 6c).[14] An unsymmetric epoxide was also synthesized through the internal nucleophilic substitution of a 1,2-diol: treatment of **16aB** with benzyl(triethyl)ammonium chloride (TEBA), MsCl, and NaOH afforded the corresponding epoxide **27aB** in 71% yield, with inversion of the stereochemistry (Scheme 6d).[15]



Scheme 6. Synthetic applications of unsymmetric 1,2-diols.

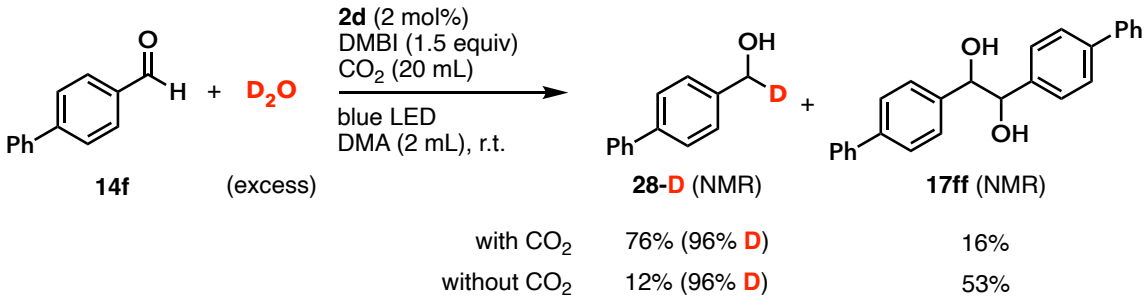
Mechanistic studies

A radical-trapping experiment and a deuteration experiment were performed to gain mechanistic insights into the photocatalytic cross-pinacol coupling. When the coupling reaction of aldehyde **14a** with **15A** was carried out in the presence of TEMPO as a radical scavenger, the formation of the cross-coupled 1,2-diol **16aA** was completely inhibited, indicating the involvement of a radical intermediate (Scheme 7).



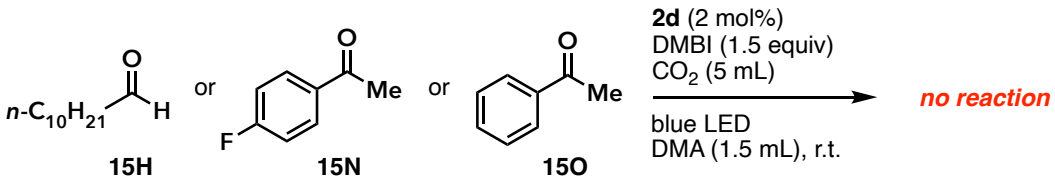
Scheme 7. Radical trapping experiment.

The deuteration experiment was performed by using D_2O, which barely reacts with radical species but reacts readily with anionic species. Biphenyl-4-carboxaldehyde (**14f**) reacted with D_2O in the presence of a CO_2 additive to give the α-*C*-deuterated alcohol **28-D** in 76% NMR yield with 96% benzylic incorporation of deuterium (Scheme 8).[6]



Scheme 8. Deuteration experiments.

The author also confirmed the inertness of the electron-rich aldehydes and ketones undecanal (**15H**), 4-fluoroacetophenone (**15N**), and acetophenone (**15O**) under the standard conditions (Scheme 9). These results support the supposition that the cross-pinacol coupling proceeds through a radical–polar crossover pathway.



Scheme 9. Inertness of carbonyl compounds serving as electrophiles.

It is assumed that CO_2 plays a key role[16] in promoting the generation of the carbinol anions.[6] When the deuteration experiment was performed under a N_2 atmosphere without a CO_2 additive, the NMR yield of alcohol **28-D** decreased to only 12%, whereas that of the dimer **17ff** increased (Scheme 8). To elucidate the role of CO_2, the author performed an electrochemical analysis of aldehyde **14a** by cyclic voltammetry (CV) in DMF in the presence or absence of the CO_2 additive (Figure 1). Under a N_2 atmosphere, aldehyde **14a** showed two successive reduction peaks (Figure 1, red). The first reversible reduction peak at −1.51 V (E_p) can be assigned to the first electron transfer to afford the carbinol radical, whereas the second irreversible peak at −2.11 V (E_p) is assigned as a second electron transfer to give the anionic species. As a rough estimate of the redox potential $E^0_{1/2}$, the author used the half-peak potential E_h (the potential at half the current in E_p).[17] The first reduction potential was approximately −1.45 V (vs. SCE), whereas the second reduction potential was approximately −2.03 V (vs. SCE), which is too high for reduction by **2d** (−1.51 V vs. SCE in MeCN);[18] therefore, one-electron reduction of aldehyde **14a** proceeded as the main pathway in the absence of CO_2, resulting in the

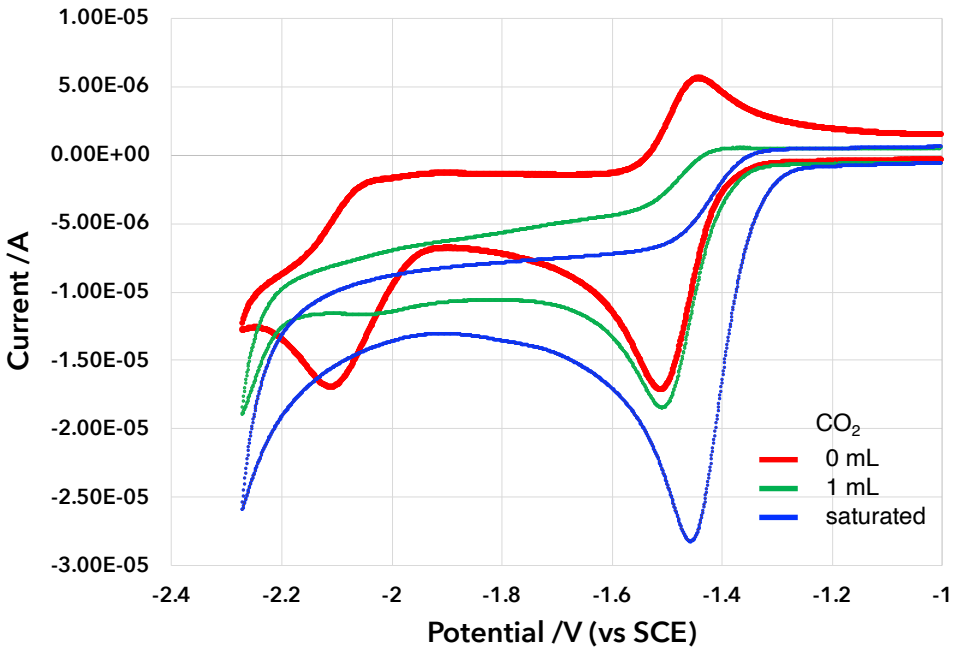
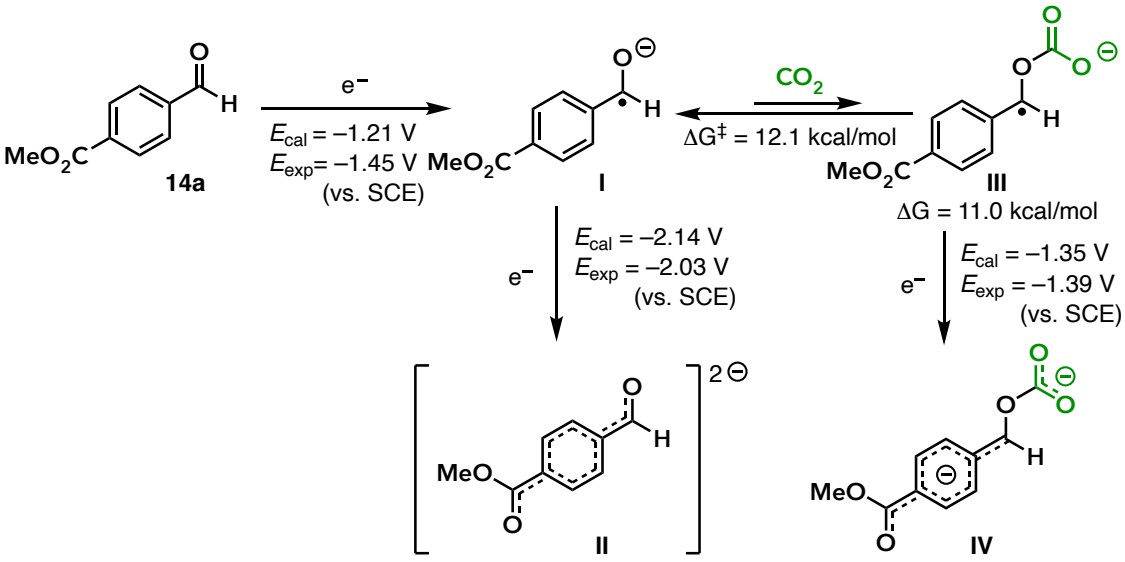


Figure 1. Cyclic voltammogram of aldehyde **14a** with various amount of CO_2.

formation of dimer **17aa** through conventional radical–radical coupling. Bubbling a certain amount of CO_2 over 30 seconds resulted in a significant change in the cyclic voltammogram of **14a**. As the amount of CO_2 additive increased, the first peak current increased and the second peak current decreased (Figure 1, green). Finally, the second peak disappeared and the first peak had twice the intensity of that observed in the absence of CO_2 and became irreversible, indicating that the rapid reaction of the carbinol radical with CO_2 generated a new intermediate (Figure 1, blue). The large current suggests that a second electron transfer also occurred in the first-peak region to produce an anionic species. Similar effects of CO_2 have been observed in the electrocarboxylation of ketones with CO_2.[19]

DFT calculations on the reduction step were performed to support the hypothesis that CO_2 promotes the generation of carbinol anion species (Scheme 10).[19c] The calculated first reduction potential (E_{cal}) of aldehyde **14a** to the carbinol radical **I** was −1.21 V (vs. SCE), which is similar to the experimental potential observed in CV (E_{exp} = −1.45 V vs. SCE). The direct successive reduction of the generated carbinol radical **I** to the dianion species **II** shows a markedly high potential (E_{cal} = −2.14 V vs. SCE), consistent with the experimental result (E_{exp} = −2.03 V vs. SCE). The negative charge on the carbinol radical **I** is localized on the oxygen derived from the aldehyde moiety, and the spin density is highest at the neighboring carbon atom. Attack by the anionic oxygen on CO_2 therefore gives the intermediate **III**; the activation barrier for this process is 12.1 kcal/mol. A subsequent one-electron reduction of intermediate **III** affords the dianion species **IV**, which serves as a carbinol anion nucleophile. The calculated reduction potential of intermediate **III** is −1.35 V (vs. SCE), which is more

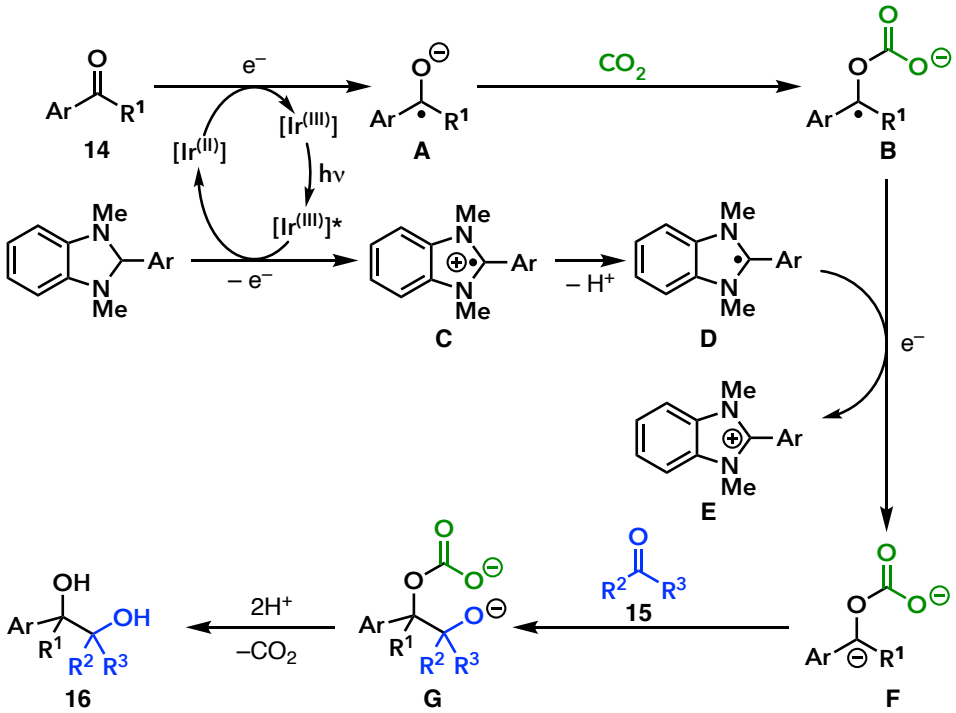


Scheme 10. Theoretical studies of the reduction step [B3LYP/6-311++G(d,p) with the CPCM solvation model (DMF)].

positive than the direct reduction potential of the carbinol radical **I**; this is consistent with the value observed in CV (E_{exp} = −1.39 V vs. SCE). The resulting negative charge on **IV** is delocalized across the aromatic ring containing the electron-withdrawing ester group. CV studies and DFT calculations support the view that carbon dioxide promotes two successive one-electron reductions to generate carbinol anion nucleophiles, suppressing the formation of the dimer by reacting rapidly with the carbinol radicals.

Reaction mechanism

A plausible mechanism is shown in Scheme 11. The excited Ir(III) photocatalyst is reduced by the DMBI to give an Ir(II) species and the DMBI radical cation **C**. Previous Stern–Volmer fluorescence quenching experiments have shown that the excited iridium photocatalyst is quenched by DMBI.[6] The Ir(II) species reduces the electron-deficient aromatic carbonyl compound **14** to give the carbinol radical **A** with regeneration of the Ir(III) photocatalyst. According to the CV measurements and DFT calculations, the carbinol radical **A** is smoothly transformed into the carbinol anion **F** through reaction of the oxygen anion in **A** with CO_2, followed by one-electron reduction by the DMBI radical **D** (−1.68 V vs. SCE for DMBI in MeCN)[7a,20] produced by deprotonation of the DMBI radical cation **C**. The carbinol anion **F** then reacts nucleophilically with the other carbonyl compound **15**; this is followed by protonation and decarboxylation to afford the final product **16**.



Scheme 11. Proposed mechanism.

Conclusion

In conclusion, the author has developed the first photocatalytic cross-pinacol coupling between two different carbonyl compounds, promoted by a CO_2 additive. The cross-pinacol coupling took place with a various combination of two aldehydes, two ketones, or an aldehyde and a ketone to afford the corresponding unsymmetric vicinal 1,2-diols in up to 91% yield, which are useful as building blocks for conversion into unsymmetric ketones, epoxides, or other products. In the coupling reaction, an umpoled carbinol anions are generated in situ through a successive one-electron reduction and the resulting carbinol anions attack the more-electron-rich carbonyl compounds serving as electrophiles. CV and DFT calculations revealed that the CO_2 additive plays a key role in the second reduction to suppress undesired dimerization.

Experimental section

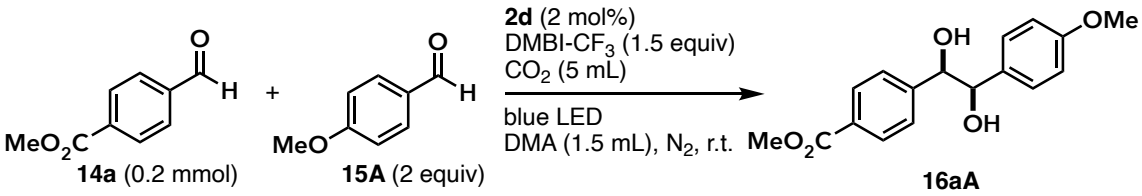
General methods

Irradiation of photoreactions was carried out using a blue LED lamp (Kessil A160WE Tuna Blue, 40 W, λ_{max} = 462 nm).[21] ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-ECS400 spectrometer (^{1}H at 396 MHz and ^{13}C at 100 MHz) and JEOL JNM-ECZ400R/S1 spectrometer (^{1}H at 400 MHz and ^{13}C at 101 MHz). NMR data were obtained in $CDCl_3$, acetone-d_6, or DMSO-d_6. Proton chemical shifts were referenced to the internal tetramethylsilane at 0.00 ppm ($CDCl_3$) or the residual proton signals of the solvents at 2.05 ppm (acetone), and 2.50 ppm (DMSO). Carbon chemical shifts were referenced to the carbon signals of the solvents at 77.16 ppm ($CDCl_3$), 29.84 ppm (acetone-d_6), and 39.52 ppm (DMSO-d_6). All NMR spectra were processed using the Delta software (JEOL). IR measurements were performed on JASCO FT/IR-460plus spectrometer in the ATR mode. GC analyses were performed with Agilent 6850 series II GC. GC-MS (EI) analyses were performed on Agilent 6890 GC/5973N MS Detector. High-resolution ESI and EI mass spectra were recorded on JEOL JMS-T100LC AccuTOF™ LC-TOFMS and JEOL JMS-T100GC AccuTOF™ GC-TOFMS equipped with Agilent 6890N GC, respectively. Flash column chromatography was performed with Hi-Flash™ Column Silica gel 40 μm 60 Å (Yamazen) or Hi-Flash™ Premium Column Silica gel 30 μm 60 Å (Yamazen). Preparative layer chromatography (PLC) was performed on silica gel plates with silica gel 60 F_{254} (Merck). Gel permeation chromatography (GPC) was carried out with a Japan Analytical Industry LC-9201.

Materials

Anhydrous DMA and DCM were purchased from KANTO. Anhydrous toluene and DMSO were purchased from FUJIFILM Wako Pure Chemical Corporation. $Ir(ppy)_2(dtbbpy)PF_6$ (**2d**),[22] 4CzIPN (**2g**),[23] DMBI reductants,[24] and ketone **14l**[25] were prepared according to the literature procedures. All aldehydes were purified by bulb-to-bulb distillation before use. Other chemicals were obtained from commercial suppliers and used without further purification.

General procedure 1 (GP1)



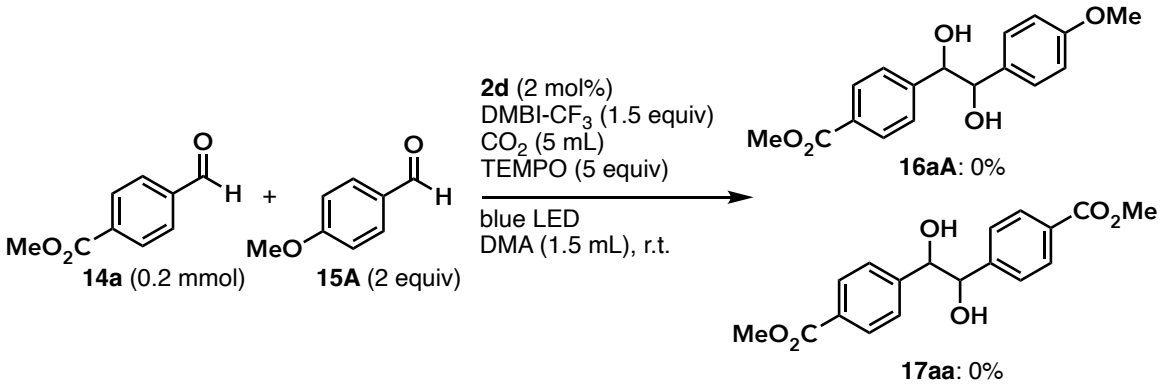
2d (3.75 mg, 0.0041 mmol, 2 mol%) and DMBI-CF_3 (88.1 mg, 0.30 mmol, 1.5 equiv) were placed in a 4 mL vial equipped with a stir bar. The vial was sealed with a rubber septum and filled with nitrogen by vacuum-refill cycles (three times). DMA (0.5 mL) was added and CO_2 (5 mL) was bubbled into the solution over 30 seconds using a syringe pump. A nitrogen balloon was attached to the vial, and *p*-anisaldehyde (**15A**) (53.8 mg, 0.40 mmol, 2 equiv) was added. A DMA solution (1 mL) of methyl 4-formylbenzoate (**14a**) (32.8 mg, 0.20 mmol) was added dropwise over 20 minutes using a syringe pump to the reaction mixture under blue light irradiation (100% light intensity from 40 W Kessil A160WE Tuna Blue. The vial was placed 2 cm away from the LED light with a fan to keep the reaction temperature at room temperature). The reaction mixture was stirred for further 40 minutes. 2 M HCl aq. was added and the resulting mixture was extracted with AcOEt (three times). The combined organic phase was washed with brine, and then dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the crude residue was purified by flash column chromatography with silica gel (gradient from 0 to 7% AcOEt/$CHCl_3$) to give 1,2-diol **16aA** as a white solid (49.0 mg, 0.16 mmol, 81%). The *syn*/*anti* ratio was assigned as 80:20 by ^{1}H NMR analysis of the crude reaction mixture.

General procedure 2 (GP2)

Benzophenone (**14m**) (36.6 mg, 0.20 mmol), **2d** (3.66 mg, 0.0040 mmol, 2 mol%) and DMBI (67.1 mg, 0.30 mmol, 1.5 equiv) were placed in a 4 mL vial equipped with a stir bar. The vial was sealed with a rubber septum and filled with nitrogen by vacuum-refill cycles (three times). DMA (1.5 mL) was added and CO_2 (20 mL) was bubbled into the solution over 30 seconds using a syringe pump. A nitrogen balloon was attached to the vial, and *p*-anisaldehyde (**15A**) (54.0 mg, 0.40 mmol, 2 equiv)

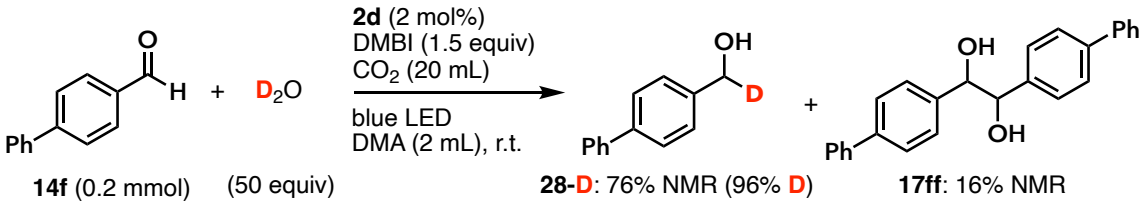
was added. The reaction mixture was stirred for 1 hour under blue light irradiation (100% light intensity from 40 W Kessil A160WE Tuna Blue. The vial was placed 2 cm away from the LED light with a fan to keep the reaction temperature at room temperature). 2 M HCl aq. was added and the resulting mixture was extracted with AcOEt (three times). The combined organic phase was washed with brine, and then dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the crude residue was purified by flash column chromatography with silica gel (gradient from 10 to 30% AcOEt/$CHCl_3$) to give 1,2-diol **16mA** as a white solid (36.3 mg, 0.11 mmol, 56%).

Radical trapping experiment



2d (3.77 mg, 0.0041 mmol, 2 mol%), DMBI-CF_3 (88.0 mg, 0.30 mmol, 1.5 equiv), and TEMPO (156.9 mg, 1.0 mmol, 5 equiv) were placed in a 4 mL vial equipped with a stir bar. The vial was sealed with a rubber septum and filled with nitrogen by vacuum-refill cycles (three times). DMA (0.5 mL) was added and CO_2 (5 mL) was bubbled into the solution over 30 seconds using a syringe pump. A nitrogen balloon was attached to the vial, and *p*-anisaldehyde (**15A**) (55.1 mg, 0.40 mmol, 2 equiv) was added. A DMA solution (1 mL) of methyl 4-formylbenzoate (**14a**) (32.9 mg, 0.20 mmol) was added dropwise over 20 minutes using a syringe pump to the reaction mixture under blue light irradiation (100% light intensity from 40 W Kessil A160WE Tuna Blue. The vial was placed 2 cm away from the LED light with a fan to keep the reaction temperature at room temperature). The reaction mixture was stirred for further 40 minutes. 2 M HCl aq. was added and the resulting mixture was extracted with AcOEt (three times). The combined organic phase was washed with brine, and then dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure. The yields of **16aA** and **17aa** were calculated by ^1H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard (**16aA**: 0%, **17aa**: 0%).

Deuteration experiment with CO_2



2d (3.79 mg, 0.0041 mmol, 2 mol%) and DMBI (67.5 mg, 0.30 mmol, 1.5 equiv) were placed in a 4 mL vial equipped with a stir bar. The vial was sealed with a rubber septum and filled with nitrogen by vacuum-refill cycles (three times). DMA (1 mL) was added and CO_2 (20 mL) was bubbled into the solution over 30 seconds using a syringe pump. A nitrogen balloon was attached to the vial, and D_2O (204.4 mg, 10 mmol, 50 equiv) was added. A DMA solution (1 mL) of biphenyl-4-carboxaldehyde (**14f**) (36.3 mg, 0.20 mmol) was added dropwise over 50 minutes using a syringe pump to the reaction mixture under blue light irradiation (100% light intensity from 40 W Kessil A160WE Tuna Blue. The vial was placed 2 cm away from the LED light with a fan to keep the reaction temperature at room temperature). The reaction mixture was stirred for further 10 minutes. 2 M HCl aq. was added and the resulting mixture was extracted with AcOEt (three times). The combined organic phase was washed with brine, and then dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure. The yield of alcohol **28-D** and homo-coupled dimer **17ff** were calculated by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard (**28-D**: 76% yield, **17ff**: 16% yield). The crude residue was purified by flash column chromatography with silica gel (gradient from 21 to 42% AcOEt/Hex) to give *C*-deuterated alcohol **28-D** (96% D, Figure 2).

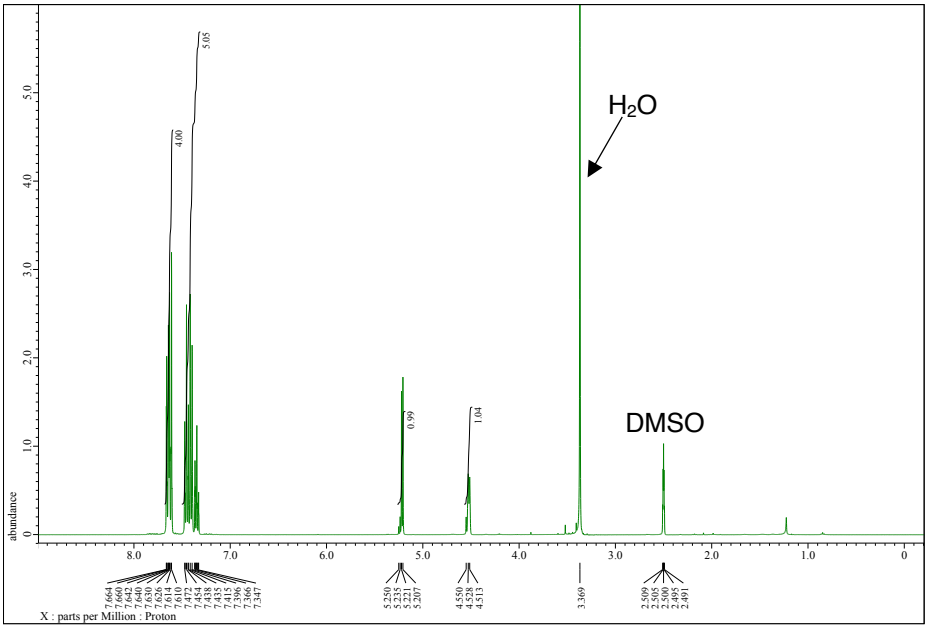
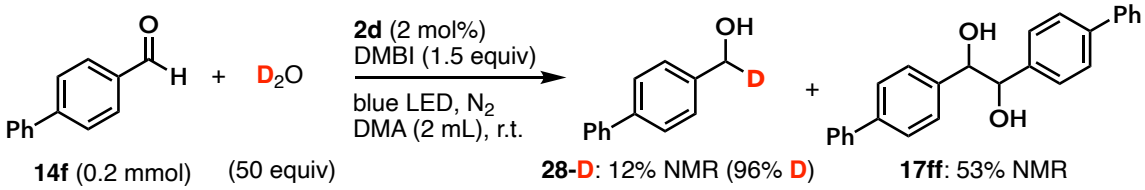


Figure 2. ^{1}H NMR Spectra of **28-D** (DMSO-d_6).

Deuteration experiment without CO_2 (under an N_2 atmosphere)



2d (3.73 mg, 0.0041 mmol, 2 mol%) and DMBI (67.3 mg, 0.30 mmol, 1.5 equiv) were placed in a 4 mL vial equipped with a stir bar. The vial was sealed with a rubber septum and filled with nitrogen by vacuum-refill cycles (three times). DMA (1 mL) was added to the mixture. A nitrogen balloon was attached to the vial, and D_2O (197.4 mg, 9.9 mmol, 50 equiv) was added. A DMA solution (1 mL) of biphenyl-4-carboxaldehyde (**14f**) (36.4 mg, 0.20 mmol) was added dropwise over 50 minutes using a syringe pump to the reaction mixture under blue light irradiation (100% light intensity from 40 W Kessil A160WE Tuna Blue. The vial was placed 2 cm away from the LED light with a fan to keep the reaction temperature at room temperature). The reaction mixture was stirred for further 10 minutes. 2 M HCl aq. was added and the resulting mixture was extracted with AcOEt (three times). The combined organic phase was washed with brine, and then dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the yield of alcohol **28-D** and homo-coupled dimer **17ff** were calculated by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard (**28-D**: 12% yield, **17ff**: 53% yield). The crude residue was purified by flash column chromatography with silica gel (gradient from 21 to 42% AcOEt/Hex) to give *C*-deuterated alcohol **28-D** (96% D, Figure 3).

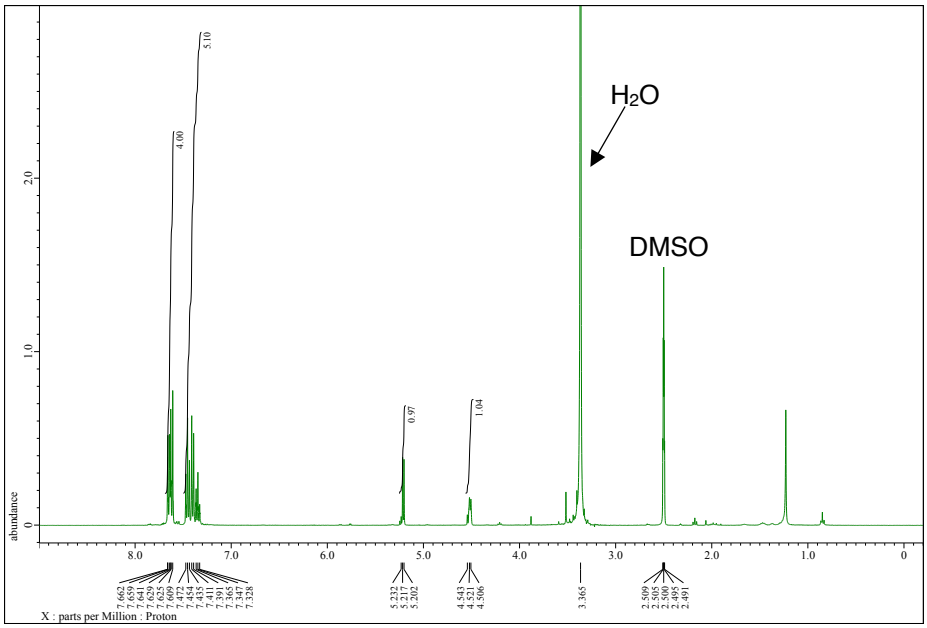
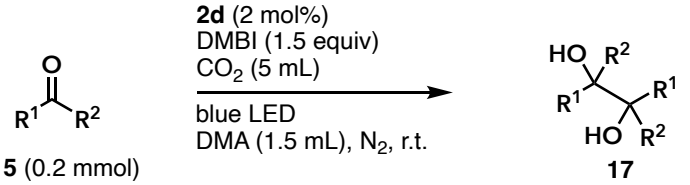
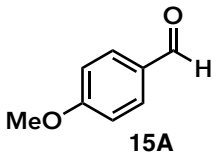
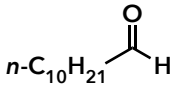
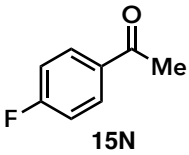
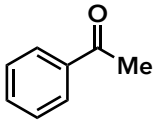


Figure 3. ^{1}H NMR Spectra of **28-D** (DMSO-d_6).

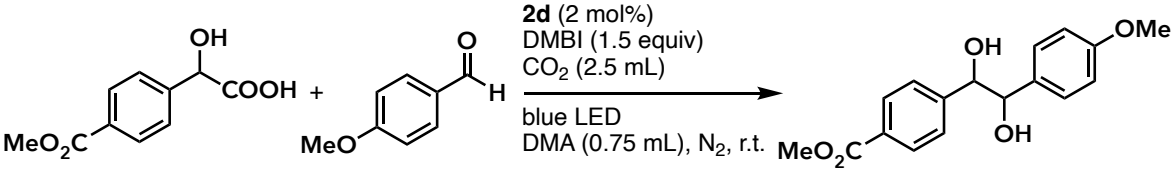
Inertness of electrophiles **15**



entry	electrophile	yield of **17** (%)[a]	recovery of **15** (%)[b]
1[c]	 **15A**	5	75
2[d]	 **15H**	0	98
3[e]	 **15N**	0	quant.
4[f]	 **15O**	0	96

[a] determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as an internal standard. [b] determined by GC using mesitylene as an internal standard. [c] GP2 using 5 mL of CO_2. [d] GP2 using 5 mL of CO_2. After the reaction, water was added instead of 2 M HCl aq. [e] GP2. After the reaction, water was added instead of 2 M HCl aq. [f] GP2.

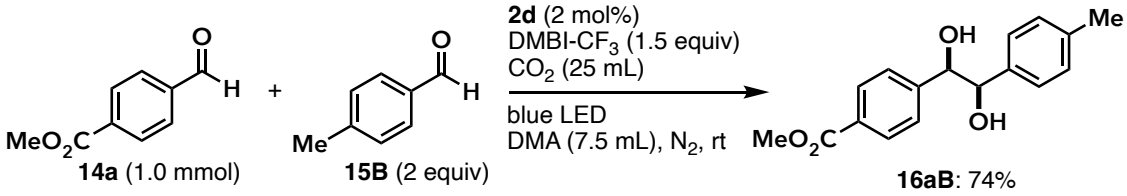
The reaction of α-hydroxycarboxylic acid **19a** with **15A**



2d (1.86 mg, 0.0020 mmol, 2 mol%) and DMBI (33.6 mg, 0.15 mmol, 1.5 equiv) were placed in a 4 mL vial equipped with a stir bar. The vial was sealed with a rubber septum and filled with nitrogen by vacuum-refill cycles (three times). DMA (0.25 mL) was added and CO_2 (2.5 mL) was bubbled into the solution over 30 seconds using a syringe pump. A nitrogen balloon was attached to the vial, and *p*-anisaldehyde (**15A**) (26.9 mg, 0.20 mmol, 2 equiv) was added. A DMA solution (0.5 mL) of α-hydroxycarboxylic acid **19a** (21.0 mg, 0.10 mmol) was added dropwise over 20 minutes using a

syringe pump to the reaction mixture under blue light irradiation (100% light intensity from 40 W Kessil A160WE Tuna Blue. The vial was placed 2 cm away from the LED light with a fan to keep the reaction temperature at room temperature). The reaction mixture was stirred for further 40 minutes. 2 M HCl aq. was added and the resulting mixture was extracted with AcOEt (three times). The combined organic phase was washed with brine, and then dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure. The yield of **16aA** and the recovery of **19a** were calculated by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard (**16aA**: 0%, **19a**: 84%).

1.0 mmol scale reaction



2d (18.5 mg, 0.020 mmol, 2 mol%) and DMBI (336.6 mg, 1.5 mmol, 1.5 equiv) were placed in a 20 mL Schlenk tube equipped with a stir bar. The Schlenk tube was filled with nitrogen by vacuum-refill cycles (three times). DMA (2.5 mL) was added and CO_2 (25 mL) was bubbled into the solution over 30 seconds using a syringe pump. A nitrogen balloon was attached to the Schlenk tube, and *p*-tolualdehyde (**15B**) (242.4 mg, 2.0 mmol, 2 equiv) was added. A DMA solution (5 mL) of methyl 4-formylbenzoate (**14a**) (164.6 mg, 1.0 mmol) was added dropwise over 50 minutes using a syringe pump to the reaction mixture under blue light irradiation (100% light intensity from 40 W Kessil A160WE Tuna Blue. The Schlenk tube was placed 2 cm away from the LED light with a fan to keep the reaction temperature at room temperature). The reaction mixture was stirred for further 10 minutes. 2 M HCl aq. was added and the resulting mixture was extracted with AcOEt (three times). The combined organic phase was washed with brine, and then dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the crude residue was purified by flash column chromatography with silica gel (gradient from 6 to 12% AcOEt/$CHCl_3$) to give **16aB** (210.9 mg, 0.73 mmol, 74%; *syn*/*anti* = 81:19).

Cyclic voltammetry

Cyclic voltammetry was measured on an ALS electrochemical analyzer model 612E by using a glassy carbon working electrode, a Pt counter electrode, and Ag/Ag^+ electrode in acetonitrile with 0.1 M TBAP+0.01 M $AgNO_3$ as the reference electrode (Figure 4). Samples in 4 mL DMF (24 mL cell, [*n*-Bu_4NBF_4] = 0.1 M, [methyl 4-formylbenzoate] =1 mM,) were degassed by purging nitrogen and then CO_2 (0–10 mL) was bubbled into the solution over 30 seconds using a syringe pump immediately prior to the measurements. The voltammograms were taken at room temperature under an N_2 atmosphere. The scan rate was 0.1 V/s. Saturated CO_2 solutions were prepared by bubbling CO_2 over 20 minutes. CV measurements of them were performed under a CO_2 atmosphere. Ferrocene was used as the internal standard. Potentials (vs. SCE) were calculated according to $E_{SCE} = E_{Fc/Fc+} + 0.38$ V.[20]

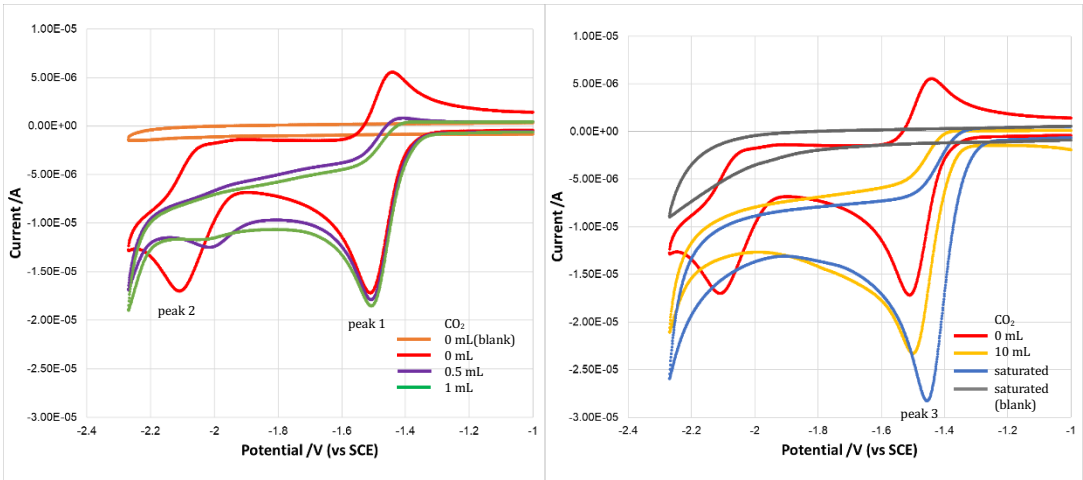


Figure 4. Cyclic voltammograms of aldehyde **14a** with various amounts of CO_2. Orange line: blank, red line: **14a**, purple line; **14a** with 0.5 mL CO_2, green line; **14a** with 1 mL CO_2, yellow line; **14a** with 10 mL CO_2, blue line; **14a** under CO_2, gray line; blank under CO_2.

Peak potential of peak 1 (E_p1): –1.51 V (vs. SCE)

Half peak potential of peak 1 ($E_{p/2}1$): –1.45 V (vs. SCE)

Peak potential of peak 2 (E_p2): –2.11 V (vs. SCE)

Half peak potential of peak 2 ($E_{p/2}2$): –2.03 V (vs. SCE)

Peak potential of peak 3 (E_p3): –1.46 V (vs. SCE)

Half peak potential of peak 3 ($E_{p/2}3$): –1.39 V (vs. SCE)

Computational methods

All calculations were carried out with the Gaussian16 program.[26] Geometry optimizations and

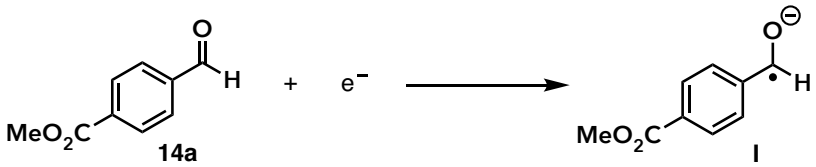
frequency calculations for all molecules were performed at the (U)B3LYP/6-311++G(d,p)[27,28] using the CPCM solvation model (DMF).

Calculated redox potential:[17]

Redox potentials $E_{1/2}^{0,\mathrm{calc}}$ were calculated according to eq. (1), where n_e is the number of electrons transferred (in all calculations here, n_e= 1), F is the Faraday constant (23.0605 kcal/mol·V), $E_{1/2}^{0,\mathrm{SHE}}$ is the absolute value for the standard hydrogen electrode (4.281 V)[29] and $E_{1/2}^{0,\mathrm{SCE}}$ is the potential of the saturated calomel electrode relative to SHE in DMF (–0.099 V),[29] and $\Delta G_{1/2}$ is the Gibbs free energy difference in DMF between reduced and oxidized forms.

$$E_{1/2}^{0,\mathrm{calc}} = -\frac{\Delta G_{1/2}}{n_e F} - E_{1/2}^{0,\mathrm{SHE}} + E_{1/2}^{0,\mathrm{SCE}} \qquad (1)$$

Example:



G(**14a**) = –573.510785 Hartree

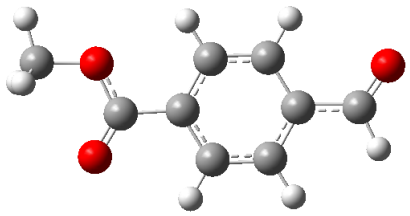
G(**I**) = –573.627335 Hartree

$\Delta G_{1/2}$ = G(**I**)–G(**14a**) = –573.627335–(–573.510785) = –0.11655 Hartree = –73.14 kcal/mol

$E_{1/2}^{0,\mathrm{calc}}$ = –(–73.14/23.0605)–4.281–0.099 =–1.21 V (vs SCE)

Cartesian Coordinates:

Methyl 4-formylbenzoate (**14a**)



Zero-point correction = 0.151674 (Hartree/Particle)

Thermal correction to Energy = 0.162615

Thermal correction to Enthalpy = 0.163559

Thermal correction to Gibbs Free Energy = 0.113889

Sum of electronic and zero-point Energies = -573.473000

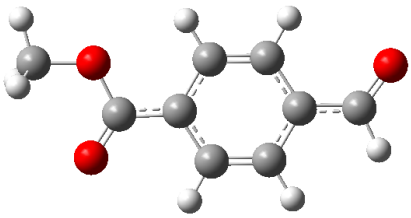
Sum of electronic and thermal Energies = -573.462059

Sum of electronic and thermal Enthalpies = -573.461115

Sum of electronic and thermal Free Energies = -573.510785

C	-3.68208617	0.10994877	-0.00004058
O	-4.35964720	-0.90022002	0.00003675
H	-4.16189412	1.10675699	-0.00001207
C	-2.20274225	0.13317037	-0.00003878
C	-1.54343317	1.36812115	-0.00005885
C	-1.45979841	-1.05580438	-0.00001849
C	-0.15458479	1.41745470	-0.00005932
H	-2.11988769	2.28682957	-0.00007458
C	-0.07380911	-1.00853428	-0.00001923
H	-1.97919582	-2.00633433	-0.00000229
C	0.58547091	0.23064462	-0.00004154
H	0.36536170	2.36663851	-0.00007470
H	0.50291294	-1.92339162	-0.00000485
C	2.07749814	0.33253143	-0.00004858
O	2.68597867	1.38331310	0.00001911
O	2.67418454	-0.86727011	0.00004262
C	4.11881506	-0.87450145	0.00014013
H	4.49778286	-0.37561179	0.89209056
H	4.40090942	-1.92396579	0.00020566
H	4.49790150	-0.37569087	-0.89180416

Radical anion **I**



Zero-point correction = 0.148965 (Hartree/Particle)

Thermal correction to Energy = 0.159949

Thermal correction to Enthalpy = 0.160894

Thermal correction to Gibbs Free Energy = 0.110977

Sum of electronic and zero-point Energies = -573.589347

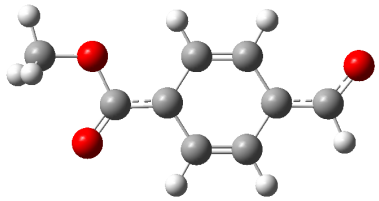
Sum of electronic and thermal Energies = -573.578363

Sum of electronic and thermal Enthalpies = -573.577418

Sum of electronic and thermal Free Energies = -573.627335

C	-3.66865700	0.11524900	-0.00024400
O	-4.40173600	-0.91073900	0.00052200
H	-4.14875900	1.11355100	0.00048000
C	-2.24314800	0.13948700	-0.00020200
C	-1.53571400	1.38194400	-0.00015000
C	-1.45392800	-1.05616200	-0.00017400
C	-0.16315400	1.42939700	-0.00011800
H	-2.10556300	2.30735000	-0.00016000
C	-0.08071300	-1.00767400	-0.00013600
H	-1.96325300	-2.01347700	-0.00020000
C	0.61778100	0.23474600	-0.00011400
H	0.34990000	2.38399700	-0.00010700
H	0.48826300	-1.92967300	-0.00013200
C	2.06034300	0.33119800	-0.00008500
O	2.71653800	1.37635100	0.00005600
O	2.68720100	-0.88943600	0.00006100
C	4.12113200	-0.87115200	0.00024500
H	4.50589700	-0.36880100	0.88981400
H	4.42771500	-1.91565600	0.00034200
H	4.50612600	-0.36889900	-0.88928000

Dianion **II**



Zero-point correction = 0.146115 (Hartree/Particle)

Thermal correction to Energy = 0.157468

Thermal correction to Enthalpy = 0.158412

Thermal correction to Gibbs Free Energy = 0.107356

Sum of electronic and zero-point Energies = -573.670964

Sum of electronic and thermal Energies = -573.659611

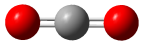
Sum of electronic and thermal Enthalpies = -573.658667

Sum of electronic and thermal Free Energies = -573.709723

C	-3.66509351	0.21550455	0.00504120
O	-4.47901251	-0.79848213	0.00956437
H	-4.11909354	1.22985021	0.00351091
C	-2.27700450	0.20743320	0.00177920
C	-1.47440906	-1.01694429	0.00429649
C	-1.49736886	1.44119563	-0.00330098
C	-0.11086184	-0.99932982	0.00108375
H	-1.99535588	-1.97018473	0.00938182
C	-0.13677058	1.45704871	-0.00558004
H	-2.03995431	2.38617234	-0.00512407
C	0.65855155	0.23234037	-0.00379382
H	0.42774295	-1.94181930	0.00396418
H	0.39025033	2.40662120	-0.00934369
C	2.05632168	0.29197132	-0.01091030
O	2.79381760	1.31660767	-0.00996519
O	2.68538326	-0.97871624	-0.02438098
C	4.10656976	-0.97902006	0.02506358

H	4.48348902	-0.52171021	0.94527077
H	4.40715187	-2.02766890	-0.00423822
H	4.54682158	-0.45256253	-0.82673400

CO_2



Zero-point correction = 0.011574 (Hartree/Particle)

Thermal correction to Energy = 0.014201

Thermal correction to Enthalpy = 0.015145

Thermal correction to Gibbs Free Energy = -0.009122

Sum of electronic and zero-point Energies = -188.638175

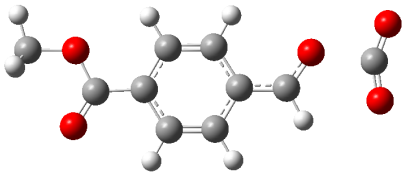
Sum of electronic and thermal Energies = -188.635548

Sum of electronic and thermal Enthalpies = -188.634604

Sum of electronic and thermal Free Energies = -188.658871

C	0.00000000	0.00000000	0.00000000
O	0.31916737	0.15043300	-1.10565212
O	-0.31916737	-0.15043300	1.10565212

Transition state in the reaction of radical anion **I** with CO_2



Zero-point correction = 0.161802 (Hartree/Particle)

Thermal correction to Energy = 0.175718

Thermal correction to Enthalpy = 0.176662

Thermal correction to Gibbs Free Energy = 0.118181

Sum of electronic and zero-point Energies = -762.223295

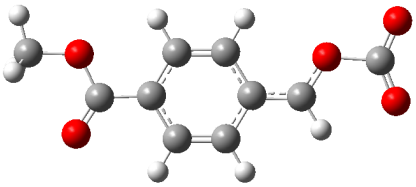
Sum of electronic and thermal Energies = -762.209379

Sum of electronic and thermal Enthalpies = -762.208435

Sum of electronic and thermal Free Energies = -762.266916

C	0.19678000	-0.90089800	0.00012800
C	0.11499600	1.54021100	0.00003500
C	-1.17847700	-0.94045000	0.00008400
H	0.76630300	-1.82263600	0.00020500
C	-1.25787900	1.49250700	-0.00000400
H	0.62085400	2.50092500	0.00002600
C	-1.94941700	0.25122100	0.00001600
H	-1.68662000	-1.89675700	0.00011700
H	-1.83470800	2.40971400	-0.00004300
C	-3.40648400	0.25130100	-0.00003100
O	-4.11861300	1.25168600	-0.00005800
O	-3.94387900	-1.00143000	-0.00004000
C	-5.37847500	-1.08392400	-0.00008200
H	-5.79376800	-0.60907100	-0.89037900
H	-5.60892500	-2.14729400	0.00002000
H	-5.79383600	-0.60888300	0.89008200
C	0.90187300	0.34521300	0.00007900
C	2.31108100	0.42170200	0.00011400
H	2.77508400	1.41354000	0.00007400
O	3.09694700	-0.60124100	0.00015000
C	4.97707900	-0.24575300	-0.00007900
O	5.09670300	0.93694400	-0.00009800
O	5.43998700	-1.33924800	-0.00016200

Radical anion **III**



Zero-point correction = 0.163271 (Hartree/Particle)

Thermal correction to Energy = 0.177193

Thermal correction to Enthalpy = 0.178138

Thermal correction to Gibbs Free Energy = 0.119930

Sum of electronic and zero-point Energies = -762.225299

Sum of electronic and thermal Energies = -762.211376

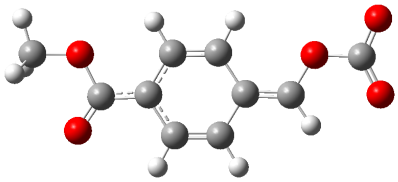
Sum of electronic and thermal Enthalpies = -762.210432

Sum of electronic and thermal Free Energies = -762.268640

C	0.32191199	-0.78482252	-0.00251751
C	0.05301522	1.64368185	-0.00516471
C	-1.04894230	-0.92747710	0.00261603
H	0.95835155	-1.66074698	-0.00349734
C	-1.31363683	1.48825414	-0.00003130
H	0.48389137	2.63924710	-0.00819275
C	-1.89952852	0.20099812	0.00396644
H	-1.48394669	-1.91871888	0.00564981
H	-1.96075210	2.35688161	0.00099037
C	-3.36443291	0.08924207	0.00934947
O	-4.13853268	1.03582224	0.01112924
O	-3.79793552	-1.19315404	0.01333822
C	-5.22462156	-1.39120660	0.01929192
H	-5.67593284	-0.95106411	-0.87065336
H	-5.36685975	-2.46934883	0.02177291
H	-5.66894647	-0.94788704	0.91117320
C	0.92446608	0.51080931	-0.00661398

C	2.31278649	0.70354746	-0.01187892
H	2.75853128	1.69153525	-0.01493667
O	3.15012850	-0.33251799	-0.01328918
C	4.64041877	-0.06028080	-0.01898063
O	5.25687481	-1.12135627	-0.02051847
O	4.95237311	1.12736602	-0.02236980

Dianion **IV**



Zero-point correction = 0.161848 (Hartree/Particle)

Thermal correction to Energy = 0.175788

Thermal correction to Enthalpy = 0.176733

Thermal correction to Gibbs Free Energy = 0.119056

Sum of electronic and zero-point Energies = -762.337266

Sum of electronic and thermal Energies = -762.323325

Sum of electronic and thermal Enthalpies = -762.322380

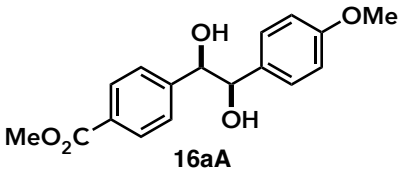
Sum of electronic and thermal Free Energies = -762.380057

C	-0.25727010	-0.84351944	0.00204754
C	-0.18484177	1.61624967	-0.01383204
C	1.10971881	-0.86723394	0.00770234
H	-0.80967328	-1.77624851	0.00595922
C	1.17650293	1.56684923	-0.00802895
H	-0.68733219	2.58006581	-0.02218701
C	1.90427973	0.32548513	0.00307668
H	1.61586137	-1.82669921	0.01604834
H	1.74260265	2.49296826	-0.01183752
C	3.32666534	0.33109307	0.00876866

O	4.07512799	1.32482367	0.00493615
O	3.88919953	-0.94128378	0.01895401
C	5.31653627	-1.00434356	0.02466139
H	5.73424425	-0.52207318	0.91169958
H	5.56515772	-2.06530759	0.03232699
H	5.74085630	-0.53336588	-0.86530231
C	-1.00724279	0.40918276	-0.00920757
C	-2.36854799	0.48753058	-0.01519832
H	-2.92246966	1.41497197	-0.02352883
O	-3.14050836	-0.67046548	-0.01066803
C	-4.55426344	-0.56861918	-0.01712387
O	-5.10943407	-1.68709543	-0.01228054
O	-5.05547526	0.57244505	-0.02690393

Spectroscopic data of products

Methyl 4-[1,2-dihydroxy-2-(4-methoxyphenyl)ethyl]benzoate



16aA

Prepared according to GP 1. Homo-coupled dimer **17aa** was formed in 5% NMR yield. The resulting crude mixture was purified by flash column chromatography (gradient from 0 to 7% AcOEt/$CHCl_3$) to give **16aA** as a white solid (49.0 mg, 81%; *syn*/*anti* = 80:20).

^{1}H NMR (400 MHz, $CDCl_3$) (*syn*)-16aA δ = 7.83 (d, *J* = 8.2 Hz, 2H), 7.10 (d, *J* = 8.2 Hz, 2H), 6.96 (d, *J* = 8.7 Hz, 2H), 6.72 (d, *J* = 8.7 Hz, 2H), 4.66 (d, *J* = 7.8 Hz, 1H), 4.53 (d, *J* = 7.8 Hz, 1H), 3.86 (s, 3H), 3.74 (s, 3H), 3.51 (br, 1H), 3.27 (br, 1H); **(*anti*)-16aA** δ = 7.89 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 7.04 (d, *J* = 8.7 Hz, 2H), 6.77 (d, *J* = 8.7 Hz, 2H), 4.85 (d, *J* = 5.0 Hz, 1H), 4.76 (d, *J* = 5.0 Hz, 1H), 3.88 (s, 3H), 3.76 (s, 3H), 2.83 (br, 1H), 2.72 (br, 1H).

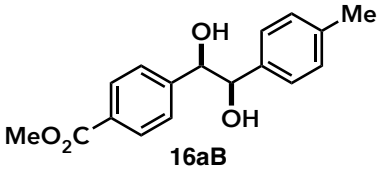
^{13}C NMR (101 MHz, acetone-d_6) δ = 167.3, 167.2, 159.9, 159.8, 148.6, 148.2, 134.6, 134.1, 129.8, 129.6, 129.4, 129.23, 129.20, 128.4, 128.3, 113.8, 113.7, 79.3, 79.0, 78.2, 78.0, 55.4, 52.2. Two carbons overlapped at 129.4, 55.4, and 52.2 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{17}H_{18}NaO_5$ ([M+Na]$^+$) 325.1046, Found *m*/*z* 325.1051.

IR (ATR): 3600–3100 (br), 1688 (s), 1279 (s), 1247 (s) cm^{-1}.

Rf: 0.30 (AcOEt/$CHCl_3$ 1:3).

Methyl 4-[1,2-dihydroxy-2-(*p*-tolyl)ethyl]benzoate



16aB

Prepared according to GP 1 using DMBI. Homo-coupled dimer **17aa** was formed in 8% NMR yield. The resulting crude mixture was purified twice by flash column chromatography (gradient from 6 to 12% AcOEt/$CHCl_3$) to give **16aB** as a white solid (43.2 mg, 76%; *syn*/*anti* = 81:19).

^{1}H NMR (396 MHz, $CDCl_3$) (*syn*)-16aB δ = 7.84 (d, *J* = 8.2 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 7.01 (d, *J* = 8.2 Hz, 2H), 6.94 (d, *J* = 7.7 Hz, 2H), 4.69 (d, *J* = 7.3 Hz, 1H), 4.56 (d, *J* = 7.7 Hz, 1H), 3.86 (s, 3H), 3.40

(br, 1H), 3.14 (br, 1H), 2.28 (s, 3H); **(*anti*)-16aB** δ = 7.90 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.6 Hz, 2H), 7.08–7.00 (m. 4H), 4.86 (d, *J* = 4.5 Hz, 1H), 4.78 (d, *J* = 5.4 Hz, 1H), 3.88 (s, 3H), 2.72 (br, 1H), 2.60 (br, 1H), 2.31 (s, 3H).

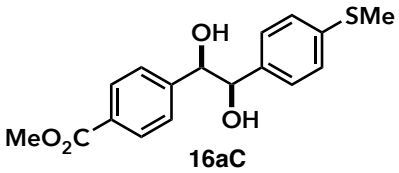
^{13}C NMR (101 MHz, acetone-d_6) δ = 167.3, 167.1, 148.6, 148.1, 139.7, 139.2, 137.5, 137.1, 129.8, 129.6, 129.4, 129.2, 129.1, 128.9, 128.4, 128.3, 128.1, 128.0, 79.31, 79.27, 78.3, 52.19, 52.16, 21.10, 21.08. Two carbons overlapped at 78.3 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{17}H_{18}NaO_4$ ([M+Na]$^+$) 309.1097, Found *m*/*z* 309.1090.

IR (ATR): 3600–3100 (br), 1692 (s), 1272 (s) cm^{-1}.

Rf: 0.34 (AcOEt/$CHCl_3$ 1:3).

Methyl 4-{1,2-dihydroxy-2-[4-(methylthio)phenyl]ethyl}benzoate



16aC

Prepared according to GP 1 using DMBI. Homo-coupled dimer **17aa** was formed in 6% NMR yield. The resulting crude mixture was purified twice by flash column chromatography (gradient from 3 to 9% AcOEt/$CHCl_3$ and gradient from 2 to 6% AcOEt/$CHCl_3$) to give **16aC** as a white solid (50.5 mg, 79%; *syn*/*anti* = 77:23).

^{1}H NMR (396 MHz, $CDCl_3$) (*syn*)-16aC δ = 7.87 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 8.2 Hz, 2H), 7.08 (d, *J* = 8.2 Hz, 2H), 6.98 (d, *J* = 8.6 Hz, 2H), 4.69 (d, *J* = 7.3 Hz, 1H), 4.59 (d, *J* = 7.7 Hz, 1H), 3.88 (s, 3H), 3.25 (br, 1H), 3.06 (br, 1H), 2.44 (s, 3H); **(*anti*)-16aC** δ = 7.92 (d, *J* = 8.6 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 8.6 Hz, 2H), 7.05 (d, *J* = 8.6 Hz, 2H), 4.89 (d, *J* = 4.1 Hz, 1H), 4.81 (d, *J* = 5.0 Hz, 1H), 3.89 (s, 3H), 2.63 (br, 1H), 2.54 (br, 1H), 2.45 (s, 3H).

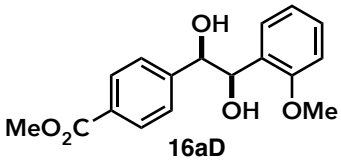
^{13}C NMR (101 MHz, acetone-d_6) δ = 167.3, 167.1, 148.5, 148.1, 139.6, 139.1, 138.3, 138.0, 129.9, 129.7, 129.5, 129.3, 128.8, 128.6, 128.4, 128.3, 126.33, 126.29, 79.1, 79.0, 78.1, 78.0, 52.21, 52.18, 15.5, 15.4.

HRMS (ESI$^+$): Calcd for $C_{17}H_{18}NaO_4S$ ([M+Na]$^+$) 341.0818, Found *m*/*z* 341.0826.

IR (ATR): 3600–3100 (br), 1687 (s), 1280 (s) cm^{-1}.

Rf: 0.30 (AcOEt/$CHCl_3$ 1:3).

Methyl 4-[1,2-dihydroxy-2-(2-methoxyphenyl)ethyl]benzoate



16aD

Prepared according to GP 1. Homo-coupled dimer **17aa** was formed in <4% NMR yield. The resulting crude mixture was purified twice by flash column chromatography (gradient from 0 to 2% AcOEt/$CHCl_3$) to give **16aD** as a white solid (47.6 mg, 79%; *syn*/*anti* = 72:28).

^{1}H NMR (400 MHz, acetone-d_6) (*syn*)-16aD δ = 7.86 (d, *J* = 8.2 Hz, 2H), 7.48 (dd, *J* = 7.3, 1.8 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 1H), 6.94–6.89 (m, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 5.08 (dd, *J* = 5.5, 5.5 Hz, 1H), 4.81 (dd, *J* = 5.0, 5.0 Hz, 1H), 4.52 (d, *J* = 5.0 Hz, 1H), 4.41 (d, *J* = 5.5 Hz, 1H), 3.85 (s, 3H), 3.58 (s, 3H); **(*anti*)-16aD** δ = 7.78 (d, *J* = 8.2 Hz, 2H), 7.22–7.15 (m, 3H), 7.09 (dd, *J* = 7.3, 1.4 Hz, 1H), 6.94–6.89 (m, 1H), 6.76 (dd, *J* = 7.3, 7.3 Hz, 1H), 5.34 (dd, *J* = 4.6 Hz, 1H), 5.04 (dd, *J* = 4.6, 4.6 Hz, 1H), 4.59 (d, *J* = 4.6 Hz, 1H), 4.32 (d, *J* = 4.6 Hz, 1H), 3.84 (s, 3H), 3.74 (s, 3H).

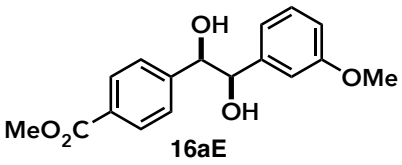
^{13}C NMR (101 MHz, acetone-d_6) δ = 167.3, 167.2, 157.2, 157.1, 149.1, 148.0, 131.0, 130.2, 129.6, 129.4, 129.3, 129.1, 128.81, 128.78, 128.7, 128.5, 128.4, 127.7, 121.0, 120.7, 110.9, 110.7, 77.8, 76.4, 73.2, 72.4, 55.6, 55.4, 52.2, 52.1.

HRMS (ESI$^+$): Calcd for $C_{17}H_{18}NaO_5$ ([M+Na]$^+$) 325.1046, Found *m*/*z* 325.1038.

IR (ATR): 3600–3100 (br), 1725 (s), 1270 (s), 1240 (s) cm^{-1}.

Rf: 0.21 (AcOEt/$CHCl_3$ 1:5).

Methyl 4-[1,2-dihydroxy-2-(3-methoxyphenyl)ethyl]benzoate



16aE

Prepared according to GP 1. Homo-coupled dimer **17aa** was formed in <3% NMR yield. The resulting crude mixture was purified by flash column chromatography (gradient from 0 to 10% AcOEt/$CHCl_3$) to give **16aE** as colorless oil (53.3 mg, 88%; *syn*/*anti* = 78:22).

^{1}H NMR (400 MHz, $CDCl_3$) (*syn*)-16aE δ = 7.84 (d, *J* = 8.2 Hz, 2H), 7.18–7.07 (m, 1H), 7.13 (d, *J* = 8.2 Hz, 2H), 6.76–6.73 (m, 1H), 6.65 (s, 1H), 6.59 (d, *J* = 7.8 Hz, 1H), 4.68 (d, *J* = 7.3 Hz, 1H), 4.56 (d, *J* = 7.3

Hz, 1H), 3.86 (s, 3H), 3.67 (s, 3H), 3.48 (br, 1H), 3.33 (br, 1H); **(*anti*)-16aE** δ = 7.89 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 2H), 7.18–7.07 (m, 1H), 6.79–6.77 (m, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 6.68 (s, 1H), 4.85 (d, *J* = 4.6 Hz, 1H), 4.79 (d, *J* = 5.0 Hz, 1H), 3.87 (s, 3H), 3.67 (s, 3H), 2.87 (br, 1H), 2.82 (br, 1H).

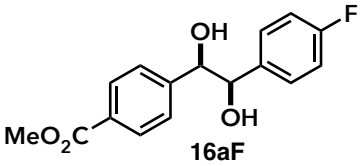
^{13}C NMR (101 MHz, acetone-*d*$_6$) δ = 167.2, 167.1, 160.14, 160.10, 148.4, 148.1, 144.3, 143.9, 129.8, 129.6, 129.38, 129.36, 129.2, 128.4, 128.2, 120.35, 120.26, 113.6, 113.5, 113.4, 79.3, 79.1, 78.3, 78.1, 55.2, 52.2. Two carbons overlapped at 129.38, 113,4, 55.2, and 52.2 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{17}H_{18}NaO_5$ ([M+Na]$^+$) 325.1046, Found *m*/*z* 325.1048.

IR (ATR): 3700–3100 (br), 1714 (s), 1278 (vs) cm^{-1}.

Rf: 0.24 (AcOEt/$CHCl_3$ 1:3).

Methyl 4-[2-(4-fluorophenyl)-1,2-dihydroxyethyl]benzoate



16aF

Prepared according to GP 1. Homo-coupled dimer **17aa** was formed in 2% NMR yield. The resulting crude mixture was purified by flash column chromatography (gradient from 0 to 15% AcOEt/$CHCl_3$) to give **16aF** as a white solid (45.3 mg, 77%; *syn*/*anti* = 73:27).

^{1}H NMR (396 MHz, acetone-*d*$_6$) (*syn*)-16aF δ = 7.84 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.19–7.16 (m, 2H), 7.00–6.93 (m, 2H), 4.83 (d, *J* = 3.6 Hz, 1H), 4.80–4.77 (m, 1H), 4.77 (d. *J* =3.6 Hz, 1H), 4.74 (dd, *J* = 6.8, 3.6 Hz, 1H), 3.85 (s, 3H); **(*anti*)-16aF** δ = 7.87 (d, *J* = 8.6 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.28–7.24 (m, 2H), 7.00–6.93 (m, 2H), 4.91 (dd, *J* = 4.8, 4.8 Hz, 1H), 4.87 (dd, *J* =4.8, 4.8 Hz, 1H), 4.64 (d, *J* = 4.1 Hz, 1H), 4.59 (d, *J* = 4.1 Hz, 1H), 3.86 (s, 3H).

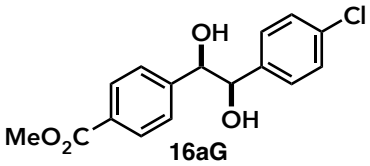
^{13}C NMR (101 MHz, acetone-*d*$_6$) δ = 167.2, 167.1, 162.83 (d, *J* = 243.7 Hz), 162.79 (d, *J* = 242.8 Hz), 148.3, 147.9, 138.7 (d, *J* = 2.9 Hz), 138.4 (d, *J* = 2.9 Hz), 130.0, 129.9, 129.8, 129.7, 129.4, 129.3, 128.3, 128.2, 115.0 (d, *J* = 21.2 Hz), 114.8 (d, *J* = 20.2 Hz), 79.1, 78.6, 78.1, 77.7, 52.2. Two carbons overlapped at 52.2 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{16}H_{15}FNaO_4$ ([M+Na]$^+$) 313.0847, Found *m*/*z* 313.0840.

IR (ATR): 3600–3100 (br), 1695 (s), 1276 (s) cm^{-1}.

Rf: 0.24 (AcOEt/$CHCl_3$ 1:3).

Methyl 4-[2-(4-chlorophenyl)-1,2-dihydroxyethyl]benzoate



16aG

Prepared according to GP 1. Homo-coupled dimer **17aa** was formed in 2% NMR yield. The resulting crude mixture was purified twice by flash column chromatography (gradient from 0 to 10% AcOEt/$CHCl_3$) to give **16aG** as a white solid (54.5 mg, 89%; *syn*/*anti* = 69:31).

^{1}H NMR (396 MHz, acetone-d_6) (*syn*)-16aG δ = 7.85 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.6 Hz, 2H), 7.16 (d, *J* = 8.6 Hz, 2H), 4.85 (d, *J* = 3.6 Hz, 1H), 4.80 (d, *J* =3.6 Hz, 1H), 4.81–4.79 (m, 1H), 4.76 (dd, *J* = 6.3, 3.6 Hz, 1H), 3.85 (s, 3H); **(*anti*)-16aG** δ = 7.88 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.25 (s, 4H), 4.91 (dd, *J* = 5.0, 5.0 Hz, 1H), 4.87 (dd, *J* = 5.4, 4.5 Hz, 1H), 4.68 (d, *J* = 4.1 Hz, 1H), 4.64 (d, *J* = 4.1 Hz, 1H), 3.86 (s, 3H).

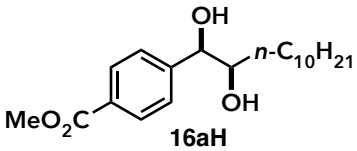
^{13}C NMR (101 MHz, acetone-d_6) δ = 167.2, 167.1, 148.2, 147.8, 141.6, 141.3, 133.2, 133.0, 129.91, 129.87, 129.7, 129.5, 129.3, 128.4, 128.25, 128.19, 78.9, 78.5, 78.0, 77.7, 52.2. Two carbons overlapped at 129.7, 128.19, and 52.2 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{16}H_{15}ClNaO_4$ ([M+Na]$^+$) 329.0551, Found *m*/*z* 329.0550.

IR (ATR): 3600–3100 (br), 1687 (s), 1276 (s) cm^{-1}.

Rf: 0.17 (AcOEt/$CHCl_3$ 1:5).

Methyl 4-(1,2-dihydroxydodecyl)benzoate



16aH

Prepared according to GP 1 using DMBI. Homo-coupled dimer **17aa** was formed in 7% NMR yield. The resulting crude mixture was purified by flash column chromatography (gradient from 12 to 25% AcOEt/$CHCl_3$) to give **16aH** as a white solid (53.2 mg, 78%; *syn*/*anti* = 56:44).

^{1}H NMR (396 MHz, $CDCl_3$) (*syn*)-16aH δ = 8.00–7.98 (m, 2H), 7.42–7.38 (m, 2H), 4.47 (d, *J* = 6.8 Hz, 1H), 3.91 (s, 3H), 3.67–3.62 (m, 1H), 1.44–1.21 (m, 18 H), 0.87 (t, *J* = 7.3 Hz, 3H); **(*anti*)-16aH** δ = 8.00–7.98 (m, 2H), 7.42–7.38 (m, 2H), 4.75 (d, *J* = 4.1 Hz, 1H), 3.91 (s, 3H), 3.85–3.81 (m, 1H), 1.44–

1.21 (m, 18 H), 0.87 (t, *J* = 7.3 Hz, 3H).

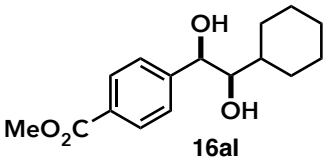
^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ = 166.4, 166.3, 149.6, 149.1, 128.52, 128.47, 128.0, 127.9, 127.4, 127.3, 76.1, 75.8, 74.25, 74.22, 52.0, 32.1, 32.0, 31.3, 29.1, 29.04, 28.98, 28.7, 25.4, 25.3, 22.1, 14.0. Two carbons overlapped at 52.0, 28.7, 22.1, and 14.0 ppm, and four carbons overlapped at 29.04 and 28.98 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{20}H_{32}NaO_4$ ([M+Na]$^+$) 359.2193, Found *m*/*z* 359.2189.

IR (ATR): 3600–3100 (br), 2917 (s), 2849 (s), 1693 (s), 1287 (s) cm^{-1}.

Rf: 0.23 (AcOEt/$CHCl_3$ 1:5).

Methyl 4-(2-cyclohexyl-1,2-dihydroxyethyl)benzoate



16al

Prepared according to GP 1. Homo-coupled dimer **17aa** was formed in <7% NMR yield. The resulting crude mixture was purified twice by flash column chromatography (gradient from 0 to 15% AcOEt/$CHCl_3$ and gradient from 0 to 10% AcOEt/$CHCl_3$) to give **16al** as a white solid (39.2 mg, 71%; *syn*/*anti* = 63:37).

^{1}H NMR (400 MHz, acetone-*d*$_6$) (*syn*)-16al δ = 7.96 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 2H), 4.77 (dd, *J* = 5.0, 5.0 Hz, 1H), 4.43 (d, *J* = 5.0 Hz, 1H), 3.87 (s, 3H), 3.64 (d, *J* = 6.0 Hz, 1H), 3.37 (ddd, *J* = 5.0, 5.0, 5.0 Hz, 1H), 1.94–1.88 (m, 1H), 1.72–1.61 (m, 4H), 1.34–1.15 (m, 6H); **(*anti*)-16al** δ = 7.93 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 8.2 Hz, 2H), 4.69 (dd, *J* = 6.0, 6.0 Hz, 1H), 4.48 (d, *J* = 4.6 Hz, 1H), 3.87 (s, 3H), 3.51–3.46 (m, 2H), 1.94–1.88 (m, 1H), 1.72–1.61 (m, 4H), 1.34–1.15 (m, 6H).

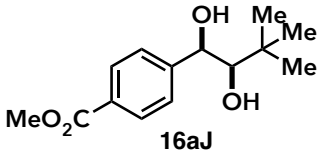
^{13}C NMR (101 MHz, acetone-*d*$_6$) δ = 167.3, 167.2, 150.4, 150.2, 129.9, 129.8, 129.7, 129.5, 128.5, 127.8, 80.4, 79.5, 74.7, 74.3, 52.22, 52.18, 40.6, 40.1, 31.1, 31.0, 28.2, 27.4, 27.3, 27.2, 27.1, 27.0, 26.95, 26.87.

HRMS (ESI$^+$): Calcd for $C_{16}H_{22}NaO_4$ ([M+Na]$^+$) 301.1410, Found *m*/*z* 301.1403.

IR (ATR): 3600–3100 (br), 2923 (m), 2849 (m), 1718 (s), 1275 (s) cm^{-1}.

Rf: 0.23 (AcOEt/$CHCl_3$ 1:5).

Methyl 4-(1,2-dihydroxy-3,3-dimethylbutyl)benzoate



16aJ

Prepared according to GP 1 using DMBI. Homo-coupled dimer **17aa** was formed in 22% NMR yield. DMA solution of **14a** was added dropwise over 50 minutes, and the reaction mixture was stirred for further 10 minutes. The resulting crude mixture was purified twice by flash column chromatography (gradient from 10 to 35% AcOEt/Hex and gradient from 0 to 8% AcOEt/$CHCl_3$) to give **16aJ** as a white solid (26.7 mg, 53%; *syn*/*anti* = 92:8).

^{1}H NMR (396 MHz, acetone-d_6) (*syn*)-16aJ δ = 7.95 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 2H), 4.91 (s, 1H), 4.38 (br, 1H), 3.89 (br, 1H), 3.87 (s, 3H), 3.30 (s, 1H), 1.01 (s, 9H); **(*anti*)-16aJ** δ = 7.92 (d, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 8.6 Hz, 2H), 4.72 (d, *J* = 5.9 Hz, 1H), 4.38 (br, 1H), 3.87 (s, 3H), 3.53–3.47 (m, 2H), 0.96 (s, 9H).

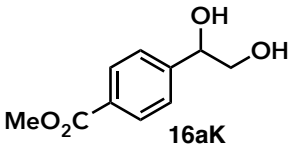
^{13}C NMR (**101 MHz, acetone-d_6**) **(*syn*)-16aJ** δ = 167.2, 152.3, 129.9, 129.6, 127.2, 82.5, 72.0, 52.2, 36.0, 27.0; **(*anti*)-16aJ** δ = 167.3, 151.1, 129.7, 129.5, 129.1, 82.0, 75.8, 52.2, 35.6, 27.2.

HRMS (ESI$^+$) (*syn*)-16aJ Calcd for $C_{14}H_{20}NaO_4$ ([M+Na]$^+$) 275.1254, Found *m*/*z* 275.1248; **(*anti*)-16aJ** Found *m*/*z* 275.1261.

IR (ATR): 3600–3100 (br), 2951 (m), 2903 (m), 1723 (s), 1278 (s) cm^{-1}.

Rf: 0.29 (AcOEt/$CHCl_3$ 1:3).

Methyl 4-(1,2-dihydroxyethyl)benzoate (CAS: 75164-88-4)[30]



16aK

Prepared according to GP 1. Homo-coupled dimer **17aa** was formed in 13% NMR yield. The resulting crude mixture was purified by flash column chromatography (gradient from 35 to 50% AcOEt/$CHCl_3$) to give **16aK** as a yellow oil (18.8 mg, 48%).

^{1}H NMR (396 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 4.88 (dd, *J* = 8.2, 3.6 Hz, 1H), 3.91 (s, 3H), 3.79 (dd, *J* = 11.3, 3.6 Hz, 1H), 3.64 (dd, *J* = 11.3, 8.2 Hz, 1H), 2.99 (br, 1H), 2.41

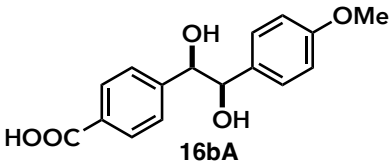
(br, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.1, 145.8, 129.9, 129.8, 126.1, 74.4, 68.0, 52.3.

EI-MS: Calcd for $C_{10}H_{12}O_4$ ([M]$^+$) 196, Found *m*/*z* 196.

Rf: 0.21 (AcOEt/$CHCl_3$ 1:1).

4-[1,2-Dihydroxy-2-(4-methoxyphenyl)ethyl]benzoic acid



16bA

Prepared according to GP 1 using DMBI and 10 mL of CO_2. Homo-coupled dimer **17bb** was formed in <4% NMR yield. DMA solution of **14b** was added dropwise over 50 minutes, and the reaction mixture was stirred for further 10 minutes. The resulting crude mixture was purified by flash column chromatography (gradient from 0 to 7% MeOH/($CHCl_3$/AcOH, v/v = 100:1)) to give **16bA** as a white solid (52.6 mg, 91%; *syn*/*anti* = 80:20).

^{1}H NMR (396 MHz, acetone-d_6) (*syn*)-16bA δ = 7.86 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.06 (d, *J* = 8.6 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 2H), 4.74 (d, *J* = 7.3 Hz, 1H), 4.63 (d, *J* = 7.3 Hz, 1H), 3.73 (s, 3H); **(*anti*)-16bA** δ = 7.90 (d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.16 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 9.1 Hz, 2H), 4.88 (d, *J* = 5.4 Hz, 1H), 4.80 (d, *J* = 5.4 Hz, 1H), 3.75 (s, 3H).

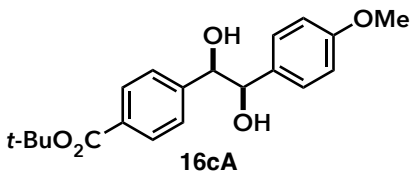
^{13}C NMR (101 MHz, DMSO-d_6) δ = 167.6, 167.5, 158.21, 158.16, 148.5, 147.6, 135.0, 134.0, 129.3, 128.4, 128.3, 127.5, 127.3, 112.8, 77.4, 77.0, 76.8, 76.5, 55.02, 54.97. Two carbons overlapped at 129.3, 128,4, 128.3, and 112.8 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^-$): Calcd for $C_{16}H_{15}O_5$ ([M–H]$^-$) 287.0925, Found *m*/*z* 287.0931.

IR (ATR): 3600–3200 (br), 1685 (s), 1247 (s) cm^{-1}.

Rf: 0.29 (MeOH/$CHCl_3$ 1:20).

tert-Butyl 4-[1,2-dihydroxy-2-(4-methoxyphenyl)ethyl]benzoate



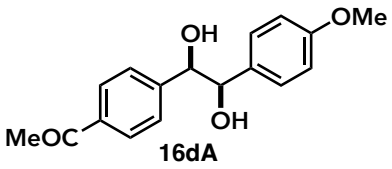
16cA

Prepared according to GP 1 using DMBI. Homo-coupled dimer **17cc** was formed in <10% NMR yield.

The resulting crude mixture was purified three times by flash column chromatography (gradient from 0 to 10% AcOEt/$CHCl_3$), followed by GPC to give **16cA** as a white solid (33.7 mg, 51%; *syn*/*anti* = 77:23).

^{1}H NMR (400 MHz, acetone-d_6) (*syn*)-16cA δ = 7.78 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 2H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.75 (d, *J* = 8.7 Hz, 2H), 4.74 (d, *J* = 7.3 Hz, 1H), 4.62 (d, *J* = 7.3 Hz, 1H), 3.73 (s, 3H), 1.56 (s, 9H); **(*anti*)-16cA** δ = 7.82 (d, *J* = 8.7 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.16 (d, *J* = 8.2 Hz, 2H), 6.79 (d, *J* = 9.2 Hz, 2H), 4.88 (d, *J* = 5.5 Hz, 1H), 4.80 (d, *J* = 5.5 Hz, 1H), 3.75 (s, 3H), 1.58 (s, 9H).
^{13}C NMR (101 MHz, acetone-d_6) δ = 166.1, 166.0, 159.9, 159.8, 148.1, 147.7, 134.6, 134.2, 131.6, 131.4, 129.3, 129.2, 129.1, 128.15, 128.07, 113.9, 113.7, 81.1, 81.0, 79.3, 79.1, 78.3, 78.1, 55.4, 28.3. Two carbons overlapped at 129.2, 55.4, and 28.3 ppm, determined by the quantitative ^{13}C NMR analysis.
HRMS (ESI$^+$): Calcd for $C_{20}H_{24}NaO_5$ ([M+Na]$^+$) 367.1516, Found *m*/*z* 367.1518.
IR (ATR): 3600–3100 (br), 2972 (m), 2916 (m), 1706 (s), 1297 (s), 1246 (s) cm^{-1}.
Rf: 0.21 (AcOEt/$CHCl_3$ 1:5).

1-{4-[1,2-Dihydroxy-2-(4-methoxyphenyl)ethyl]phenyl}ethan-1-one



16dA

Prepared according to GP 1 using DMBI, 5 equivalents of **15A**, and 20 mL of CO_2. Homo-coupled dimer **17dd** was formed in <18% NMR yield. The resulting crude mixture was purified twice by flash column chromatography (gradient from 45 to 72% AcOEt/Hex) to give **16dA** as a white solid (26.6 mg, 46%; *syn*/*anti* = 75:25).

^{1}H NMR (396 MHz, acetone-d_6) (*syn*)-16dA δ = 7.81 (d, *J* = 8.6 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 7.07 (d, *J* = 8.6 Hz, 2H), 6.75 (d, *J* = 9.1 Hz, 2H), 4.75 (d, *J* = 6.8 Hz, 1H), 4.63 (d, *J* = 7.3 Hz, 1H), 3.73 (s, 3H), 2.52 (s, 3H); **(*anti*)-16dA** δ = 7.85 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.17 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 9.1 Hz, 2H), 4.88 (d, *J* = 5.4 Hz, 1H), 4.80 (d, *J* = 5.4 Hz, 1H), 3.75 (s, 3H), 2.54 (s, 3H).
^{13}C NMR (100 MHz, acetone-d_6) δ = 197.8, 197.7, 159.9, 159.8, 148.6, 148.1, 137.0, 136.9, 134.7, 134.2, 129.2, 128.4, 128.34, 128.28, 128.2, 113.8, 113.7, 79.2, 79.0, 78.3, 78.0, 55.4, 26.7. Two carbons

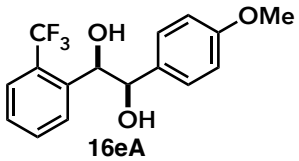
overlapped at 129.2, 55,4, and 26.7 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{17}H_{18}NaO_4$ ([M+Na]$^+$) 309.1097, Found *m*/*z* 309.1094.

IR (ATR): 3600–3100 (br), 1660 (s), 1274 (s), 1242 (s) cm^{-1}.

Rf: 0.24 (AcOEt/Hex 1:1).

1-(4-Methoxyphenyl)-2-(2-(trifluoromethyl)phenyl)ethane-1,2-diol



16eA

Prepared according to GP 1 using DMBI and 20 mL of CO_2. Homo-coupled dimer **17ee** was formed in 3% NMR yield. The resulting crude mixture was purified twice by flash column chromatography (gradient from 0 to 7% AcOEt/$CHCl_3$ and gradient from 0 to 4% AcOEt/$CHCl_3$) to give **16eA** as a white solid (38.0 mg, 62%; *syn*/*anti* = 67:33).

^{1}H NMR (396 MHz, $CDCl_3$) (*syn*)-16eA δ = 7.82 (d, *J* = 7.7 Hz, 1H), 7.64–7.31 (m, 3H), 7.15 (d, *J* = 8.6 Hz, 2H), 6.81–6.77 (m, 2H), 5.15 (br, 1H), 4.82 (br, 1H), 3.75 (s, 3H), 2.96 (br, 1H), 2.85 (br, 1H); **(*anti*)-16eA** δ = 7.64–7.31 (m, 4H), 7.11 (d, *J* = 8.6 Hz, 2H), 6.81–6.77 (m, 2H), 5.33 (d, *J* = 5.0 Hz, 1H), 4.82 (br, 1H), 3.78 (s, 3H), 2.61 (br, 1H), 2.34 (br, 1H).

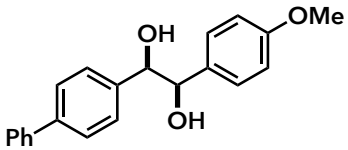
^{13}C NMR (101 MHz, acetone-*d*$_6$) δ = 160.0, 159.8, 142.8, 142.4, 134.8, 134.7, 132.7, 132.4, 130.9, 130.4, 129.8, 128.7, 128.4, 128.3 (q, *J* = 29.9 Hz), 128.1, 127.8 (q, *J* = 29.9 Hz), 125.9 (q, *J* = 6.7 Hz), 125.74 (q, *J* = 273.6 Hz), 125.67 (q, *J* = 5.8 Hz), 125.5 (q, *J* = 273.6 Hz), 113.9, 113.6, 77.9, 77.6, 74.2, 73.7, 55.42, 55.38.

HRMS (ESI$^+$): Calcd for $C_{16}H_{15}F_3NaO_3$ ([M+Na]$^+$) 335.0866, Found *m*/*z* 335.0857.

IR (ATR): 3600–3100 (br), 1309 (s), 1251 (s) cm^{-1}.

Rf: 0.29 (AcOEt/$CHCl_3$ 1:5).

1-(4-Methoxyphenyl)-2-(4-phenylphenyl)ethane-1,2-diol



16fA

Prepared according to GP 1 using DMBI, 10 equivalents of **15A**, and 20 mL of CO_2. Homo-coupled

dimer **17ff** was formed in <23% NMR yield. DMA solution of **14f** was added dropwise over 50 minutes, and the reaction mixture was stirred for further 1 hour. The resulting crude mixture was purified by PLC to give **16fA** as a white solid (35.0 mg, 54%; *syn*/*anti* = 63:37).

^{1}H NMR (396 MHz, acetone-d_6) (*syn*)-16fA δ = 7.66–7.20 (m, 9H), 7.10 (d, *J* = 8.6 Hz, 2H), 6.76 (d, *J* = 8.6 Hz, 2H), 4.70 (d, *J* = 7.3 Hz, 1H), 4.65 (d, *J* = 7.3 Hz, 1H), 3.73 (s, 3H); **(*anti*)-16fA** δ = 7.66–7.20 (m, 11H), 6.80 (d, *J* = 9.1 Hz, 2H), 4.84 (d, *J* = 5.9 Hz, 1H), 4.80 (d, *J* = 5.4 Hz, 1H), 3.75 (s, 3H).

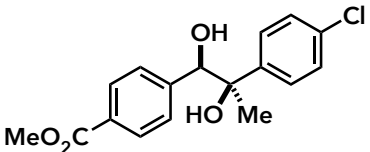
^{13}C NMR (101 MHz, acetone-d_6) δ = 159.9, 159.8, 142.5, 141.9, 141.8, 141.6, 140.5, 140.3, 135.1, 134.5, 129.7, 129.33, 129.28, 128.8, 128.7, 128.0, 127.9, 127.57, 127.56, 126.8, 126.7, 113.8, 113.7, 79.4, 79.2, 78.4, 78.2, 55.4. Two carbons overlapped at 129.7 and 55.4 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{21}H_{20}NaO_3$ ([M+Na]$^+$) 343.1305, Found *m*/*z* 343.1315.

IR (ATR): 3700–3100 (br), 1250 (s) cm^{-1}.

Rf: 0.20 (AcOEt/$CHCl_3$ 1:10).

Methyl 4-[2-(4-chlorophenyl)-1,2-dihydroxypropyl]benzoate



16aL

Prepared according to GP 1 using 5 equivalents of **15L**, and 20 mL of CO_2. Homo-coupled dimer **17aa** was formed in 5% NMR yield. The resulting crude mixture was purified twice by flash column chromatography (gradient from 0 to 5% AcOEt/$CHCl_3$) to give **16aL** as a white solid (42.9 mg, 67%; *syn*/*anti* = 82:18).

^{1}H NMR (396 MHz, $CDCl_3$) (*syn*)-16aL δ = 7.86 (d, *J* = 8.6 Hz, 2H), 7.26 (d, *J* = 8.6 Hz, 2H), 7.22 (d, *J* = 8.6 Hz, 2H), 7.10 (d, *J* = 8.6 Hz, 2H), 4.79 (d, *J* = 2.3 Hz, 1H), 3.88 (s, 3H), 3.03 (d, *J* = 3.2 Hz, 1H), 2.89 (s, 1H), 1.36 (s, 3H); **(*anti*)-16aL** δ = 7.80 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.6 Hz, 2H), 7.11–7.05 (m, 4H), 4.74 (d, *J* = 3.2 Hz, 1H), 3.87 (s, 3H), 2.93 (d, *J* = 3.6 Hz, 1H), 2.74 (s, 1H), 1.61 (s, 3H).

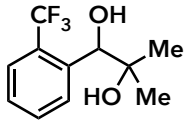
^{13}C NMR (101 MHz, acetone-d_6) δ = 167.2, 147.8, 147.6, 145.74, 145.68, 132.7, 132.5, 129.8, 129.6, 129.14, 129.10, 129.0, 128.9, 128.84, 128.75, 128.1, 128.0, 80.9, 80.6, 76.9, 76.8, 52.2, 52.1, 26.2, 25.7. Two carbons overlapped at 167.2 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI+): Calcd for $C_{17}H_{17}ClNaO_4$ ([M+Na]+) 343.0708, Found *m/z* 343.0712.

IR (ATR): 3600–3200 (br), 1687 (s), 1284 (s), 1090 (s) cm^{-1}.

Rf: 0.25 (AcOEt/$CHCl_3$ 1:8).

2-Methyl-1-[2-(trifluoromethyl)phenyl]propane-1,2-diol



16eM

Prepared according to GP 1 using DMBI, 5 equivalents of **15M**, and 20 mL of CO_2. Homo-coupled dimer **17ee** was formed in 2% NMR yield. The resulting crude mixture was purified twice by flash column chromatography (gradient from 0 to 10% AcOEt/$CHCl_3$) to give **16eM** as a white solid (33.9 mg, 71%).

^{1}H NMR (396 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 8.2 Hz, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.56 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.40 (dd, *J* = 7.7, 7.7 Hz, 1H), 4.90 (d, *J* = 3.6 Hz, 1H), 2.88 (d, *J* = 4.5 Hz, 1H), 2.43 (s, 1H), 1.37 (s, 3H), 0.98 (s, 3H).

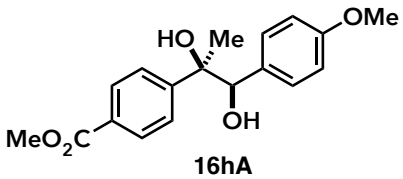
^{13}C NMR (101 MHz, $CDCl_3$): δ = 140.2, 132.0, 129.6, 128.4 (q, *J* = 29.9 Hz), 128.0, 125.6 (q, *J* = 5.8 Hz), 124.5 (q, *J* = 273.6 Hz), 73.8 (q, *J* = 1.9 Hz), 73.5, 28.6, 25.3.

HRMS (ESI+): Calcd for $C_{11}H_{13}F_3NaO_2$ ([M+Na]+) 257.0760, Found *m/z* 257.0753.

IR (ATR): 3600–3100 (br), 2978 (m), 2939 (m), 1308 (s) cm^{-1}.

Rf: 0.28 (AcOEt/$CHCl_3$ 1:5).

Methyl 4-[1,2-dihydroxy-1-(4-methoxyphenyl)propan-2-yl]benzoate



16hA

Prepared according to GP 1 using DMBI. Homo-coupled dimer **17hh** was formed in <2% NMR yield. The resulting crude mixture was purified twice by flash column chromatography (gradient from 0 to 10% AcOEt/$CHCl_3$ and gradient from 0 to 5% AcOEt/$CHCl_3$) to give **16hA** as a white solid (44.9 mg, 71%; *syn*/*anti* = 85:15).

^{1}H NMR (396 MHz, $CDCl_3$) (*syn*)-16hA δ = 7.95 (d, *J* = 8.6 Hz, 2H), 7.41 (d, *J* = 8.6 Hz, 2H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.77 (d, *J* = 8.6 Hz, 2H), 4.75 (s, 1H), 3.90 (s, 3H), 3.77 (s, 3H), 2.94 (s, 1H), 2.73 (s, 1H), 1.38 (s, 3H); **(*anti*)-16hA** δ = 7.86 (d, *J* = 8.6 Hz, 2H), 7.25 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 6.68 (d, *J* = 9.1 Hz, 2H), 4.71 (s, 1H), 3.88 (s, 3H), 3.73 (s, 3H), 2.82 (s, 1H), 2.70 (s, 1H), 1.63 (s, 3H).

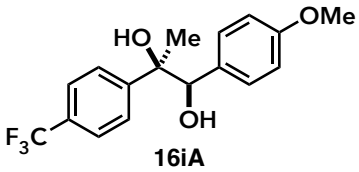
^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.23, 167.16, 159.4, 159.3, 150.6, 149.1, 131.4, 131.1, 129.4, 128.94, 128.89, 128.8, 128.6, 126.3, 126.1, 113.3, 113.1, 80.5, 80.4, 77.3, 77.1, 55.33, 55.26, 52.23, 52.18, 26.1, 24.1. Two carbons overlapped at 129.4 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{18}H_{20}NaO_5$ ([M+Na]$^+$) 339.1203, Found *m*/*z* 339.1201.

IR (ATR): 3700–3200 (br), 1687 (s), 1286 (s), 1248 (s) cm^{-1}.

Rf: 0.23 (AcOEt/$CHCl_3$ 1:5).

1-(4-Methoxyphenyl)-2-[4-(trifluoromethyl)phenyl]propane-1,2-diol



16iA

Prepared according to GP 1 using DMBI and 20 mL of CO_2. Homo-coupled dimer **17ii** was formed in <4% NMR yield. DMA solution of **14i** was added dropwise over 50 minutes, and the reaction mixture was stirred for further 10 minutes. The resulting crude mixture was purified twice by flash column chromatography (gradient from 23 to 40% AcOEt/Hex) to give **16iA** as a white solid (38.1 mg, 59%; *syn*/*anti* = 66:34).

^{1}H NMR (396 MHz, $CDCl_3$) (*syn*)-16iA δ = 7.57 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.6 Hz, 2H), 7.06 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 4.77 (s, 1H), 3.79 (s, 3H), 2.83 (s, 1H), 2.54 (s, 1H), 1.38 (s, 3H); **(*anti*)-16iA** δ = 7.48 (d, *J* = 8.6 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 6.93 (d, *J* = 8.6 Hz, 2H), 6.71 (d, *J* = 8.6 Hz, 2H), 4.72 (s, 1H), 3.75 (s, 3H), 2.70 (s, 1H), 2.51 (s, 1H), 1.63 (s, 3H).

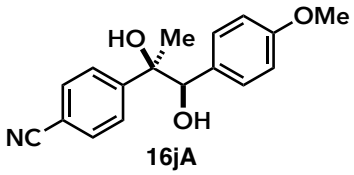
^{13}C NMR (101 MHz, acetone-*d*$_6$) δ = 159.9, 159.7, 152.4, 151.7, 134.1, 133.9, 130.00, 129.95, 128.7 (q, *J* = 31.8 Hz), 128.6 (q, *J* = 31.8 Hz), 128.0, 127.9, 125.6 (q, *J* = 270.7 Hz), 124.9 (q, *J* = 3.9 Hz), 124.7 (q, *J* = 3.9 Hz), 113.3, 113.2, 80.8, 80.5, 77.3, 77.1, 55.4, 55.3, 26.2, 25.8. Two carbons overlapped at 125.6 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{17}H_{17}F_3NaO_3$ ([M+Na]$^+$) 349.1022, Found *m*/*z* 349.1028.

IR (ATR): 3600–3100 (br), 1326 (s), 1244 (s) cm^{-1}.

Rf: 0.21 (AcOEt/Hex 1:2).

4-[1,2-Dihydroxy-1-(4-methoxyphenyl)propan-2-yl]benzonitrile



16jA

Prepared according to GP 1 using DMBI. Homo-coupled dimer **17jj** was formed in 5% NMR yield. The resulting crude mixture was purified three times by flash column chromatography (gradient from 23 to 40% AcOEt/Hex) to give **16jA** as a white solid (38.2 mg, 68%; *syn*/*anti* = 78:22).

^{1}H NMR (396 MHz, $CDCl_3$) (*syn*)-16jA δ = 7.58 (d, *J* = 8.6 Hz, 2H), 7.46 (d, *J* = 8.6 Hz, 2H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 9.1 Hz, 2H), 4.73 (s, 1H), 3.79 (s, 3H), 2.93 (s, 1H), 2.66 (br, 1H), 1.39 (s, 3H); **(*anti*)-16jA** δ = 7.48 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 6.70 (d, *J* = 8.6 Hz, 2H), 4.70 (s, 1H), 3.75 (s, 3H), 2.88 (s, 1H), 2.66 (br, 1H), 1.63 (s, 3H).

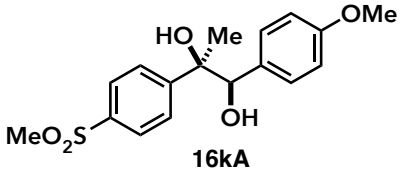
^{13}C NMR (101 MHz, acetone-d_6) δ = 159.9, 159.7, 153.3, 152.6, 133.9, 133.8, 131.9, 131.7, 129.94, 129.90, 128.3, 119.7, 113.3, 113.2, 110.8, 110.6, 80.7, 80.4, 77.4, 77.2, 55.4, 55.3, 26.1, 25.7. Two carbons overlapped at 128.3 and 119.7 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{17}H_{17}NNaO_3$ ([M+Na]$^+$) 306.1101, Found *m*/*z* 306.1099.

IR (ATR): 3700–3100 (br), 2226 (m), 1245 (s) cm^{-1}.

Rf: 0.21 (AcOEt/Hex 1:2).

1-(4-Methoxyphenyl)-2-[4-(methylsulfonyl)phenyl]propane-1,2-diol



16kA

Prepared according to GP 1 using DMBI. Homo-coupled dimer **17kk** was formed in 4% NMR yield. The resulting crude mixture was purified by PLC to give **16kA** as a white solid (57.1 mg, 85%; *syn*/*anti* = 77:23).

^{1}H NMR (400 MHz, acetone-d_6) (*syn*)-16kA δ = 7.82 (d, *J* = 8.7 Hz, 2H), 7.69 (d, *J* = 8.7 Hz, 2H), 7.12 (d, *J* = 8.7 Hz, 2H), 6.77 (d, *J* = 8.7 Hz, 2H), 4.83 (s, 1H), 3.75 (s, 3H), 3.09 (s, 3H), 1.45 (s, 3H); **(*anti*)-**

16kA δ = 7.76 (d, *J* = 8.7 Hz, 2H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.70 (d, *J* = 8.7 Hz, 2H), 4.76 (s, 1H), 3.71 (s, 3H), 3.06 (s, 3H), 1.63 (s, 3H).

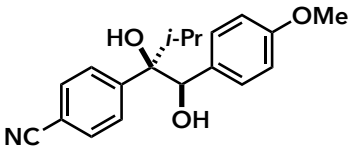
^{13}C NMR (101 MHz, acetone-*d*$_6$) δ = 159.9, 159.7, 153.9, 153.1, 140.2, 140.0, 133.9, 133.8, 130.0, 128.2, 128.1, 127.1, 126.9, 113.3, 113.2, 80.7, 80.4, 77.4, 77.2, 55.4, 55.3, 44.4, 26.0, 25.9. Two carbons overlapped at 130.0 and 44.4 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{17}H_{20}NaO_5S$ ([M+Na]$^+$) 359.0924, Found *m*/*z* 359.0921.

IR (ATR): 3600–3300 (br), 1398 (m), 1288 (s), 1253 (s), 1146 (s) cm^{-1}.

Rf: 0.37 (AcOEt/Hex 3:2).

4-[1,2-Dihydroxy-1-(4-methoxyphenyl)-3-methylbutan-2-yl]benzonitrile



16lA

Prepared according to GP 1 using DMBI. The resulting crude mixture was purified twice by flash column chromatography (gradient from 12 to 35% AcOEt/Hex) to give **16lA** as a white solid (43.6 mg, 69%; *syn*/*anti* = 80:20).

^{1}H NMR (396 MHz, acetone-*d*$_6$) (*syn*)-16lA δ = 7.61 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 6.97 (d, *J* = 8.6 Hz, 2H), 6.64 (d, *J* = 8.6 Hz, 2H), 5.09 (s, 1H), 4.58 (br, 1H), 3.78 (s, 1H), 3.69 (s, 3H), 2.61 (sep, *J* = 6.8 Hz, 1H), 1.13 (d, *J* = 6.8 Hz, 3H), 0.65 (d, *J* = 6.8 Hz, 3H); **(*anti*)-16lA** δ = 7.53 (d, *J* = 8.6 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.08 (d, *J* = 8.6 Hz, 2H), 6.67–6.63 (m, 2H), 5.25 (s, 1H), 4.16 (s, 1H), 3.68 (s, 3H), 2.91 (br, 1H), 2.45 (sep, *J* = 6.8 Hz, 1H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H).

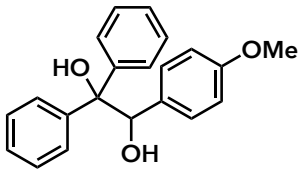
^{13}C NMR (100 MHz, acetone-*d*$_6$) δ = 159.6, 150.7, 148.9, 134.5, 134.2, 131.3, 131.1, 130.3, 130.0, 129.2, 129.0, 119.8, 119.6, 113.3, 113.0, 110.41, 110.36, 81.9, 81.4, 77.0, 76.2, 55.3, 35.5, 34.1, 18.6, 17.79, 17.75, 16.7. Two carbons overlapped at 159.6 and 55,3 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{19}H_{21}NNaO_3$ ([M+Na]$^+$) 334.1414, Found *m*/*z* 334.1411.

IR (ATR): 3700–3200 (br), 2963 (m), 2233 (m), 1250 (s) cm^{-1}.

Rf: 0.23 (AcOEt/Hex 1:3).

2-(4-Methoxyphenyl)-1,1-diphenylethane-1,2-diol (CAS: 4237-52-9)[4f]



16mA

Prepared according to GP 2. Homo-coupled dimer **17mm** was not formed. The resulting crude mixture was purified by flash column chromatography (gradient from 10 to 30% AcOEt/$CHCl_3$) to give **16mA** as a white solid (36.3 mg, 56%).

^{1}H NMR (396 MHz, DMSO-*d*$_6$): δ = 7.58 (d, *J* = 7.3 Hz, 2H), 7.31–7.25 (m, 4H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.11 (dd, *J* = 7.3 Hz, 2H), 7.05–7.00 (m, 3H), 6.62 (d, *J* = 9.1 Hz, 2H), 5.53 (d, *J* = 4.5 Hz, 1H), 5.44 (d, *J* = 5.0 Hz, 1H), 5.43 (s, 1H), 3.65 (s, 3H).

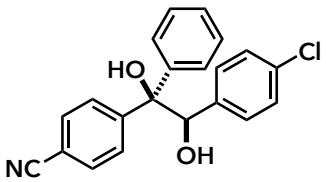
^{13}C NMR (101 MHz, DMSO-*d*$_6$): δ = 157.8, 146.8, 146.2, 134.0, 129.8, 127.4, 127.2, 126.5, 126.0, 125.8, 111.9, 79.8, 76.1, 54.8. Two carbons overlapped at 127.2 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{21}H_{20}NaO_3$ ([M+Na]$^+$) 343.1305, Found *m*/*z* 343.1302.

IR (ATR): 3700–3100 (br), 1247 (s) cm^{-1}.

Rf: 0.23 (AcOEt/$CHCl_3$ 1:5).

4-[2-(4-Chlorophenyl)-1,2-dihydroxy-1-phenylethyl]benzonitrile



16nG

Prepared according to GP 2. The resulting crude mixture was purified by flash column chromatography (gradient from 10 to 35% AcOEt/Hex) to give **16nG** as a white solid (61.7 mg, 85%; *syn*/*anti* = 57:43, determined by the quantitative ^{13}C NMR analysis).

^{1}H NMR (400 MHz, acetone-*d*$_6$) δ = 7.88 (d, *J* = 8.2 Hz, 2H), 7.74–7.69 (m, 4H), 7.53–7.47 (m, 4H), 7.36–7.33 (m, 4H), 7.27–7.09 (m, 12H), 5.83 (s, 2H), 5.08 (br, 2H), 4.95 (s, 2H).

^{13}C NMR (101 MHz, acetone-*d*$_6$) δ = 152.7, 151.4, 146.3, 145.0, 140.8, 140.6, 133.1, 133.0, 132.1,

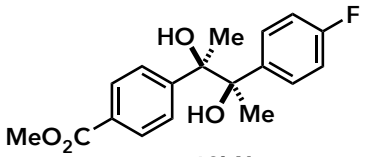
131.2, 131.1, 129.5, 128.7, 128.5, 128.3, 128.2, 127.8, 127.7, 127.6, 127.5, 127.4, 119.5, 119.4, 111.0, 110.8, 81.1, 81.0, 77.1, 76.9. Two carbons overlapped at 132.1 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{21}H_{16}ClNNaO_2$ ([M+Na]$^+$) 372.0762, Found *m/z* 372.0767.

IR (ATR): 3600–3100 (br), 2238 (m), 2227 (m) cm^{-1}.

Rf: 0.25 (AcOEt/Hex 1:3).

Methyl 4-[3-(4-fluorophenyl)-2,3-dihydroxybutan-2-yl]benzoate



16hN

Prepared according to GP 1 using DMBI and 20 mL of CO_2. Homo-coupled dimer **17hh** was formed in <4% NMR yield. DMA solution of **14h** was added dropwise over 50 minutes, and the reaction mixture was stirred for further 10 minutes. The resulting crude mixture was purified twice by flash column chromatography (gradient from 10 to 25% AcOEt/Hex) to give **16hN** as a colorless oil (42.0 mg, 67%; *syn*/*anti* = 82:18).

^{1}H NMR (396 MHz, acetone-d_6) (*syn*)-16hN δ = 7.77 (d, *J* = 9.1 Hz, 2H), 7.32 (d, *J* = 8.6 Hz, 2H), 7.23–7.18 (m, 2H), 6.86 (dd, *J* = 9.1 Hz, 2H), 4.45 (s, 1H), 4.41 (s, 1H), 3.85 (s, 3H), 1.63 (s, 3H), 1.61 (s, 3H); **(*anti*)-16hN** δ = 7.86 (d, *J* = 9.1 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 2H), 7.50–7.46 (m, 2H), 6.98-6.94 (m, 2H), 4.29 (s, 1H), 4.26 (s, 1H), 3.87 (s, 3H), 1.49 (s, 3H), 1.48 (s, 3H).

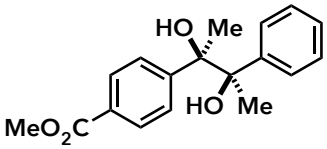
^{13}C NMR (101 MHz, acetone-d_6) δ = 167.4, 167.3, 162.5 (d, *J* = 242.8 Hz), 162.4 (d, *J* = 242.8 Hz), 152.5, 152.0, 142.7 (d, *J* = 2.9 Hz), 142.3 (d, *J* = 2.9 Hz), 130.3 (d, *J* = 7.7 Hz), 130.1 (d, *J* = 7.7 Hz), 129.0, 128.9, 128.62, 128.58, 128.43, 128.38, 114.0 (d, *J* = 22.2 Hz), 113.8 (d, *J* = 20.2 Hz), 78.9, 78.6, 78.5, 78.2, 52.14, 52.12, 25.6, 25.4, 25.2, 25.0.

HRMS (ESI$^+$): Calcd for $C_{18}H_{19}FNaO_4$ ([M+Na]$^+$) 341.1160, Found *m/z* 341.1154.

IR (ATR): 3700–3200 (br), 1703 (s), 1280 (s) cm^{-1}.

Rf: 0.26 (AcOEt/Hex 1:3).

Methyl 4-(2,3-dihydroxy-3-phenylbutan-2-yl)benzoate



16hO

Prepared according to GP 1 using DMBI and 20 mL of CO_2. Homo-coupled dimer **17hh** was formed in <1% NMR yield. DMA solution of **14h** was added dropwise over 50 minutes, and the reaction mixture was stirred for further 10 minutes. The resulting crude mixture was purified by flash column chromatography (gradient from 15 to 35% AcOEt/Hex) to give **16hO** as a colorless oil (38.2 mg, 64%; *syn*/*anti* = 86:14).

^{1}H NMR (400 MHz, $CDCl_3$) (*syn*)-16hO δ = 7.88 (d, *J* = 8.7 Hz, 2H), 7.28–7.14 (m, 7H), 3.90 (s, 3H), 2.83 (s, 1H), 2.66 (s, 1H), 1.52 (s, 3H), 1.49 (s, 3H); **(*anti*)-16hO** δ = 7.86 (d, *J* = 8.7 Hz, 2H), 7.30 (d, *J* = 8.7 Hz, 2H), 7.28–7.14 (m, 5H), 3.89 (s, 3H), 2.53 (s, 1H), 2.37 (s, 1H), 1.59 (s, 3H), 1.58 (s, 3H).

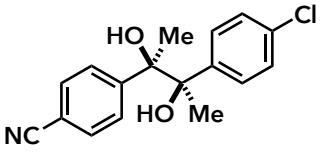
^{13}C NMR (101 MHz, acetone-d_6) δ = 167.3, 151.9, 146.0, 128.92, 128.88, 128.6, 128.52, 128.49, 128.33, 128.27, 127.5, 127.3, 127.1, 127.0, 79.0, 78.7, 78.6, 78.5, 52.1, 25.53, 25.46, 25.12, 25.10. Two carbons overlapped, at 167.3, 151.9, 146.0, 128.33, and 52.1 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{18}H_{20}NaO_4$ ([M+Na]$^+$) 323.1254, Found *m*/*z* 323.1246.

IR (ATR): 3700–3100 (br), 1703 (s), 1279 (s) cm^{-1}.

Rf: 0.28 (AcOEt/Hex 1:2).

4-[3-(4-Chlorophenyl)-2,3-dihydroxybutan-2-yl]benzonitrile



16jL

Prepared according to GP 2 using 5 mL of CO_2. Homo-coupled dimer **17jj** was formed in <6% NMR yield. The resulting crude mixture was purified by flash column chromatography (gradient from 10 to 35% AcOEt/Hex) to give **16jL** as a white solid (30.3 mg, 51%; *syn*/*anti* = 50:50).

^{1}H NMR (396 MHz, acetone-d_6) δ = 7.71 (d, *J* = 8.2 Hz, 2H), 7.64 (d, *J* = 8.6 Hz, 2H), 7.51 (d, *J* = 8.6 Hz, 4H), 7.40 (d, *J* = 8.6 Hz, 2H), 7.26 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 9.1 Hz, 2H), 7.12 (d, *J* = 9.1 Hz, 2H),

4.60 (s, 1H), 4.54 (s, 1H), 4.43 (s, 1H), 4.39 (s, 1H), 1.68 (s, 3H), 1.65 (s, 3H), 1.47 (s, 3H), 1.44 (s, 3H).

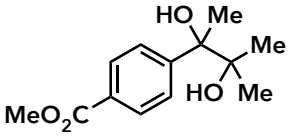
^{13}C NMR (101 MHz, acetone-d_6) δ = 152.7, 152.4, 145.6, 145.3, 132.7, 132.5, 131.3, 131.1, 130.2, 129.9, 129.5, 129.2, 127.6, 127.3, 119.7, 110.8, 110.6, 78.7, 78.3, 78.1, 25.4, 25.2, 25.0, 24.9. Two carbons overlapped at 119.7 and 78.3 ppm, determined by the quantitative ^{13}C NMR analysis.

HRMS (ESI$^+$): Calcd for $C_{17}H_{16}ClNNaO_2$ ([M+Na]$^+$) 324.0762, Found *m/z* 324.0763.

IR (ATR): 3600–3200 (br), 2231 (m), 1092 (s) cm^{-1}.

Rf: 0.24 (AcOEt/Hex 1:3).

Methyl 4-(2,3-dihydroxy-3-methylbutan-2-yl)benzoate



16hM

Prepared according to GP 1 using DMBI, 50 equivalents of **15M**, and 20 mL of CO_2. Homo-coupled dimer **17hh** was formed in <18% NMR yield. DMA solution of **14h** was added dropwise over 50 minutes, and the reaction mixture was stirred for further 10 minutes. The resulting crude mixture was purified by flash column chromatography (gradient from 0 to 10% AcOEt/$CHCl_3$) to give **16hM** as a colorless oil (25.5 mg, 54%).

^{1}H NMR (396 MHz, acetone-d_6): δ = 7.92 (d, *J* = 8.6 Hz, 2H), 7.72 (d, *J* = 8.6 Hz, 2H), 4.22 (s, 1H), 3.87 (s, 3H), 3.62 (br, 1H), 1.63 (s, 3H), 1.12 (s, 3H), 1.11 (s, 3H).

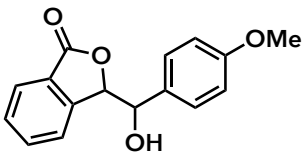
^{13}C NMR (**100 MHz, acetone-d_6**): δ = 167.3, 152.9, 128.95, 128.87, 128.2, 78.7, 74.9, 52.2, 25.7, 25.6, 24.6.

HRMS (ESI$^+$): Calcd for $C_{13}H_{18}NaO_4$ ([M+Na]$^+$) 261.1097, Found *m/z* 261.1097.

IR (ATR): 3700–3100 (br), 1705 (s), 1281 (s) cm^{-1}.

Rf: 0.23 (AcOEt/$CHCl_3$ 1:5).

3-[hydroxy(4-methoxyphenyl)methyl]-1(3*H*)-isobenzofuranone (CAS: 81428-85-5)



23gA

Prepared according to GP 1. Homo-coupled dimer **17gg** was not detected. The resulting crude mixture was purified by flash column chromatography (gradient from 10 to 30% AcOEt/$CHCl_3$) to give **23gA** as a pale yellow oil (25.2 mg, 47%; *dr* = 67:33).

^{1}H NMR (396 MHz, acetone-d_6) major-23gA δ = 7.77–7.61 (m, 2H), 7.57–7.52 (m, 1H), 7.38–7.36 (m, 1H), 7.28 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 5.73 (d, *J* = 4.5 Hz, 1H), 5.11 (d, *J* = 5.0 Hz, 1H), 3.76 (s, 3H); **minor-23gA** δ = 7.77–7.61 (m, 2H), 7.57–7.52 (m, 1H), 7.38–7.36 (m, 2H), 7.19 (d, *J* = 7.7 Hz, 1H), 6.92 (d, *J* = 9.1 Hz, 2H), 5.73 (d, *J* = 4.5 Hz, 1H), 5.15 (d, *J* = 4.5 Hz, 1H), 3.80 (s, 3H).

^{13}C NMR (**100 MHz, acetone-d_6**): δ = 170.6, 170.5, 160.31, 160.27, 148.3, 148.1, 134.3, 134.1, 132.7, 129.9, 129.3, 128.9, 128.0, 127.9, 125.5, 125.4, 124.7, 124.5, 114.2, 114.0, 84.7, 84.5, 74.4, 74.0, 55.5, 55.4. Two carbons overlapped at 132.7 and 129.9 ppm, determined by the quantitative ^{13}C NMR analysis.

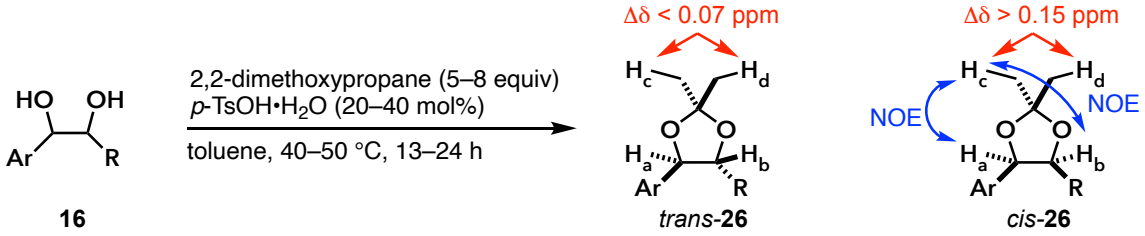
HRMS (ESI$^+$): Calcd for $C_{16}H_{14}NaO_4$ ([M+Na]$^+$) 293.0784, Found *m*/*z* 293.0792.

IR (ATR): 3700–3100 (br), 1754 (s), 1248 (s) cm^{-1}.

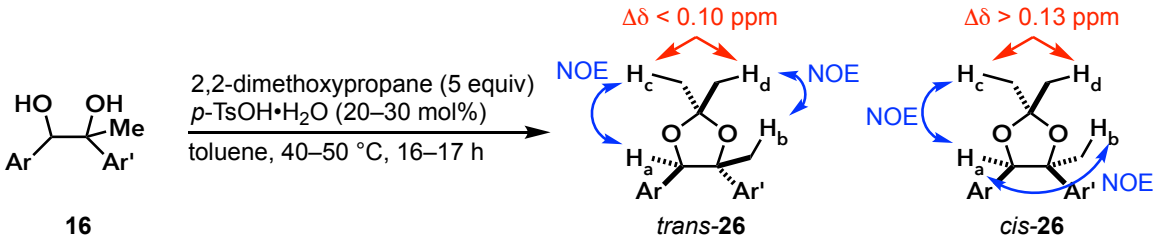
Rf: 0.18 (AcOEt/$CHCl_3$ 1:4).

Stereochemistry of 1,2-diols

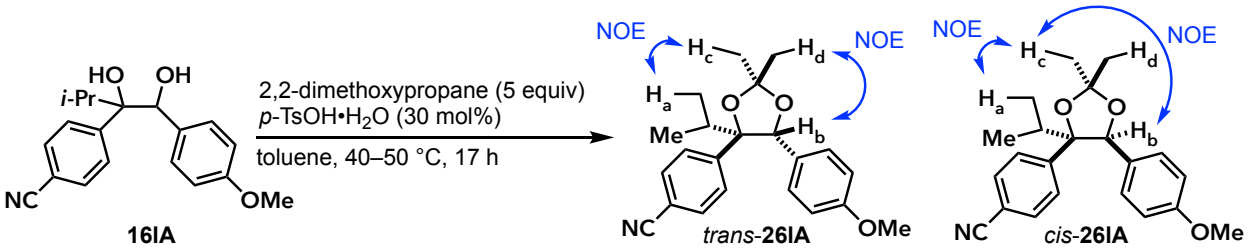
The stereochemistry of 1,2-diol products **16** was confirmed by ^{1}H NMR and NOESY analyses of the corresponding 1,2-acetonides **26** prepared through the acetalization of the 1,2-diols with 2,2-dimethoxypropane according to the reported methods.[14]



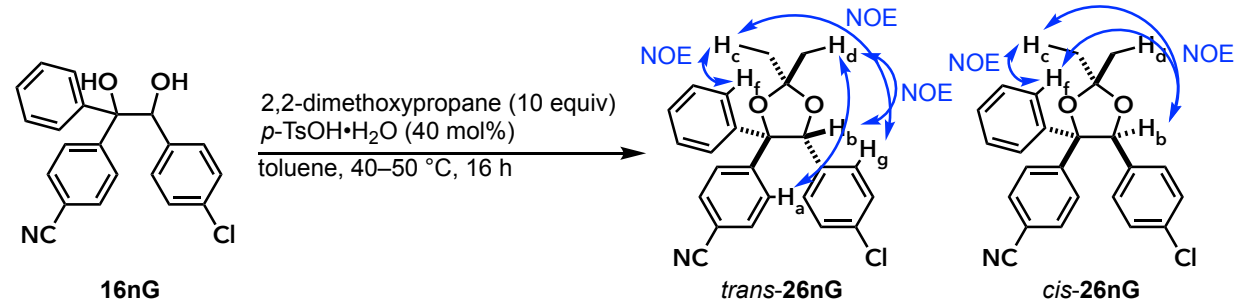
16aA–16aJ, **16bA–16fA**: In ^{1}H NMR of the *trans*-**26**, the two singlets' shifts of the *gem* methyl groups differed less than 0.07 ppm since they have a *pseudo*-C_2 symmetry, while in that of the *cis*-**26**, they split up more than 0.15 ppm.[31] NOESY analyses also supported the stereochemistry. In the NOESY of *cis*-**26**, the cross peaks of H_a/H_c, and H_b/H_c were observed.



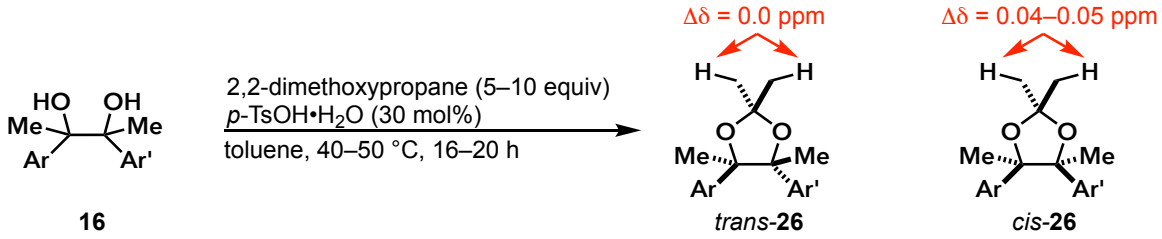
16aL, **16hA**, **16iA**, **16jA**, **16kA**: In ^{1}H NMR of the *trans*-**26**, the two singlets' shifts of the *gem* methyl groups differed less than 0.10 ppm, while in that of the *cis*-**26**, they split up more than 0.13 ppm.[31] NOESY analyses also supported the stereochemistry. In the NOESY of *cis*-**26**, the cross peaks of H_a/H_b and H_a/H_c were observed, while in that of *trans*-**26**, the cross peaks of H_a/H_c and H_b/H_d were observed and no cross peak of H_a/H_b was observed.



16lA: In the NOESY of *cis*-**26lA**, the cross peaks of H_a/H_c and H_b/H_c were observed, while in that of *trans*-**26lA**, the cross peaks of H_a/H_c and H_b/H_d were observed.



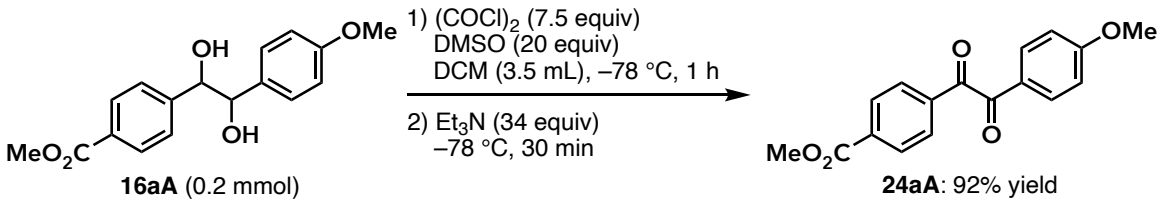
16nG: In the NOESY of *cis*-**26nG**, the cross peaks of H_b/H_c, H_c/H_f, and H_b/H_f were observed, while in that of *trans*-**26nG**, the cross peaks of H_a/H_d, H_b/H_d, H_c/H_g, and H_c/H_f were observed.



16hN, **16hO**, **16jL**: In ^{1}H NMR of the *trans*-**26**, the *gem* methyl protons were overlapped since they have a *pseudo*-C_2 symmetry, while in that of the *cis*-acetonide, they split up 0.04–0.05 ppm.[31]

Synthetic applications of unsymmetric 1,2-diols

Oxidation:[13]



16aA (0.2 mmol) **24aA**: 92% yield

Oxalyl chloride (194.5 mg, 1.5 mmol, 7.5 equiv) was placed in a Schlenk tube equipped with a stir bar and dissolved in DCM (1 mL) under nitrogen. A solution of DMSO (309.3 mg, 4.0 mmol, 20 equiv) in DCM (1 mL) was added to the Schlenk tube at −78 °C. The mixture was stirred for 2 minutes, and then a solution of 1,2-diol **16aA** (60.8 mg, 0.20 mmol) in DCM (1.5 mL) was added. After the reaction mixture was stirred for 1 hour at −78 °C, triethylamine (684.2 mg, 6.8 mmol, 34 equiv) was added, and the mixture was stirred for further 30 minutes. The reaction mixture was diluted with methyl *tert*-butyl ether (MTBE), washed with water, 2 M HCl aq., water, sat. $NaHCO_3$ aq., and brine, and then dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the crude residue was purified by PLC to give diketone **24aA** as a pale yellow solid (55.0 mg, 0.18 mmol, 92%).

Methyl 4-[2-(4-methoxyphenyl)-2-oxoacetyl]benzoate

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 8.7 Hz, 2H), 8.04 (d, *J* = 8.7 Hz, 2H), 7.95 (d, *J* = 9.2 Hz, 2H), 6.99 (d, *J* = 9.2 Hz, 2H), 3.96 (s, 3H), 3.89 (s, 3H).

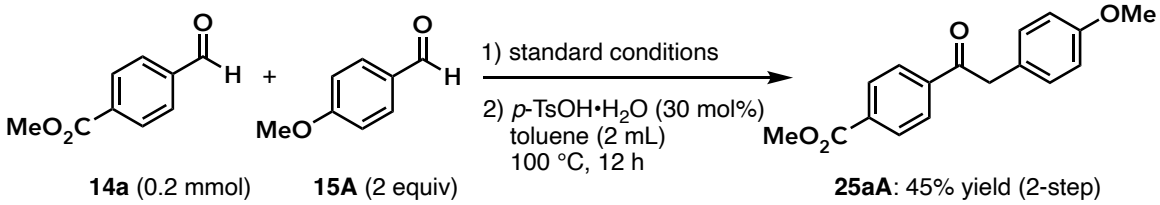
^{13}C NMR (**101 MHz, $CDCl_3$**): δ = 194.1, 192.5, 166.1, 165.4, 136.4, 135.3, 132.6, 130.2, 129.9, 125.9, 114.6, 55.8, 52.8.

HRMS (ESI$^+$): Calcd for $C_{17}H_{14}NaO_5$ ([M+Na]$^+$) 321.0733, Found *m/z* 321.0731.

IR (ATR): 1725 (s), 1672 (s), 1655 (s), 1285 (s), 1263 (s) cm^{-1}.

Rf: 0.28 (AcOEt/Hex 1:3).

Treatment with *p*-TsOH·H_2O:



14a (0.2 mmol) **15A** (2 equiv) **25aA**: 45% yield (2-step)

2d (3.78 mg, 0.0041 mmol, 2 mol%) and DMBI (67.0 mg, 0.30 mmol, 1.5 equiv) were placed in a 4 mL vial equipped with a stir bar. The vial was sealed with a rubber septum and filled with nitrogen by vacuum-refill cycles (three times). DMA (0.5 mL) was added and CO_2 (5 mL) was bubbled into the solution over 30 seconds using a syringe pump. A nitrogen balloon was attached to the vial, and *p*-anisaldehyde (**15A**) (54.8 mg, 0.40 mmol, 2 equiv) was added. A DMA solution (1 mL) of methyl 4-formylbenzoate (**14a**) (33.1 mg, 0.20 mmol) was added dropwise over 20 minutes using a syringe pump to the reaction mixture under blue light irradiation (100% light intensity from 40 W Kessil A160WE Tuna Blue. The vial was placed 2 cm away from the LED light with a fan to keep the reaction temperature at room temperature). The reaction mixture was stirred for further 40 minutes. 2 M HCl aq. was added and the resulting mixture was extracted with AcOEt (three times). The combined organic phase was washed with brine, and then dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the residue and *p*-toluenesulfonic acid monohydrate (11.0 mg, 0.058 mmol, 30 mol%) were placed in a Schlenk tube equipped with a stir bar. The Schlenk tube was filled with nitrogen by vacuum-refill cycles (three times). Toluene (2 mL) was added to the Schlenk tube, and the reaction mixture was stirred for 12 hours at 100 °C. The mixture was cooled to room temperature, diluted with AcOEt, washed with water (three times) and brine, and then dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the crude residue was purified twice by flash column chromatography with silica gel (gradient from 5 to 17% AcOEt/Hex) to give ketone **25aA** as a white solid (25.7 mg, 0.090 mmol, 45%). The structure was confirmed by ^1H, ^{13}C NMR, HMBC, HRMS, and IR analyses.

Methyl 4-[2-(4-methoxyphenyl)acetyl]benzoate

^1H NMR (396 MHz, $CDCl_3$) δ = 8.11 (d, *J* = 8.6 Hz, 2H), 8.04 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.25 (s, 2H), 3.94 (s, 3H), 3.78 (s, 3H).

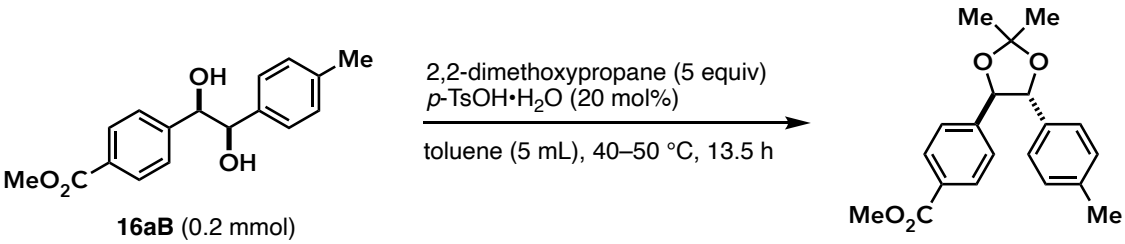
^{13}C NMR (**101 MHz, $CDCl_3$**): δ = 197.6, 166.3, 158.8, 140.0, 134.0, 130.6, 130.0, 128.6, 126.0, 114.4, 55.4, 52.6, 45.1.

HRMS (EI+): Calcd for $C_{17}H_{16}O_4$ ([M]+) 284.1043, Found *m*/*z* 284.1055.

IR (ATR): 1720 (s), 1685 (s), 1280 (s), 1252 (s) cm^{-1}.

Rf: 0.29 (AcOEt/Hex 1:5).

Acetalization:[14]



1,2-Diol **16aB** (56.9 mg, 0.20 mmol) and *p*-toluenesulfonic acid monohydrate (7.0 mg, 0.037 mmol, 20 mol%) were placed in a Schlenk tube equipped with a stir bar. To the Schlenk tube, 2,2-dimethoxypropane (107.0 mg, 1.0 mmol, 5 equiv) was added and dissolved in toluene (5 mL) under nitrogen. After stirring for 30 minutes at 50 °C, the reaction mixture was stirred for further 13 hours at 40 °C. Sat. $NaHCO_3$ aq. was added and the mixture was stirred for 30 minutes. The resulting mixture was extracted with AcOEt (three times). The combined organic phase was washed with brine, and then dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, analytically pure acetonide **26aB** was obtained as colorless oil (62.7 mg, 0.19 mmol, 96%; *trans*/*cis* = 82:18).

Methyl 4-[2,2-dimethyl-5-(*p*-tolyl)-1,3-dioxolan-4-yl]benzoate

^{1}H NMR (400 MHz, acetone-d_6) (*trans*)-26aB δ = 7.96 (d, *J* = 8.7 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.15 (s, 4H), 4.82 (d, *J* = 8.7 Hz, 1H), 4.70 (d, *J* = 8.7 Hz, 1H), 3.88 (s, 3H), 2.32 (s, 3H), 1.63 (s, 6H); **(*cis*)-26aB** δ = 7.71 (d, *J* = 8.7 Hz, 2H), 7.21 (d, *J* = 8,2 Hz, 2H), 6.97 (d, *J* = 8.2 Hz, 2H), 6.86 (d, *J* = 8.2 Hz, 2H), 5.66 (d, *J* = 7.8 Hz, 1H), 5.63 (d, *J* = 7.3 Hz, 1H), 3.79 (s, 3H), 2.11 (s, 3H), 1.77 (s, 3H), 1.57 (s, 3H).

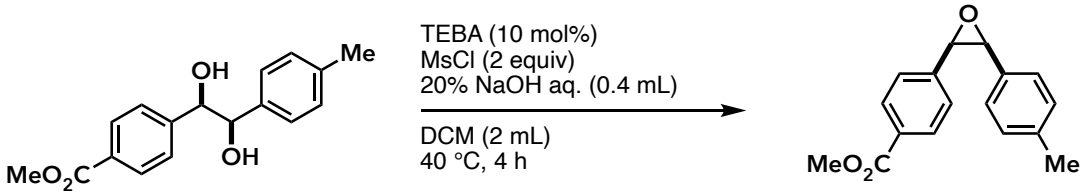
^{13}C NMR (**101 MHz, acetone-d_6**) δ = 166.99, 166.95, 145.1, 143.5, 138.8, 137.3, 135.9, 134.5, 130.9, 130.2, 129.9, 129.5, 129.3, 128.9, 128.0, 127.90, 127.86, 127.7, 110.1, 109.4, 86.2, 85.6, 81.9, 81.5, 52.3, 52.1, 27.5, 27.3, 26.9, 24.6, 21.2, 21.0.

HRMS (ESI+): Calcd for $C_{20}H_{22}NaO_4$ ([M+Na]+) 349.1410, Found *m*/*z* 349.1428.

IR (ATR): 1721 (s), 1275 (s), 1063 (s) cm^{-1}.

Rf: 0.47, 0.40 (AcOEt/Hex 1:7).

Epoxidation[15]



16aB (0.1 mmol)

27aB: 71% yield
(*trans*/*cis* = 18:82)

1,2-Diol **16aB** (28.5 mg, 0.10 mmol) and benzyl(triethyl)ammonium chloride (TEBA) (2.30 mg, 0.010 mmol, 10 mol%) were placed in a Schlenk tube equipped with a stir bar. To the Schlenk tube, 20% NaOH aq. (0.4 mL) and DCM (2 mL) were added under nitrogen. A DCM solution (1 mL) of methanesulfonyl chloride (23.8 mg, 0.21 mmol, 2 equiv) was slowly added to the mixture at 40 °C, and then the reaction mixture was stirred for 4 hours. The mixture was diluted with DCM, and washed with water (three times) and brine. The organic phase was dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the crude residue was purified by flash column chromatography with silica gel (gradient from 3 to 24% AcOEt/Hex) to give epoxide **27aB** as a white solid (19.1 mg, 0.71 mmol, 71%). The *trans*/*cis* ratio was assigned as 18:82 by ^{1}H NMR analysis of the crude reaction mixture. The stereochemistry was confirmed by the coupling constant of the vicinal protons on the epoxide (*trans*: J = 1.8 Hz, *cis*: J = 4.5 Hz).

Methyl 4-[3-(*p*-tolyl)oxiran-2-yl]benzoate

^{1}H NMR (396 MHz, $CDCl_3$) (*trans*)-27aB δ = 8.04 (d, J = 8.6 Hz, 2H), 7.40 (d, J = 8.2 Hz, 2H), 7.26–7.23 (m, 2H), 7.19 (d, J = 8.2 Hz, 2H), 3.92 (s, 3H), 3.90 (d, J = 1.8 Hz, 1H), 3.83 (d, J = 1.8 Hz, 1H), 2.37 (s, 3H); **(*cis*)-27aB** δ = 7.86 (d, J = 8.6 Hz, 2H), 7.25 (d, J = 8.2 Hz, 2H), 7.03 (d, J = 8.2 Hz, 2H), 6.97 (d, J = 8.2 Hz, 2H), 4.37 (d, J = 4.5 Hz, 1H), 4.36 (d, J = 4.5 Hz, 1H), 3.85 (s, 3H), 2.23 (s, 3H).

^{13}C NMR (**101 MHz, $CDCl_3$**) δ = 167.0, 166.9, 142.5, 140.0, 138.6, 137.5, 133.7, 130.8, 130.1, 130.0, 129.44, 129.39, 129.2, 128.8, 127.0, 126.8, 125.6, 125.5, 63.3, 62.3, 60.0, 59.5, 52.3, 52.2, 21.4, 21.2.

HRMS (EI$^+$): Calcd for $C_{17}H_{16}O_3$ ([M]$^+$) 268.1094, Found m/z 268.1089.

IR (ATR): 1714 (s), 1282 (s) cm^{-1}.

Rf: 0.47 (AcOEt/Hex 1:7).

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[10] In the reaction with **15A**, aryl aldehydes bearing electron-withdrawing groups such as ester (**14a**), carboxyl (**14b**), and trifluoromethyl (**14e**) groups afforded the corresponding dimers **17** in <4% NMR yield. On the other hand, relatively electron-rich substrate **14f** gave dimer **17ff** in ca.23% NMR yield. Reduction of electron-rich carbinol radicals should be slow to result in forming carbinol radical dimer.

[11] In the presence of 5 mL of CO_2, **16eM** was obtained in 60% NMR yield. The yield of **16eM** increased to 75% NMR yield (71% isolated yield) when 20 mL of CO_2 was used, where carboxylated product **19e** was formed less than 2% yield.

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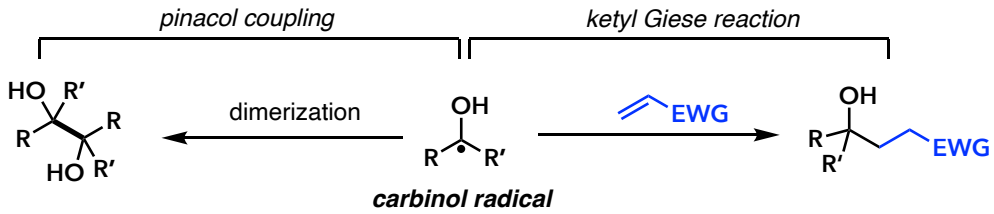
Chapter 2

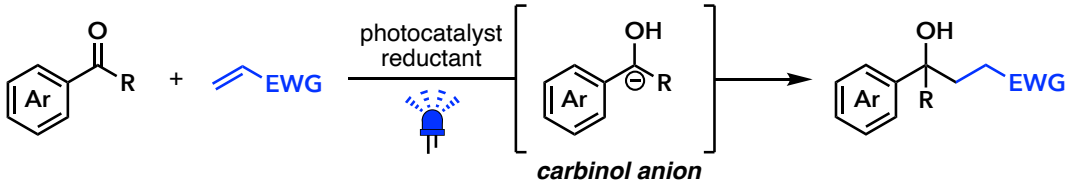
Introduction

1,4-Addition of radical species to electron-deficient olefins, the so-called Giese reaction,[1,2] is known to take place under photocatalytic conditions.[1c] However, carbinol radicals[3] are not fully compatible with the photocatalytic Giese-type 1,4-addition reaction and often dimerize to form vicinal 1,2-diols (i.e., they undergo pinacol coupling) (Scheme 1).[4–6] Indeed, well-developed research on the photocatalytic intermolecular Giese reaction of carbinol radicals has been limited to the recent pioneering reports of the groups of He and Guan,[7] and Lin.[8]



Scheme 1. Reactions of carbinol redicals; pinacol coupling vs. ketyl Giese reaction.

As already mentioned, Okumura and Uozumi, and the author developed the anionic reductive coupling of an aromatic aldehyde or ketone with a second carbonyl compound under photocatalytic conditions.[9,10] In this context, the author achieved the ionic 1,4-addition of carbonyl compounds to electron-deficient olefins through the photocatalytic carbinol cation/anion umpolung (Scheme 2).



Scheme 2. 1,4-Addition of aromatic carbonyl compounds via umpoled carbinol anions (this work).

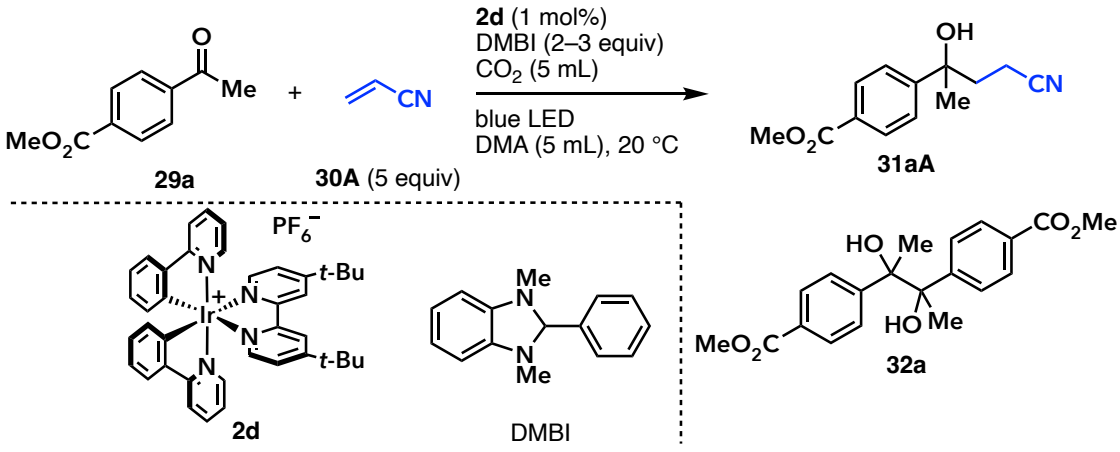
Optimization of reaction conditions

First, the author examined the reductive 1,4-addition of methyl 4-acetylbenzoate (**29a**) to acrylonitrile (**30A**) (Table 1). The reaction was smoothly promoted by the iridium complex $Ir(ppy)_2(dtbbpy)PF_6$ (**2d**; ppy = 2-phenylpyridinato; dtbbpy = 4,4′-di-*tert*-butyl-2,2′-bipyridine) and 1,3-dimethyl-2-phenyl-2,3-dihydro-1*H*-benzimidazole (DMBI) in *N*,*N*-dimethylacetamide (DMA) in the presence of CO_2 gas under blue-light irradiation (λ = 448 nm). CO_2 (5 mL) was bubbled for 30 seconds through a solution of **2d** (1 mol%), DMBI (2.0 equiv), and acrylonitrile (**30A**; 5 equiv) in DMA (4 mL).[11] The resulting solution was irradiated with blue light (LEDs; λ = 448 nm) under nitrogen at

20 °C while a solution of methyl 4-acetylbenzoate (**29a**) in DMA (1 mL) was added dropwise over 80 minutes. Irradiation was continued for a further 70 minutes to give the γ-hydroxybutyronitrile derivative **31aA** in 70% NMR yield, along with a trace of the homo-coupled dimer **32a** (Table 1, entry 1). The best result was achieved with 3.0 equivalents of DMBI, which gave a 92% NMR yield (76% isolated yield) of **31aA** (entry 2). Control experiments showed that the Ir catalyst, DMBI reductant, and blue-light irradiation were all essential for the formation of **31aA** (entries 3–5). In the absence of CO_2, the yield of **31aA** decreased to 18% and that of the dimer **32a** increased to 37% (entry 6), showing that the undesired homo-coupling of carbinol radicals through a one-electron reduction of **29a** was the dominant reaction pathway. This is consistent with the author's earlier findings that CO_2 promotes successive one-electron reductions of carbinol radicals to produce carbinol anions.[10,12]

When the reaction was carried out under the photocatalytic ketyl Giese conditions reported by He, Guan and co-workers,[7] with 1 mol% of Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 [**2c**; dF(CF_3)ppy = 2-(2,4-difluorophenyl)-5-(trifluoromethyl)pyridinato] and 2.0 equivalents of diethyl 2,6-dimethyl-1,4-

Table 1. 1,4-Addition of methyl 4-acetylbenzoate (**29a**) to acrylonitrile (**30A**).[a]



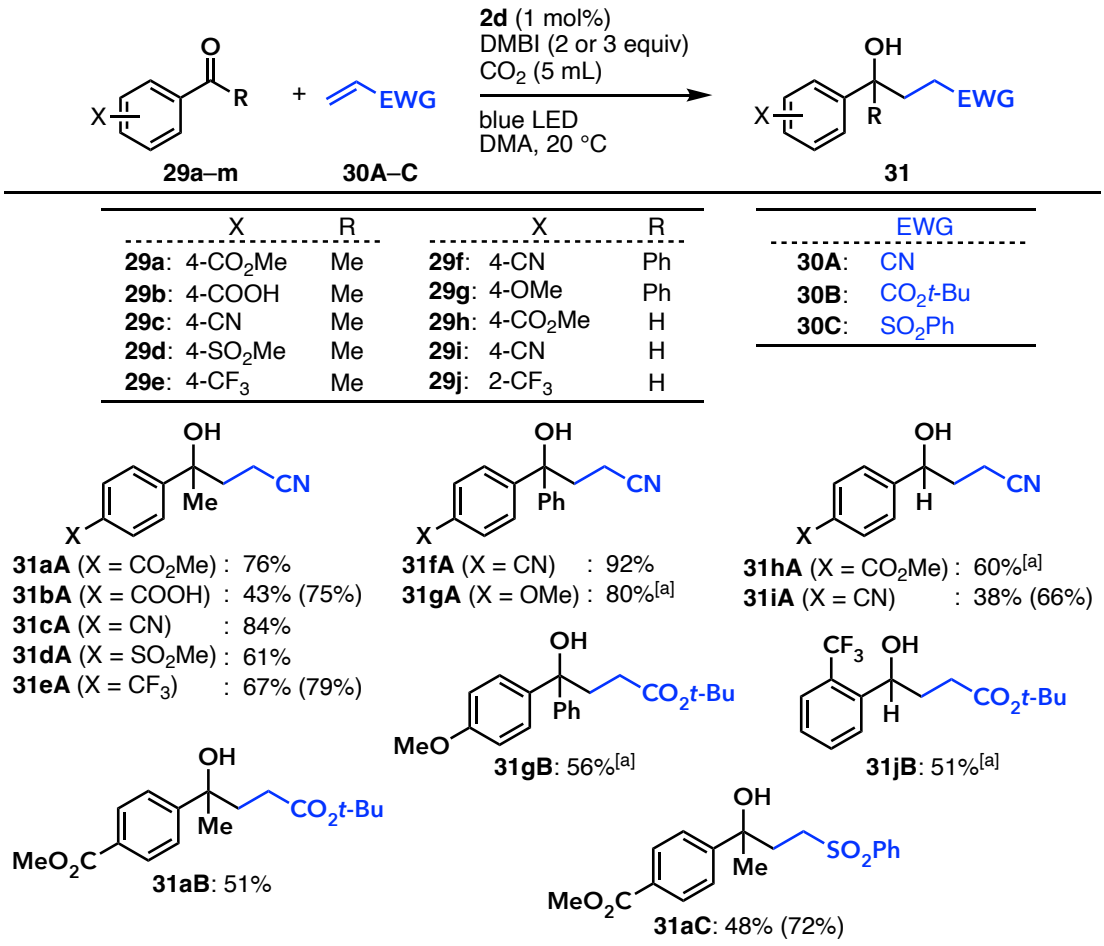
entry	variation	yield (%)[b] **31aA**	**32a**
1	none	70	1
2	DMBI (3 equiv)	92 (76)	3
3	without **2d**	0	0
4	without DMBI	0	0
5	without light	0	2
6	without CO_2	18	37
7[c]	—	11	45

[a] A 0.2 M solution of **29a** (0.2 mmol) in DMA (1 mL) was added dropwise to a solution of **30A** (1.0 mmol), **2d** (0.002 mmol), and DMBI (0.4 mmol) in DMA (4 mL), previously bubbled with CO_2 (5 mL), under blue LED irradiation (λ = 448 nm) at 20 °C for 2.5 h. [b] NMR yield. The isolated yield is shown in parentheses. [c] The reaction was carried out according to the conditions reported by He, Guan, and co-workers[7] in the presence of $B(C_6F_5)_3$ (10 mol%), Hantzsch ester (HE **20**; 2.0 equiv), and Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (**2c**; 1 mol%).

dihydropyridine-3,5-dicarboxylate (HE **20**, Hantzsch ester) in the presence of tris(pentafluorophenyl)borane [$B(C_6F_5)_3$; 10 mol%] as a co-catalyst, the homo-coupled dimer **32a** was formed as the major product in 45% yield (Table 1, entry 7). Carbonyl substrates for the intermolecular ketyl Giese reaction are limited to electron-rich aromatic compounds and, indeed, electron-deficient **29a** underwent a radical pinacol coupling rather than the ketyl Giese reaction, resulting in the formation of the homo-dimer **32a** (entry 7). Consequently, the present ionic 1,4-addition of two-electron-reduced carbinol anions is complementary to the ketyl Giese reaction.

Substrate scope

The 1,4-addition reactions of a variety of ketones were then examined (Scheme 3). 4-Acetylbenzoic acid (**29b**), with an acidic proton, gave the γ-hydroxybutyronitrile **31bA** in 43% yield (75% NMR yield). Acetophenones **29c** and **29d** bearing cyano and methylsulfanyl groups, respectively, coupled



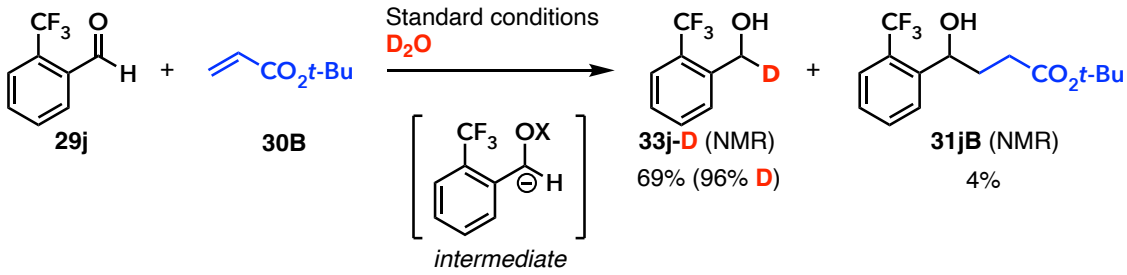
Reaction conditions: aldehyde or ketone **29** (0.2 mmol), olefin **30** (1.0 mmol, 5.0 equiv), **2d** (0.002 mmol, 1 mol%), DMBI (0.6 mmol, 3.0 equiv), DMA (5 mL), CO_2 (5 mL, bubbled), blue LED irradiation (λ = 448 nm), 20 °C, 2.5 h. Isolated yields (NMR yields in parentheses) are reported. [a] DMBI (2.0 equiv) was used.

Scheme 3. Substrate scope.

with **30A** to give the corresponding products **31cA** and **31dA** in yields of 84% and 61%. Substrate **29e**, bearing a trifluoromethyl substituent that has a high inductive effect, also underwent the coupling reaction to afford product **31eA** in 67% yield. Benzophenones **29f** and **29g** both coupled with **30A** to form products **31fA** and **31gA**, which contained sterically hindered quaternary carbinol carbons, in yields of 92% and 80%, respectively, showing that an electron-donating methoxy group is also tolerated in the reaction. The 1,4-addition of electron-deficient aromatic aldehydes **29h** and **29i**, which can readily undergo the radical pinacol coupling, also proceeded under the photocatalytic conditions. Thus, aromatic aldehydes bearing a methyl ester (**29h**) or cyano group (**29i**) gave products **31hA** and **31iA** in isolated yields of 60% and 38% (66% NMR), respectively. α,β-Unsaturated esters and sulfones were also eligible olefins: the 1,4-addition of **29a**, **29g**, or 2-(trifluoromethyl)benzaldehyde (**29j**) to *tert*-butyl acrylate (**30B**) gave the corresponding γ-hydroxy esters **31aB**, **31gB**,and **31jB** in yields of 51%, 56%, and 51%, respectively. Phenyl vinyl sulfone (**30C**) also reacted with **29a** to afford the γ-hydroxy sulfone **31aC** in 48% (72% NMR) yield.

Mechanistic study

The author then performed a deuteration experiment using D_2O, which barely reacts with radical species but reacts readily with anionic species. When the photocatalytic coupling of aldehyde **29j** and enoate **30B** was carried out under the standard conditions in the presence of D_2O, aldehyde **29j** preferentially reacted with D_2O to give the *C*-deuterated alcohol **33j-D** in 69% NMR yield with 96% incorporation of deuterium, along with 4% of the γ-hydroxy ester **31jB** (Scheme 4). This result indicated the intermediacy of a carbinol anion.

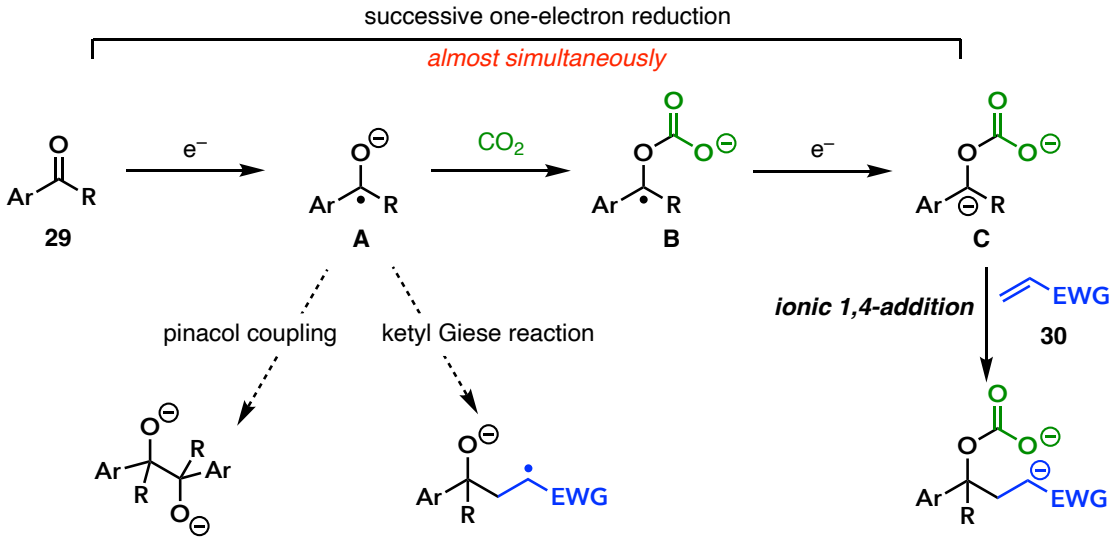


Scheme 4. Deuteration experiment.

Proposed mechanism

A plausible reaction mechanism is shown in Scheme 5. As already mentioned in Chapter 1, the first one-electron reduction (to form **A**), an *O*-carboxylation (to form **B**), and a second one-electron

reduction (to form **C**) take place almost simultaneously; these give the carbinol anion **C**, with suppression of the dimerization of carbinol radical intermediates (pinacol coupling).[10] In the deuteration experiment (Scheme 4), aldehyde **29j**, rather than olefin **30A**, reacted with D_2O under the photocatalytic conditions where the second reduction of carbinol radical **A** should proceed much faster than the ketyl Giese reaction. This strongly suggests that the resulting carbinol anion **C** reacts ionically with olefin **30** to afford the desired 1,4-addition product.



Scheme 5. Plausible reaction pathway.

Conclusion

In conclusion, the author has developed a 1,4-addition reaction of aromatic aldehydes or ketones with electron-deficient olefins under photocatalytic conditions with CO_2 as an additive to give the corresponding γ-substituted secondary or tertiary alcohols, respectively, in up to 92% yield. The reaction proceeds via umpoled carbinol anions, generated through two successive one-electron reductions to achieve an ionic 1,4-addition of the carbonyl compound.

Experimental section

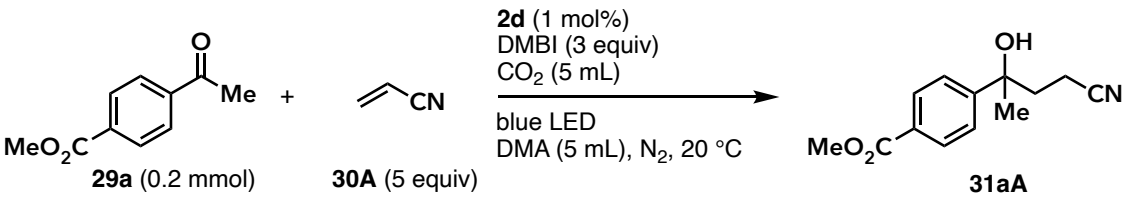
General Methods

Irradiation of photoreactions was carried out using a blue LED lamp (PER-448, λ_{max} = 448 nm, Techno Sigma Co., Ltd.). ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-ECS400 spectrometer (^{1}H at 396 MHz and ^{13}C at 100 MHz) and JEOL JNM-ECZ400R/S1 spectrometer (^{1}H at 400 MHz and ^{13}C at 101 MHz). NMR data were obtained in $CDCl_3$ or DMSO-d_6. Proton chemical shifts were referenced to the internal tetramethylsilane at 0.00 ppm ($CDCl_3$) or the residual proton signals of the solvents at 2.50 ppm (DMSO). Carbon chemical shifts were referenced to the carbon signals of the solvents at 77.16 ppm ($CDCl_3$) and 39.52 ppm (DMSO-d_6). All NMR spectra were processed using Delta NMR software (JEOL). IR measurements were performed on JASCO FT/IR-460plus spectrometer in the ATR mode. High-resolution ESI mass spectra were recorded on JEOL JMS-T100LC AccuTOF™ LC-TOFMS. Flash column chromatography was performed with Hi-Flash™ Column Silica gel 40 μm 60 Å (Yamazen) or Hi-Flash™ Premium Column Silica gel 30 μm 60 Å (Yamazen). Preparative layer chromatography (PLC) was performed on silica gel plates with silica gel 60 F_{254} (Merck). Gel permeation chromatography (GPC) was carried out with a Japan Analytical Industry LC-9201.

Materials

Anhydrous DMA and DCM were purchased from KANTO. Anhydrous DMSO was purchased from FUJIFILM Wako Pure Chemical Corporation. **2d**[13] and DMBI reductant[14] were prepared according to the literature procedures. All aldehydes were purified by bulb-to-bulb distillation before use. Other chemicals were obtained from commercial suppliers and used without further purification.

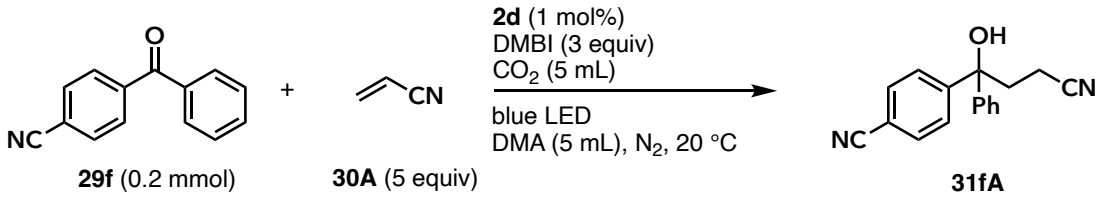
General procedure 1 (GP1)



2d (1.88 mg, 0.0021 mmol, 1 mol%) and DMBI (134.2 mg, 0.60 mmol, 3 equiv) were placed in a 20 mL Schlenk tube equipped with a stir bar. The Schlenk tube was filled with nitrogen by vacuum-refill cycles (three times). DMA (4 mL) was added and CO_2 (5 mL) was bubbled into the solution over 30 seconds using a syringe pump. A nitrogen balloon was attached to the Schlenk tube, and acrylonitrile (**30A**) (52.7 mg, 1.0 mmol, 5 equiv) was added. A DMA solution (1 mL) of methyl 4-acetylbenzoate (**29a**) (35.9 mg, 0.20 mmol) was added dropwise over 80 minutes using a syringe pump to the reaction mixture under blue light irradiation (448 nm) at 20 °C. The reaction mixture was stirred for further 70 minutes. 2 M HCl aq. was added and the resulting mixture was extracted with AcOEt (three times). The combined organic phase was washed with water (twice) and brine, and then dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the crude residue was purified by flash column chromatography with silica gel (gradient from 20 to 35% AcOEt/Hex) to give **31aA** (35.6 mg, 0.15 mmol, 76%).

Note: Assuming carbon dioxide is an ideal gas, 5 mL CO_2 is 0.2 mmol at 25 °C (P (pressure) = 1atm, R (gas constant) = 0.082 atm L/mol K). Therefore, the amount of CO_2 dissolved in DMA (5 mL) is up to 0.04 M.

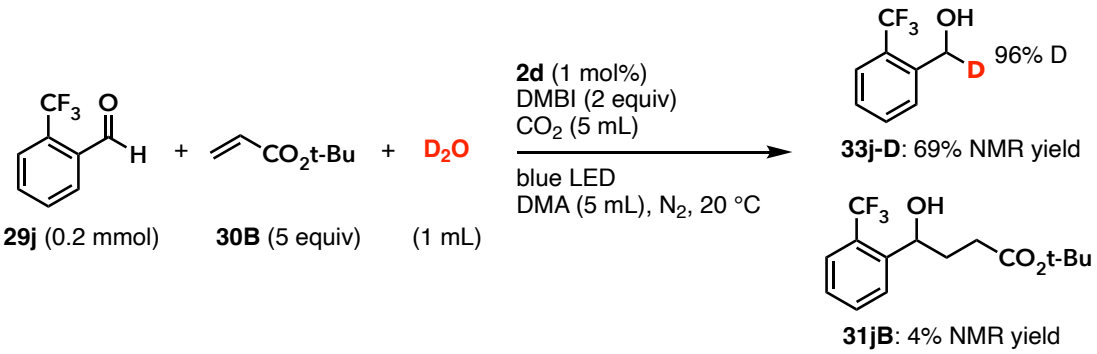
General procedure 2 (GP2)



4-Cyanobenzophenone (**29f**) (41.8 mg, 0.20 mmol), **2d** (1.85 mg, 0.0020 mmol, 1 mol%), and DMBI (134.9 mg, 0.60 mmol, 3 equiv) were placed in a 20 mL Schlenk tube equipped with a stir bar. The Schlenk tube was filled with nitrogen by vacuum-refill cycles (three times). DMA (4 mL) was added and CO_2 (5 mL) was bubbled into the solution over 30 seconds using a syringe pump. A nitrogen

balloon was attached to the Schlenk tube, and acrylonitrile (**30A**) (52.7 mg, 1.0 mmol, 5 equiv) was added. The reaction mixture was stirred for 150 minutes under blue light irradiation (448 nm) at 20 °C. 2 M HCl aq. was added and the resulting mixture was extracted with AcOEt (three times). The combined organic phase was washed with water (twice) and brine, and then dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the crude residue was purified by PLC (33% AcOEt/Hex, and then 40% AcOEt/Hex) and flash column chromatography with silica gel (50% MTBE/Hex) to give **31fA** (48.7 mg, 0.19 mmol, 92%).

Deuteration experiment



2d (1.86 mg, 0.0020 mmol, 1 mol%) and DMBI (89.2 mg, 0.40 mmol, 2 equiv) were placed in a 20 mL Schlenk tube equipped with a stir bar. The Schlenk tube was filled with nitrogen by vacuum-refill cycles (three times). DMA (4 mL) was added and CO_2 (5 mL) was bubbled into the solution over 30 seconds using a syringe pump. A nitrogen balloon was attached to the Schlenk tube, and then *tert*-butyl acylate (**30B**) (128.6 mg, 1.0 mmol, 5 equiv) and D_2O (1 mL) were added to the solution. A DMA solution (1 mL) of 2-(trifluoromethyl)benzaldehyde (**29j**) (34.5 mg, 0.20 mmol) was added dropwise over 80 minutes using a syringe pump to the reaction mixture under blue light irradiation (448 nm) at 20 °C. The reaction mixture was stirred for further 70 minutes. 2 M HCl aq. was added and the resulting mixture was extracted with AcOEt (three times). The combined organic phase was washed with water (twice) and brine, and then dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the yields of alcohol **33j-D** and γ-hydroxy ester **31jB** were calculated by ^1H NMR analysis using anisole as an internal standard (**33j-D**: 69% yield, **31jB**: 4% yield, Figure 1). The crude residue was purified by PLC (25% AcOEt/Hex) to give *C*-deuterated alcohol **33j-D** (96% D, Figure 2).[15]

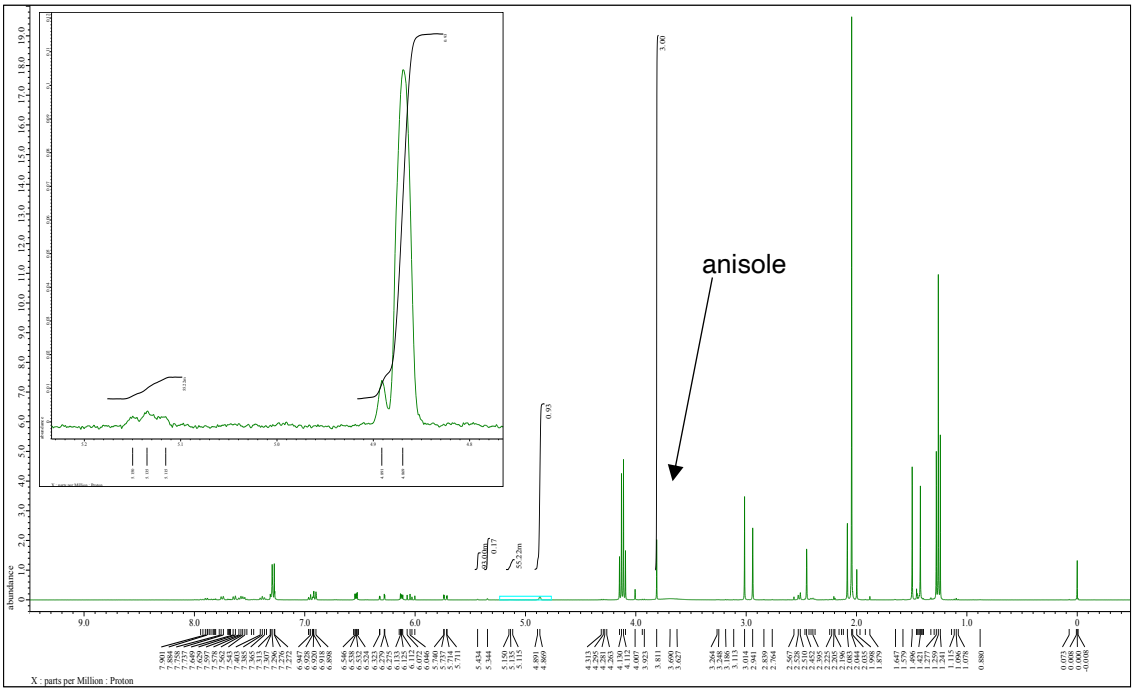


Figure 1. Crude ^{1}H NMR spectra (396 MHz, $CDCl_3$).

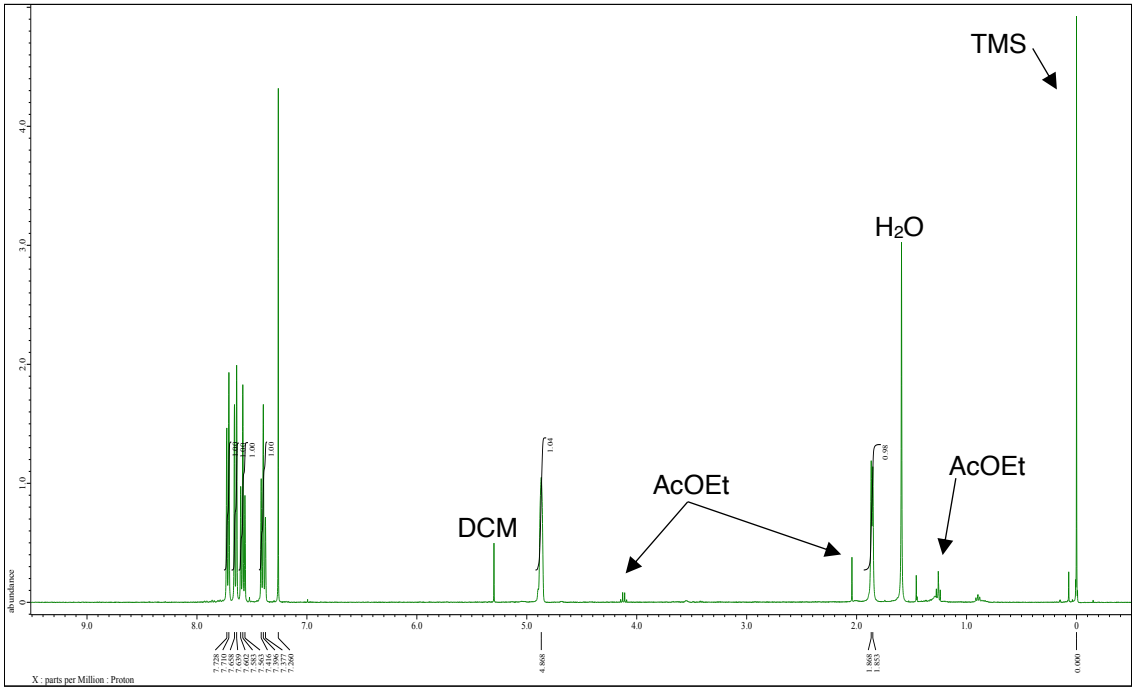
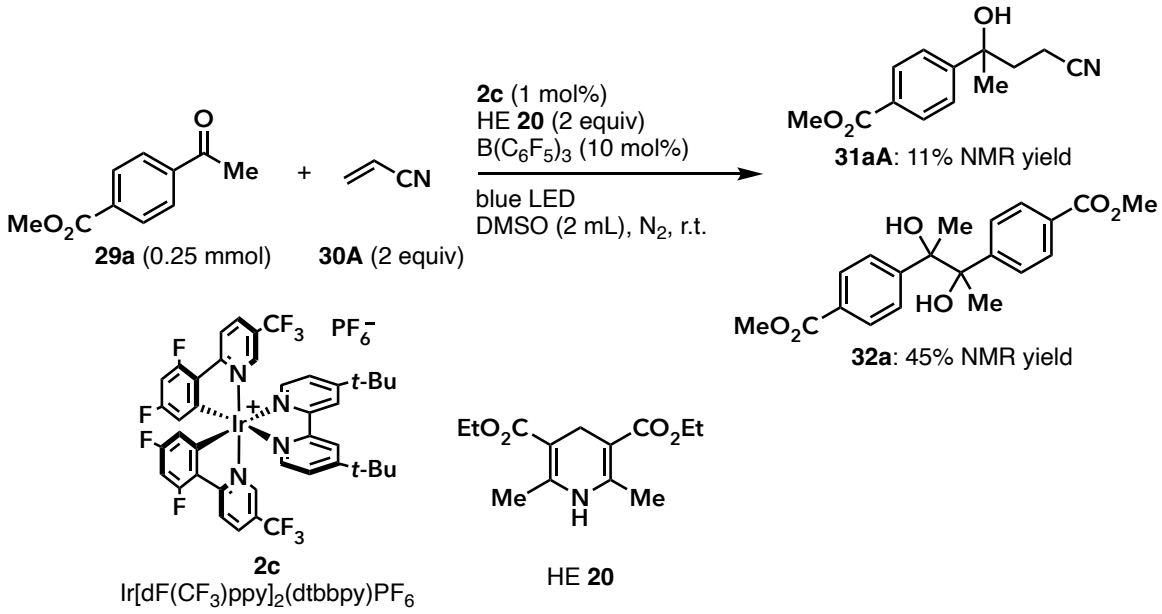


Figure 2. ^{1}H NMR Spectra of **33j-D** (396 MHz, $CDCl_3$).

Photocatalytic ketyl Giese reaction of ketone **29a** with olefin **30A**

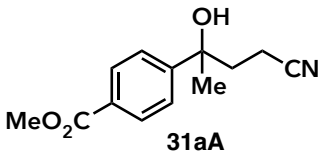
The reaction of ketone **29a** with olefin **30A** was carried out under the photocatalytic ketyl Giese conditions reported by the groups of He and Guan.[7]



Methyl 4-acetylbenzoate (**29a**) (44.6 mg, 0.20 mmol), **2c** (2.80 mg, 0.0025 mmol, 1 mol%), Hantzsch ester (HE **20**) (127.1 mg, 0.50 mmol, 2 equiv), and $B(C_6F_5)_3$ (13.2 mg, 0.026 mmol, 10 mol%) were placed in a 4 mL vial equipped with a stir bar. The vial was sealed with a rubber septum and filled with nitrogen by vacuum-refill cycles (three times). A nitrogen balloon was attached to the vial, and then DMSO (2 mL) and acrylonitrile (**30A**) (26.0 mg, 0.49 mmol, 2 equiv) were added to the solution. The reaction mixture was stirred for 36 hours under blue light irradiation (100% light intensity from 40 W Kessil A160WE Tuna Blue; λ_{max} = 462 nm.[16] The vial was placed 2 cm away from the LED light with a fan to keep the reaction temperature at room temperature). Water was added and the resulting mixture was extracted with AcOEt (three times). The combined organic phase was dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the yields of γ-hydroxybutyronitrile **31aA** and homo-dimer **32a** were calculated by ^1H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard (**31aA**: 11% yield, **32a**: 45% yield).

Spectroscopic data of products

Methyl 4-(4-cyano-2-hydroxybutan-2-yl)benzoate



31aA

Prepared according to GP 1. The resulting crude mixture was purified by flash column chromatography with silica gel (gradient from 20 to 35% AcOEt/Hex) to give **31aA** (35.6 mg, 76%, white solid).

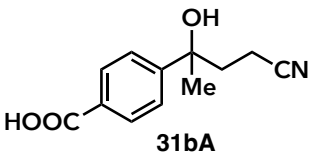
^{1}H NMR (396 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.6 Hz, 2H), 7.49 (d, *J* = 8.6 Hz, 2H), 3.92 (s, 3H), 2.46–2.38 (m, 1H), 2.18 (t, *J* = 7.7 Hz, 2H), 2.10–2.02 (m, 1H), 1.99 (s, 1H), 1.64 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.9, 150.7, 130.0, 129.3, 124.9, 120.0, 73.7, 52.3, 39.5, 30.7, 12.2.

HRMS (ESI$^+$): Calcd for $C_{13}H_{15}NNaO_3^+$ ([M+Na]$^+$) 256.0944, Found *m/z* 256.0951.

IR (ATR): 3454 (m), 2257 (m), 1719 (s), 1279 (s) cm^{-1}.

4-(4-Cyano-2-hydroxybutan-2-yl)benzoic acid



31bA

Prepared according to GP 1. The resulting crude mixture was purified by flash column chromatography with silica gel (1/1/98 = MeOH/AcOH/$CHCl_3$) to give **31bA** (18.6 mg, 43%, white solid).

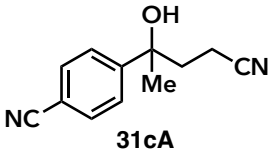
^{1}H NMR (396 MHz, DMSO-*d_6*): δ = 7.89 (d, *J* = 8.6 Hz, 2H), 7.55 (d, *J* = 8.6 Hz, 2H), 5.37 (br, 1H), 2.44–2.32 (m, 1H), 2.22–1.98 (m, 3H), 1.45 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d_6*): δ = 167.4, 152.4, 129.3, 129.1, 125.2, 120.8, 72.2, 38.6, 29.7, 11.4.

HRMS (ESI$^-$): Calcd for $C_{12}H_{12}NO_3^-$ ([M–H]$^-$) 218.0823, Found *m/z* 218.0816.

IR (ATR): 3600–3200 (br), 2259 (w), 1684 (s) cm^{-1}.

4-(4-Cyano-2-hydroxybutan-2-yl)benzonitrile



31cA

Prepared according to GP 1. The resulting crude mixture was purified by PLC (10% MTBE/DCM) and flash column chromatography with silica gel (5% MTBE/DCM) to give **31cA** (33.7 mg, 84%, gray solid).

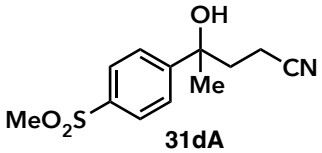
^{1}H NMR (396 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.6 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 2.47–2.39 (m, 1H), 2.17 (t, *J* = 7.3 Hz, 2H), 2.12–2.04 (m, 1H), 1.87 (s, 1H), 1.65 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.1, 132.5, 125.8, 119.8, 118.7, 111.3, 73.5, 39.4, 30.6, 12.1.

HRMS (ESI$^+$): Calcd for $C_{12}H_{12}N_2NaO^+$ ([M+Na]$^+$) 223.0842, Found *m*/*z* 223.0847.

IR (ATR): 3442 (s), 2253 (m), 2226 (s) cm^{-1}.

4-Hydroxy-4-[4-(methylsulfonyl)phenyl]pentanenitrile



31dA

Prepared according to GP 1. The resulting crude mixture was purified by flash column chromatography with silica gel (50% AcOEt/Hex) to give **31dA** (31.0 mg, 61%, gray solid).

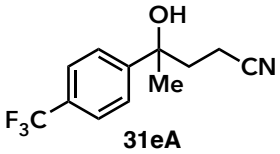
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 8.7 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 2H), 3.07 (s, 3H), 2.48–2.40 (m, 1H), 2.19 (t, *J* = 7.3 Hz, 2H), 2.14–2.07 (m, 1H), 1.86 (s, 1H), 1.67 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 151.9, 139.8, 127.9, 126.0, 119.7, 73.7, 44.7, 39.6, 30.8, 12.2.

HRMS (ESI$^+$): Calcd for $C_{12}H_{15}NNaO_3S^+$ ([M+Na]$^+$) 276.0665, Found *m*/*z* 276.0673.

IR (ATR): 3429 (m), 2257 (m), 1308 (s), 1151 (s) cm^{-1}.

4-Hydroxy-4-[4-(trifluoromethyl)phenyl]pentanenitrile



31eA

Prepared according to GP 1. The resulting crude mixture was purified by flash column chromatography with silica gel (33% AcOEt/Hex, and then 40% MTBE/Hex) to give **31eA** (32.4 mg, 67%, dark green solid).

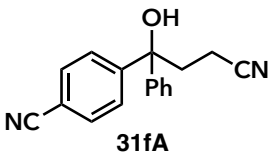
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.7 Hz, 2H), 7.54 (d, *J* = 8.2 Hz, 2H), 2.47–2.39 (m, 1H), 2.18 (t, *J* = 7.8 Hz, 2H), 2.12–2.04 (m, 1H), 1.79 (s, 1H), 1.65 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 149.7, 129.8 (q, *J* = 32.8 Hz), 125.7 (q, *J* = 3.9 Hz), 125.3, 124.2 (q, *J* = 271.7 Hz), 120.0, 73.6, 39.6, 30.8, 12.2.

HRMS (ESI$^+$): Calcd for $C_{12}H_{12}F_3NNaO^+$ ([M+Na]$^+$) 266.0763, Found *m*/*z* 266.0762.

IR (ATR): 3457 (m), 2256 (m), 1320 (s) cm^{-1}.

4-(3-Cyano-1-hydroxy-1-phenylpropyl)benzonitrile



31fA

Prepared according to GP 2. The resulting crude mixture was purified by PLC (33% AcOEt/Hex, and then 40% AcOEt/Hex) and flash column chromatography with silica gel (50% MTBE/Hex) to give **31fA** (48.7 mg, 92%, dark green gum).

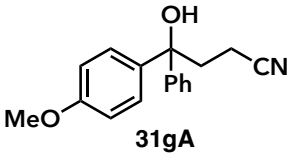
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.7 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.40–7.30 (m, 5H), 2.71–2.66 (m, 2H), 2.44–2.35 (m, 1H), 2.27–2.19 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 150.3, 144.2, 132.5, 129.1, 128.4, 126.8, 125.8, 119.8, 118.6, 111.6, 77.4, 37.5, 12.2.

HRMS (ESI$^+$): Calcd for $C_{17}H_{14}N_2NaO^+$ ([M+Na]$^+$) 285.0998, Found *m*/*z* 285.0998.

IR (ATR): 3600–3100 (br), 2228 (m) cm^{-1}.

4-Hydroxy-4-(4-methoxyphenyl)-4-phenylbutanenitrile



31gA

Prepared according to GP 2 using 2 equivalents of DMBI. The resulting crude mixture was purified by PLC (33% AcOEt/Hex) to give **31gA** (42.8 mg, 80%, dark green oil).

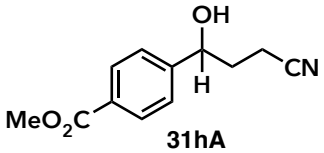
^{1}H NMR (396 MHz, $CDCl_3$): δ = 7.36–7.24 (m, 7H), 6.85 (d, *J* = 9.1 Hz, 2H), 3.78 (s, 3H), 2.61 (t, *J* = 8.6 Hz, 2H), 2.36–2.21 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.1, 145.3, 137.6, 128.7, 127.7, 127.3, 126.0, 120.4, 114.0, 77.1, 55.4, 38.0, 12.4.

HRMS (ESI$^+$): Calcd for $C_{17}H_{17}NNaO_2^+$ ([M+Na]$^+$) 290.1151, Found *m*/*z* 290.1157.

IR (ATR): 3600–3100 (br), 2249 (m), 1248 (s) cm^{-1}.

Methyl 4-(3-cyano-1-hydroxypropyl)benzoate



31hA

Prepared according to GP 1 using 2 equivalents of DMBI. The resulting crude mixture was purified by flash column chromatography with silica gel (gradient from 25 to 45% AcOEt/Hex) to give **31hA** (26.5 mg, 60%, dark green oil).

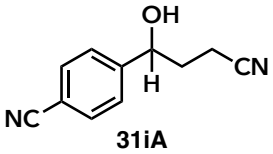
^{1}H NMR (396 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 4.94–4.90 (m, 1H), 3.92 (s, 3H), 2.60 (dt, *J* = 16.8, 7.7 Hz, 1H), 2.43 (dt, *J* = 17.2, 6.3 Hz, 1H), 2.26 (d, *J*= 3.2 Hz, 1H), 2.05 (ddd, *J* = 7.3, 7.3, 7.3 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.9, 148.2, 130.2, 130.1, 125.7, 119.5, 72.0, 52.4, 34.3, 13.9.

HRMS (ESI$^+$): Calcd for $C_{12}H_{13}NNaO_3^+$ ([M+Na]$^+$) 242.0788, Found *m*/*z* 242.0782.

IR (ATR): 3600–3100 (br), 2247 (m), 1717 (s), 1278 (s) cm^{-1}.

4-(3-Cyano-1-hydroxypropyl)benzonitrile



31iA

Prepared according to GP 1. The resulting crude mixture was purified by PLC (50% AcOEt/Hex and then 5% MeOH/$CHCl_3$) and GPC to give **31iA** (14.1 mg, 38%, pale yellow oil).

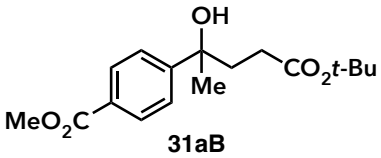
^{1}H NMR (396 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 8.6 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H), 4.95–4.91 (m, 1H), 2.63 (dt, *J* = 17.2, 7.7 Hz, 1H), 2.53 (d, *J* = 3.2 Hz, 1H), 2.45 (dt, *J* = 16.8, 6.3 Hz, 1H), 2.04–1.99 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.6, 132.7, 126.5, 119.4, 118.7, 112.0, 71.5, 34.3, 13.8.

HRMS (ESI$^+$): Calcd for $C_{11}H_{10}N_2NaO^+$ ([M+Na]$^+$) 209.0685, Found *m*/*z* 209.0690.

IR (ATR): 3700–3100 (br), 2228 (s) cm^{-1}.

Methyl 4-[5-(*tert*-butoxy)-2-hydroxy-5-oxopentan-2-yl]benzoate



31aB

Prepared according to GP 1. The resulting crude mixture was purified by flash column chromatography with silica gel (gradient from 15 to 28% AcOEt/Hex) to give **31aB** (31.6 mg, 51%, white solid).

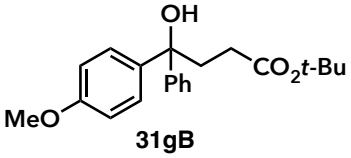
^{1}H NMR (396 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.6 Hz, 2H), 7.50 (d, *J* = 8.6 Hz, 2H), 3.91 (s, 3H), 2.96 (s, 1H), 2.25–2.07 (m, 4H), 1.57 (s, 3H), 1.41 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.2, 167.2, 152.7, 129.7, 128.6, 125.1, 81.0, 74.2, 52.2, 38.4, 31.0, 30.7, 28.2.

HRMS (ESI$^+$): Calcd for $C_{17}H_{24}NaO_5^+$ ([M+Na]$^+$) 331.1516, Found *m*/*z* 331.1526.

IR (ATR): 3600–3300 (br), 1720 (s), 1697 (s), 1275 (s) cm^{-1}.

tert-Butyl 4-hydroxy-4-(4-methoxyphenyl)-4-phenylbutanoate



31gB

Prepared according to GP 2 using 2 equivalents of DMBI. The resulting crude mixture was purified by flash column chromatography with silica gel (gradient from 10 to 20% AcOEt/Hex) to give **31gB** (38.1 mg, 56%, pale yellow oil).

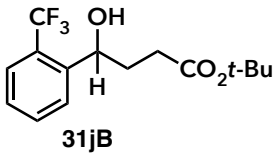
^{1}H NMR (396 MHz, $CDCl_3$): δ = 7.42–7.38 (m, 2H), 7.35–7.27 (m, 4H), 7.23–7.15 (m, 1H), 6.83 (d, *J* = 9.1 Hz, 2H), 3.78 (s, 3H), 2.77 (s, 1H), 2.57 (t, *J* = 6.8 Hz, 2H), 2.32–2.18 (m, 2H), 1.42 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.3, 158.5, 147.0, 139.2, 128.3, 127.4, 126.9, 126.1, 113.6, 80.7, 77.4, 55.4, 36.7, 30.6, 28.2.

HRMS (ESI$^+$): Calcd for $C_{21}H_{26}NaO_4^+$ ([M+Na]$^+$) 365.1723, Found *m*/*z* 365.1723.

IR (ATR): 3700–3200 (br), 1722 (m), 1248 (s) cm^{-1}.

tert-Butyl 4-hydroxy-4-[2-(trifluoromethyl)phenyl]butanoate



31jB

Prepared according to GP 1 using 2 equivalents of DMBI. The resulting crude mixture was purified by flash column chromatography with silica gel (step gradient, from 10 to 15% AcOEt/Hex) and PLC (25% AcOEt/Hex) to give **31jB** (31.5 mg, 51%, brown oil).

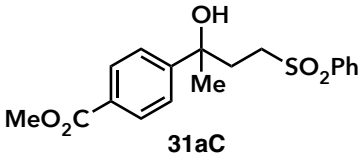
^{1}H NMR (396 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 7.7 Hz, 1H), 7.62–7.57 (m, 2H), 7.37 (dd, *J* = 7.7, 7.7 Hz, 1H), 5.14 (t, *J* = 5.4 Hz, 1H), 2.91 (br, 1H), 2.52–2.37 (m, 2H), 2.03–1.97 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.6, 143.7, 132.4, 127.8, 127.6, 126.8 (q, *J* = 29.9 Hz), 125.6 (q, *J* = 5.8 Hz), 124.5 (q, *J* = 274.5 Hz), 81.0, 69.2, 34.3, 32.8, 28.2.

HRMS (ESI$^+$): Calcd for $C_{15}H_{19}F_3NaO_3^+$ ([M+Na]$^+$) 327.1179, Found *m*/*z* 327.1180.

IR (ATR): 3600–3100 (br), 1726 (m), 1311 (s) cm^{-1}.

Methyl 4-[2-hydroxy-4-(phenylsulfonyl)butan-2-yl]benzoate



31aC

Prepared according to GP 1. The resulting crude mixture was purified by flash column chromatography with silica gel (40% AcOEt/Hex) to give **31aC** (33.3 mg, 48%, white solid).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 8.2 Hz, 2H), 7.83 (d, *J* = 7.3 Hz, 2H), 7.65 (t, *J* = 7.3 Hz, 1H), 7.54 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.41 (d, *J* = 8.2 Hz, 2H), 3.92 (s, 3H), 3.23–3.16 (m, 1H), 2.84–2.77 (m, 1H), 2.25 (t, *J* = 8.7 Hz, 2H), 1.97 (s, 1H), 1.60 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.9, 150.8, 139.1, 133.9, 130.0, 129.5, 129.2, 128.1, 124.8, 73.6, 52.3, 52.0, 36.3, 31.3.

HRMS (ESI^+): Calcd for $C_{18}H_{20}NaO_5S^+$ ($[M+Na]^+$) 371.0924, Found m/z 371.0929.

IR (ATR): 3465 (m), 1715 (s), 1265 (s), 1145 (s) cm^{-1}.

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General Conclusion

The research reported in this thesis has focused on the development of electrophilic addition reactions to carbonyl compounds through the photocatalytic carbinol cation/anion umpolung.

In Chapter 1, the author has developed the cross-pinacol coupling of two different carbonyl compounds through successive one-electron transfer processes under photocatalytic conditions. In the reaction, an umpoled anionic carbinol synthon was generated in situ to react nucleophilically with a second electrophilic carbonyl compound. It was revealed that a CO_2 additive promoted the photocatalytic generation of the carbinol synthon to suppress undesired radical dimerization. A wide variety of aromatic and aliphatic carbonyl substrates underwent the cross-pinacol coupling to afford the corresponding unsymmetric vicinal 1,2-diols, in which even a combination of carbonyl reactants with similar structures such as two aldehydes and two ketones were also well tolerated with high cross-coupling selectivity.

In Chapter 2, the author has developed a 1,4-addition reaction of aromatic aldehydes or ketones to electron-deficient olefins under photocatalytic conditions. In the reaction, an umpoled carbinol anion generated in situ through two successive one-electron reductions of the carbonyl compound reacted nucleophilically with the electron-deficient olefin. Various electron-deficient aromatic aldehydes and ketones successfully underwent the reaction to afford the corresponding γ-functionalized alcohols.

Collectively, these results showed the high utility of the photocatalytic carbinol cation/anion umpolung strategy to achieve unconventional electrophilic addition reactions to carbonyl compounds. A CO_2 additive plays a key role in the second one-electron reduction step to promote the reduction of carbinol radicals and suppress the formation of homo-coupled dimers. The author believes that these works in this thesis may pave the way to novel electrophilic addition reactions to carbonyl compounds.

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