Supplementary File

Base-Promoted Chemodivergent Formation of 1,4-Benzoxazepin-5(4*H*)-ones and 1,3-Benzoxazin-4(4*H*)-ones Switched by Solvents

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1. Synthesis of known compound 1 (a modified literature method: [1])

A typical procedure for the synthesis of **1a**:



A mixture of propylamine (0.885 g, 15.0 mmol), K_2CO_3 (2.070 g, 15.0 mmol) and CH₃CN (25 mL) in a 100-mL round-bottomed flask was stirred at 70 °C for a few minutes, and then 2-fluorobenzoyl chloride (1.585 g, 10.0 mmol) was added dropwise to the mixture (*ca.* 0.5 h). The obtained reaction mixture was heated for additional 4 h and then cooled to room temperature, water (50 mL) was added and the mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic phases were dried over MgSO₄. The filtered solution was concentrated under reduced pressure, and the crude residue was purified by column chromatography on silica gel with the use of petroleum ether/ethyl acetate (gradient mixture ratio from 20:1 to 4:1 in volume) to afford **1a** as a pale yellow oil in 90% yield (1.635 g).

1b ~ 1m were prepared in 2.0 mmol-scale of benzoyl chlorides.

	Ľ		U	1	
Compound	Weight (g)	Yield (%)	Compound	Weight (g)	Yield (%)
1a ^b	1.635	90	1g	0.383	88
1b	0.279	91	1h	0.358	92
1c	0.325	90	1i	0.393	93
1d	0.333	85	1j	0.348	81
1e	0.330	85	11	0.351	78
lf	0.353	87	1m	0.390	78

Table S1. Yields in both weight and percentage for known compound 1^{a} .

^{*a*} Unless otherwise noted, the reactions were carried out by using 2.0 mmol of benzoyl chlorides and 3.0 mmol of amines.

^b 2-Fluorobenzoyl chloride and *n*-propylamine were used in 10.0 mmol and 15.0 mmol, respectively. Twice reactions were performed, and the yields are almost same.

Structures of Compound 1



2. Copies of ¹H NMR spectra of the prepared 1



¹H NMR spectrum of **1a**

2-*Fluoro-N-propylbenzamide* (**1a**): ¹H NMR (400 MHz, CDCl₃): δ 8.00 (apparent td, J = 7.8, 1.8 Hz, 1H), 7.35-7.42 (m, 1H), 7.18 (apparent td, J = 7.8, 0.8 Hz, 1H), 7.06-7.01 (m, 1H), 6.79 (s_{br}, 1H), 3.38 (tq, J = 7.4, 1.6 Hz, 2H), 1.59 (apparent hex, J = 7.4 Hz, 2H), 0.93 (t, J = 7.4 Hz, 3H).

¹H NMR spectrum of **1b**



2-*Fluoro-N-methylbenzamide* (**1b**): ¹H NMR (400 MHz, CDCl₃): δ 7.97 (apparent td, *J* = 7.8, 1.8 Hz, 1H), 7.37-7.44 (m, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.08-7.03 (m, 2H), 7.06 (s, 1H), 2.99 (d, *J* = 4.8 Hz, 3H).

¹H NMR spectrum of **1c**



2-*Fluoro-N-isopropylbenzamide* (**1c**): ¹H NMR (400 MHz, CDCl₃): δ 8.06 (apparent td, J = 8.0, 1.8 Hz, 1H), 7.41-7.46 (m, 1H), 7.24 (t, J = 8.0 Hz, 1H), 7.11-7.06 (m, 1H), 6.59 (s_{br}, 1H), 4.26-4.35 (m, 1H), 1.27 (d, J = 7.0 Hz, 6H).

¹H NMR spectrum of **1d**



2-*Fluoro-N-t-butylbenzamide* (**1d**): ¹H NMR (400 MHz, CDCl₃): δ 7.98 (apparent td, J = 8.0, 1.8 Hz, 1H), 7.34-7.41 (m, 1H), 7.18 (apparent td, J = 8.0, 0.8 Hz, 1H), 7.05-7.00 (m, 1H), 6.65 (d, J = 12.4 Hz, 1H), 1.46 (s, 9H).

¹H NMR spectrum of **1e**



2-*Fluoro-N-t-amylbenzamide* (**1e**): ¹H NMR (400 MHz, CDCl₃): δ 8.02 (apparent td, J = 8.0, 1.8 Hz, 1H), 7.38-7.45 (m, 1H), 7.22 (t, J = 8.0 Hz, 1H), 7.10-7.05 (m, 1H), 6.51 (d, J = 12.8 Hz, 1H), 1.83(q, J = 7.8 Hz, 2H), 1.42 (s, 6H), 0.92 (t, J = 7.8 Hz, 3H).

¹H NMR spectrum of **1f**



2-*Fluoro-N-cyclopentylbenzamide* (**1f**): ¹H NMR (400 MHz, CDCl₃): δ 8.09 (apparent td, *J* = 8.0, 1.8 Hz, 1H), 7.41-7.48 (m, 1H), 7.25 (apparent td, *J* = 8.0, 0.8 Hz, 1H), 7.12-7.07 (m, 1H), 6.69 (s_{br}, 1H), 4.38-4.48 (m, 1H), 2.04-2.14 (m, 2H), 1.60-1.80 (m, 4H), 1.48-1.56 (m, 2H).

¹H NMR spectrum of **1g**



2-*Fluoro-N-cyclohexylbenzamide* (**1g**): ¹H NMR (400 MHz, CDCl₃): δ 8.09 (apparent td, J = 8.0, 1.8 Hz, 1H), 7.41-7.48 (m, 1H), 7.25 (apparent td, J = 8.0, 0.8 Hz, 1H), 7.12-7.07 (m, 1H), 6.62 (s_{br}, 1H), 3.98-4.07 (m, 1H), 1.99-2.06 (m, 2H), 1.60-1.78 (m, 4H), 1.18-1.50 (m, 4H).

¹H NMR spectrum of **1h**



2-*Fluoro-N-propyl-3-methylbenzamide* (**1h**): ¹H NMR (400 MHz, CDCl₃): δ 8.00 (apparent t, J = 7.8 Hz, 1H), 7.17 (apparent t, J = 7.8 Hz, 1H), 6.99 (apparent t, J = 7.8 Hz, 1H), 6.80 (s_{br}, 1H), 3.33 (tq, J = 7.3, 1.2 Hz, 2H), 2.18 (d, J = 2.4 Hz, 3H), 1.55 (apparent hex, J = 7.3 Hz, 2H), 0.89 (t, J = 7.3 Hz, 3H).

¹H NMR spectrum of **1i**



2-*Fluoro-4-methoxyl-N-propylbenzamide* (**1i**): ¹H NMR (400 MHz, CDCl₃): δ 8.03 (apparent t, J = 9.6 Hz, 1H), 6.76 (dd, J = 9.6, 2.4 Hz, 1H), 6.71 (s_{br}, 1H), 6.59 (dd, J = 9.6, 2.4 Hz, 1H), 3.83 (s, 3H), 3.42 (tq, J = 7.6, 1.2 Hz, 2H), 1.64 (apparent hex, J = 7.6 Hz, 2H), 0.98 (t, J = 7.6 Hz, 3H).

¹H NMR spectrum of **1**j



2-*Fluoro-5-chloro-N-propylbenzamide* (**1j**): ¹H NMR (400 MHz, CDCl₃): δ 8.07 (dd, J = 6.8, 3.0 Hz, 1H), 7.41 (ddd, J = 8.8, 4,4, 3.0 Hz, 1H), 7.07 (dd, J = 10.4, 8.8 Hz, 1H), 6.71 (s_{br}, 1H), 3.44 (tq, J = 7.6, 1.2 Hz, 2H), 1.65 (apparent hex, J = 7.6 Hz, 2H), 0.99 (t, J = 7.6 Hz, 3H).

¹H NMR spectrum of **1**l



2-*Fluoro-5-nitro-N-propylbenzamide* (**11**): ¹H NMR (400 MHz, CDCl₃): δ 8.98 (dd, J = 6.8, 3.0 Hz, 1H), 8.35 (ddd, J = 8.8, 4,4, 3.0 Hz, 1H), 7.31 (dd, J = 10.4, 8.8 Hz, 1H), 6.71 (s_{br}, 1H), 3.48 (tq, J = 7.6, 1.2 Hz, 2H), 1.68 (apparent hex, J = 7.6 Hz, 2H), 1.01 (t, J = 7.6 Hz, 3H).

¹H NMR spectrum of **1m**



2-*Fluoro-5-trifluoromethyl-N-propylbenzamide* (**1m**): ¹H NMR (400 MHz, CDCl₃): δ 8.44 (dd, J = 6.8, 2.8 Hz, 1H), 7.7,-7.75 (m, 1H), 7.22-7.28 (m, 1H), 6.72 (s_{br}, 1H), 3.47 (tq, J = 7.6, 1.2 Hz, 2H), 1.67 (apparent hex, J = 7.6 Hz, 2H), 1.00 (t, J = 7.6 Hz, 3H).

3. Copies of NMR spectra of 2

¹H NMR spectrum of **2a**



¹³C NMR spectrum of **2a**



¹H NMR spectrum of **2b**



¹³C NMR spectrum of **2b**



¹H NMR spectrum of **2c**



¹³C NMR spectrum of **2c**



¹H NMR spectrum of **2d**



¹³C NMR spectrum of 2d



¹H NMR spectrum of **2e**



¹³C NMR spectrum of 2e



¹H NMR spectrum of 2f



^{13}C NMR spectrum of 2f



¹H NMR spectrum of **2g**



¹³C NMR spectrum of **2g**



¹H NMR spectrum of 2h



¹³C NMR spectrum of **2h**



¹H NMR spectrum of **2i**



¹³C NMR spectrum of 2i



¹H NMR spectrum of **2**j



¹³C NMR spectrum of **2j**



¹H NMR spectrum of **2k**



¹³C NMR spectrum of **2k**



4. Copies of NMR spectra of 3

¹H NMR spectrum of **3a**



¹³C NMR spectrum of **3a**



¹H NMR spectrum of **3b**



¹³C NMR spectrum of **3b**



¹H NMR spectrum of **3c**



¹³C NMR spectrum of **3c**



¹H NMR spectrum of **3d**



¹³C NMR spectrum of **3d**



¹H NMR spectrum of **3g**



¹³C NMR spectrum of **3g**



¹H NMR spectrum of **3h**



¹³C NMR spectrum of **3h**



¹H NMR spectrum of **3i**



¹³C NMR spectrum of **3i**



¹H NMR spectrum of **3**j



¹³C NMR spectrum of **3j**



¹H NMR spectrum of **3**l



¹³C NMR spectrum of **3**l



¹H NMR spectrum of **3m**



¹³C NMR spectrum of **3m**



5. X-ray structural details of 2g and 3g

Crystal Structure of C₁₆H₁₉NO₂

The low temperature $(173 \pm 2^{\circ}\text{K})$ single-crystal X-ray experiments were performed on a SuperNova diffractometer with Cu K_a radiation. Unit cell was obtained and refined by 4943 reflections with $5.3^{\circ} < \theta < 71.2^{\circ}$. No decay was observed in data collection. Raw intensities were corrected for Lorentz and polarization effects, and for absorption by empirical method. Direct phase determination yielded the positions of all non-hydrogen atoms. All non-hydrogen atoms were subjected to anisotropic refinement. All hydrogen atoms were generated geometrically with C-H bonds of 0.93–0.98 Å according to criteria described in the SHELXTL manual (SHELXTL. Structure Determination Programs, Version 5.10, Bruker AXS Inc., Madison, WI, USA, 1997). They were included in the refinement with $U_{iso}(H) = 1.2U_{eq}$ or $1.5U_{eq}$ (for methyl C) of their parent atoms. The final full-matric least-square refinement on F^2 converged with R1 = 0.0783 and wR2 = 0.1804 for 4525 observed reflections [I $\geq 2\sigma(I)$]. The final difference electron density map shows no features. Details of crystal parameters, data collection and structure refinement are given in Table S2-1.

Data collection was controlled by CrysAlisPro, Agilent Technologies, Version 1.171.36.32 (Oxford Diffraction Ltd., Abingdon, Oxfordshire, OX, UK, 2013). Computations were performed using the SHELXTL NT ver. 5.10 program package (Bruker AXS Inc., Madison, WI, USA) on an IBM PC 586 computer. Analytic expressions of atomic scattering factors were employed, and anomalous dispersion corrections were incorporated [2,3]. Crystal drawings were produced with XP (SHELXTL. Structure Determination Programs, Version 5.10, Bruker AXS Inc., Madison, WI, USA).

Table S2-1. Details of Data Collection, Processing and Structure Refinement.

Sample code	2g			
Molecular formula	$C_{16}H_{19}N_{16}$	NO_2		
Molecular weight	257.32			
Color and habit	colorles	ss block		
Crystal size	0.20×0	$0.22 \times 0.30 \text{ m}$	ım	
Crystal system	monocl	inic		
Space group	Pn (No.	. 7)		
Unit cell parameters	a = 6.5092(2)	2) Å $\alpha = 9$	90.00°	
	b = 6.5112(2)	2) Å $\beta = 9$	92.429(3)°	
	c = 32.8651(9)	(Θ) Å $\gamma =$	90.00°	
	V = 1391.60	$5(7) Å^3 Z = 4$	F(000)	= 552
Density (calcd)	1.228 g	/cm ³		
Diffractometer SuperNova, Dual, Cu at home/near, AtlasS2				AtlasS2
Radiation Cu K_{α} , $\lambda = 1.54178$ Å				
Temperature	Temperature 173±2K			
Scan type	ω-scan			
Data collection range	-7 < h <	< 7, -7 < k < 5	5, $-38 < l < 40;$	$\theta_{max} = 71.3^{\circ}$
Reflections measured 7	Cotal: 9158 U	nique (<i>n</i>): 46	18 Observed [I 2	≥ 2σ(I)]: 4525
Absorption coefficient	0.641 m	nm ⁻¹		
Minimum and maximum tran	smission 0.837	7, 1.000		
No. of variables, <i>p</i>	34	45		
Weighting scheme v	$v = \frac{1}{\sigma^2(F_o^2) + (0)}$	$\frac{1}{.01P)^2 + 4.5P}$	$P = (F_0^2 + 2)$.F _c ²)/3
$R1 = \frac{\sum F_{o} - F_{c} }{\sum F_{o} } \text{ (for all reflect})$	tions)	0.0792	0.0783 (for ob	served data)
$wR2 = \sqrt{\frac{\Sigma[w(F_{o}^{2} - F_{c}^{2})^{2}]}{\Sigma w(F_{o}^{2})^{2}}} \text{ (for }$	all reflections)	0.1808	0.1804 (for ob	served data)
Goof = S = $\sqrt{\frac{\Sigma[w(F_o^2 - F_c^2)^2]}{n - p}}$	1.	129		
Largest and mean Δ/σ	0.	.000, 0.000		
Residual extrema in final diff	erence map -0.	368 to 0.465	<i>e</i> Å ⁻³	

Atoms	x	У	Z	Ueq.
O(1)	1.1150(7)	0.1624(8)	0.43578(16)	0.0316(12)
O(2)	0.7661(7)	0.1040(7)	0.33275(14)	0.0263(10)
N(1)	0.7816(8)	0.2226(8)	0.41622(17)	0.0223(11)
C(1)	0.9631(10)	0.1176(10)	0.41397(19)	0.0227(13)
C(2)	0.5970(10)	0.1751(10)	0.3935(2)	0.0239(14)
C(3)	0.5866(10)	0.1266(10)	0.3544(2)	0.0247(14)
C(4)	0.8799(11)	-0.0643(10)	0.3468(2)	0.0253(14)
C(5)	0.9045(12)	-0.2286(12)	0.3207(2)	0.0325(16)
C(6)	1.0272(14)	-0.3946(12)	0.3334(3)	0.0408(19)
C(7)	1.1219(13)	-0.3932(12)	0.3719(3)	0.0381(18)
C(8)	1.1002(12)	-0.2271(11)	0.3972(2)	0.0303(16)
C(9)	0.9729(10)	-0.0605(10)	0.3855(2)	0.0225(13)
C(10)	0.7728(11)	0.3854(10)	0.4478(2)	0.0243(14)
C(11)	0.7023(11)	0.2949(10)	0.4881(2)	0.0258(14)
C(12)	0.7140(13)	0.4597(11)	0.5211(2)	0.0325(16)
C(13)	0.5794(13)	0.6440(12)	0.5085(2)	0.0383(18)
C(14)	0.6406(13)	0.7286(11)	0.4674(2)	0.0348(17)
C(15)	0.6297(12)	0.5631(11)	0.4347(2)	0.0300(16)
C(16)	0.3920(13)	0.0875(14)	0.3299(2)	0.0385(19)
O(3)	1.1552(7)	0.5931(8)	0.12773(15)	0.0295(11)
O(4)	0.8499(7)	0.5264(7)	0.23087(14)	0.0252(10)
N(2)	0.8301(8)	0.6539(8)	0.14775(16)	0.0207(11)
C(17)	1.0142(10)	0.5483(10)	0.1495(2)	0.0230(14)
C(18)	0.6563(10)	0.6054(10)	0.1701(2)	0.0238(14)
C(19)	0.6625(10)	0.5531(10)	0.2092(2)	0.0230(13)
C(20)	0.9587(10)	0.3587(10)	0.2159(2)	0.0226(13)
C(21)	0.9862(11)	0.1917(11)	0.2413(2)	0.0290(15)
C(22)	1.1033(12)	0.0287(11)	0.2277(2)	0.0326(16)
C(23)	1.1874(12)	0.0330(11)	0.1896(2)	0.0318(16)
C(24)	1.1570(10)	0.2046(11)	0.1648(2)	0.0270(15)
C(25)	1.0335(10)	0.3683(10)	0.1777(2)	0.0221(13)
C(26)	0.8070(10)	0.8154(10)	0.1160(2)	0.0227(13)
C(27)	0.7220(11)	0.7248(10)	0.0756(2)	0.0253(14)
C(28)	0.7179(12)	0.8913(11)	0.0427(2)	0.0323(16)
C(29)	0.5897(14)	1.0748(13)	0.0551(2)	0.0393(19)
C(30)	0.6690(12)	1.1602(11)	0.0962(2)	0.0338(17)
C(31)	0.6715(12)	0.9930(10)	0.1290(2)	0.0280(15)
C(32)	0.4783(12)	0.5135(13)	0.2339(2)	0.0340(17)

Table S2-2. Atomic coordinates and equivalent isotropic temperature factors* (Å²).

 $*U_{eq.}$ defined as one third of the trace of the orthogonalized U tensor.

Molecule I		Molecule II	
O(1)-C(1)	1.232(8)	O(3)-C(17)	1.223(9)
O(2)-C(4)	1.390(8)	O(4)-C(19)	1.397(8)
O(2)-C(3)	1.401(8)	O(4)-C(20)	1.402(8)
N(1)-C(1)	1.370(9)	N(2)-C(17)	1.380(8)
N(1)-C(2)	1.421(8)	N(2)-C(18)	1.411(9)
N(1)-C(10)	1.485(8)	N(2)-C(26)	1.486(8)
C(1)-C(9)	1.493(9)	C(17)-C(25)	1.497(9)
C(2)-C(3)	1.325(10)	C(18)-C(19)	1.327(10)
C(3)-C(16)	1.494(10)	C(19)-C(32)	1.499(9)
C(4)-C(5)	1.383(10)	C(20)-C(25)	1.367(9)
C(4)-C(9)	1.385(9)	C(20)-C(21)	1.378(9)
C(5)-C(6)	1.397(12)	C(21)-C(22)	1.392(11)
C(6)-C(7)	1.383(12)	C(22)-C(23)	1.386(11)
C(7)-C(8)	1.375(11)	C(23)-C(24)	1.392(10)
C(8)-C(9)	1.408(10)	C(24)-C(25)	1.411(9)
C(10)-C(15)	1.535(9)	C(26)-C(31)	1.527(9)
C(10)-C(11)	1.537(10)	C(26)-C(27)	1.532(9)
C(11)-C(12)	1.526(9)	C(27)-C(28)	1.533(9)
C(12)-C(13)	1.532(11)	C(28)-C(29)	1.523(11)
C(13)-C(14)	1.526(11)	C(29)-C(30)	1.530(11)
C(14)-C(15)	1.522(10)	C(30)-C(31)	1.533(10)
C(4)-O(2)-C(3)	111.1(5)	C(19)-O(4)-C(20)	111.1(5)
C(1)-N(1)-C(2)	125.1(5)	C(17)-N(2)-C(18)	125.5(5)
C(1)-N(1)-C(10)	116.9(5)	C(17)-N(2)-C(26)	116.3(5)
C(2)-N(1)-C(10)	117.7(5)	C(18)-N(2)-C(26)	117.7(5)
O(1)-C(1)-N(1)	121.5(6)	O(3)-C(17)-N(2)	121.9(6)
O(1)-C(1)-C(9)	119.7(6)	O(3)-C(17)-C(25)	120.3(6)
N(1)-C(1)-C(9)	118.8(6)	N(2)-C(17)-C(25)	117.7(6)
C(3)-C(2)-N(1)	124.7(6)	C(19)-C(18)-N(2)	124.7(6)
C(2)-C(3)-O(2)	120.6(6)	C(18)-C(19)-O(4)	121.1(6)
C(2)-C(3)-C(16)	124.8(7)	C(18)-C(19)-C(32)	125.2(6)
O(2)-C(3)-C(16)	114.6(6)	O(4)-C(19)-C(32)	113.7(6)
C(5)-C(4)-C(9)	121.6(7)	C(25)-C(20)-C(21)	123.4(6)
C(5)-C(4)-O(2)	118.6(6)	C(25)-C(20)-O(4)	119.4(6)
C(9)-C(4)-O(2)	119.7(6)	C(21)-C(20)-O(4)	117.2(6)
C(4)-C(5)-C(6)	119.6(7)	C(20)-C(21)-C(22)	117.8(7)
C(7)-C(6)-C(5)	119.6(7)	C(23)-C(22)-C(21)	121.2(7)
C(8)-C(7)-C(6)	120.3(7)	C(22)-C(23)-C(24)	119.5(7)
C(7)-C(8)-C(9)	121.0(7)	C(23)-C(24)-C(25)	119.9(7)

Table S2-3. Bond lengths (Å) and bond angles (°).

(Table S2-3. continued)

C(4)-C(9)-C(8)	117.7(6)	C(20)-C(25)-C(24)	118.1(6)
C(4)-C(9)-C(1)	124.1(6)	C(20)-C(25)-C(17)	125.5(6)
C(8)-C(9)-C(1)	117.8(6)	C(24)-C(25)-C(17)	116.1(6)
N(1)-C(10)-C(15)	112.6(5)	N(2)-C(26)-C(31)	112.4(5)
N(1)-C(10)-C(11)	110.5(5)	N(2)-C(26)-C(27)	111.0(5)
C(15)-C(10)-C(11)	109.3(6)	C(31)-C(26)-C(27)	110.1(6)
C(12)-C(11)-C(10)	109.6(6)	C(26)-C(27)-C(28)	109.5(5)
C(11)-C(12)-C(13)	110.3(6)	C(29)-C(28)-C(27)	111.0(6)
C(14)-C(13)-C(12)	110.7(7)	C(28)-C(29)-C(30)	110.7(6)
C(15)-C(14)-C(13)	111.3(6)	C(29)-C(30)-C(31)	110.9(6)
C(14)-C(15)-C(10)	109.1(6)	C(26)-C(31)-C(30)	109.2(6)

Atoms	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O(1)	0.021(3)	0.038(3)	0.035(3)	-0.009(2)	-0.006(2)	0.005(2)
O(2)	0.025(2)	0.028(3)	0.026(2)	0.005(2)	0.0039(19)	0.000(2)
N(1)	0.020(3)	0.020(3)	0.026(3)	-0.005(2)	0.000(2)	0.001(2)
C(1)	0.025(3)	0.023(3)	0.021(3)	-0.003(3)	0.003(3)	-0.003(3)
C(2)	0.014(3)	0.023(3)	0.035(4)	-0.002(3)	0.000(3)	0.001(3)
C(3)	0.020(3)	0.024(3)	0.030(4)	0.002(3)	0.003(3)	-0.001(3)
C(4)	0.027(3)	0.021(3)	0.028(3)	0.004(3)	-0.003(3)	-0.006(3)
C(5)	0.035(4)	0.036(4)	0.027(4)	-0.007(3)	0.006(3)	-0.006(3)
C(6)	0.048(5)	0.029(4)	0.045(5)	-0.013(3)	-0.001(4)	0.004(4)
C(7)	0.040(5)	0.027(4)	0.047(5)	-0.002(3)	0.002(4)	0.011(3)
C(8)	0.033(4)	0.027(4)	0.031(4)	0.002(3)	-0.004(3)	0.005(3)
C(9)	0.019(3)	0.022(3)	0.027(3)	-0.002(3)	0.004(3)	-0.003(3)
C(10)	0.028(3)	0.019(3)	0.026(3)	-0.003(3)	0.000(3)	-0.001(3)
C(11)	0.029(4)	0.022(3)	0.026(3)	-0.001(3)	0.004(3)	0.001(3)
C(12)	0.042(4)	0.029(4)	0.026(4)	-0.003(3)	0.005(3)	0.006(3)
C(13)	0.043(5)	0.035(4)	0.038(4)	-0.011(3)	0.006(4)	0.006(4)
C(14)	0.043(5)	0.019(3)	0.043(4)	-0.003(3)	-0.001(4)	0.005(3)
C(15)	0.034(4)	0.024(4)	0.032(4)	-0.001(3)	-0.001(3)	0.008(3)
C(16)	0.036(4)	0.051(5)	0.028(4)	0.002(3)	-0.006(3)	-0.008(4)
O(3)	0.023(2)	0.034(3)	0.032(3)	0.006(2)	0.008(2)	0.002(2)
O(4)	0.027(2)	0.025(2)	0.023(2)	-0.0053(19)	0.0012(19)	0.000(2)
N(2)	0.020(3)	0.021(3)	0.022(3)	0.004(2)	0.003(2)	-0.002(2)
C(17)	0.021(3)	0.023(3)	0.025(3)	-0.002(3)	-0.003(3)	0.000(3)
C(18)	0.017(3)	0.020(3)	0.035(4)	-0.001(3)	0.002(3)	0.001(3)
C(19)	0.016(3)	0.023(3)	0.030(4)	-0.004(3)	0.003(3)	-0.005(3)
C(20)	0.020(3)	0.020(3)	0.028(3)	-0.003(3)	-0.002(3)	-0.002(3)
C(21)	0.033(4)	0.027(4)	0.027(3)	0.003(3)	0.002(3)	0.001(3)
C(22)	0.035(4)	0.025(4)	0.038(4)	0.005(3)	0.000(3)	0.004(3)
C(23)	0.033(4)	0.026(4)	0.036(4)	0.000(3)	-0.001(3)	0.008(3)
C(24)	0.023(3)	0.029(4)	0.029(4)	-0.001(3)	0.002(3)	0.006(3)
C(25)	0.023(3)	0.017(3)	0.026(3)	-0.003(2)	-0.002(3)	0.002(3)
C(26)	0.026(3)	0.018(3)	0.024(3)	0.003(3)	0.001(3)	-0.001(3)
C(27)	0.027(4)	0.017(3)	0.031(4)	-0.001(3)	-0.002(3)	0.000(3)
C(28)	0.038(4)	0.032(4)	0.027(4)	0.003(3)	-0.002(3)	-0.002(3)
C(29)	0.045(5)	0.034(4)	0.039(4)	0.004(3)	-0.006(4)	0.007(4)
C(30)	0.037(4)	0.025(4)	0.040(4)	0.004(3)	0.001(3)	0.002(3)
C(31)	0.036(4)	0.017(3)	0.031(4)	-0.003(3)	0.005(3)	0.002(3)
C(32)	0.032(4)	0.043(4)	0.028(4)	-0.001(3)	0.013(3)	-0.011(3)

Table S2-4. Anisotropic thermal parameters* (Å²).

The exponent takes the form: $-2\pi^2 \Sigma \Sigma U_{ij} h_i h_j \mathbf{a}_i^ \mathbf{a}_j^*$

Atoms	x	у	Z.	$U_{eq.}$
H(2)	0.4747	0.1783	0.4072	0.029
H(5)	0.8398	-0.2284	0.2950	0.039
H(6)	1.0451	-0.5054	0.3160	0.049
H(7)	1.2007	-0.5051	0.3807	0.046
H(8)	1.1706	-0.2247	0.4224	0.036
H(10)	0.9117	0.4408	0.4525	0.029
H(11A)	0.5621	0.2453	0.4845	0.031
H(11B)	0.7896	0.1799	0.4961	0.031
H(12A)	0.8554	0.5040	0.5255	0.039
H(12B)	0.6677	0.4030	0.5464	0.039
H(13A)	0.4363	0.6024	0.5067	0.046
H(13B)	0.5944	0.7507	0.5290	0.046
H(14A)	0.5494	0.8407	0.4594	0.042
H(14B)	0.7795	0.7824	0.4700	0.042
H(15A)	0.6715	0.6197	0.4090	0.036
H(15B)	0.4897	0.5135	0.4310	0.036
H(16A)	0.2764	0.1171	0.3461	0.058
H(16B)	0.3871	-0.0538	0.3216	0.058
H(16C)	0.3873	0.1742	0.3062	0.058
H(18)	0.5282	0.6104	0.1565	0.029
H(21)	0.9285	0.1881	0.2667	0.035
H(22)	1.1255	-0.0851	0.2444	0.039
H(23)	1.2636	-0.0779	0.1808	0.038
H(24)	1.2182	0.2113	0.1398	0.032
H(26)	0.9440	0.8709	0.1113	0.027
H(27A)	0.5841	0.6729	0.0790	0.030
H(27B)	0.8080	0.6114	0.0676	0.030
H(28A)	0.8572	0.9360	0.0381	0.039
H(28B)	0.6606	0.8348	0.0173	0.039
H(29A)	0.4473	1.0333	0.0569	0.047
H(29B)	0.5959	1.1812	0.0345	0.047
H(30A)	0.5814	1.2725	0.1042	0.041
H(30B)	0.8070	1.2137	0.0936	0.041
H(31A)	0.7249	1.0489	0.1547	0.034
H(31B)	0.5328	0.9442	0.1328	0.034
H(32A)	0.3570	0.5625	0.2193	0.051
H(32B)	0.4942	0.5839	0.2595	0.051
H(32C)	0.4657	0.3687	0.2386	0.051

Table S2-5. Coordinates and isotropic temperature factors* (Å²) for H atoms.

*The exponent takes the form: $-8\pi^2 U \sin^2\theta/\lambda^2$



 $Molecule \ I \\ ORTEP drawing of C_{16}H_{19}NO_2 \ with \ 50\% \ probability ellipsoids, showing the \\ atomic numbering scheme.$



 $\label{eq:molecule II} Molecule \ II \\ ORTEP drawing of C_{16}H_{19}NO_2 \ with \ 50\% \ probability ellipsoids, showing the atomic numbering scheme.$



С

A packing view along the b direction

Crystal Structure of C₁₆H₁₉NO₂

The low temperature $(173 \pm 2^{\circ}\text{K})$ single-crystal X-ray experiments were performed on a SuperNova diffractometer with Cu K_a radiation. Unit cell was obtained and refined by 4943 reflections with $5.3^{\circ} < \theta < 71.2^{\circ}$. No decay was observed in data collection. Raw intensities were corrected for Lorentz and polarization effects, and for absorption by empirical method. Direct phase determination yielded the positions of all non-hydrogen atoms. All non-hydrogen atoms were subjected to anisotropic refinement. All hydrogen atoms were generated geometrically with C-H bonds of 0.93–0.98 Å according to criteria described in the SHELXTL manual (SHELXTL. Structure Determination Programs, Version 5.10, Bruker AXS Inc., Madison, WI, USA, 1997). They were included in the refinement with U_{iso}(H) = 1.2U_{eq} of their parent atoms. The final full-matric least-square refinement on F^2 converged with R1 = 0.0395 and wR2 = 0.0815 for 2237 observed reflections [I $\ge 2\sigma$ (I)]. The final difference electron density map shows no features. Details of crystal parameters, data collection and structure refinement are given in Table S3-1.

Data collection was controlled by CrysAlisPro, Agilent Technologies, Version 1.171.36.32 (Oxford Diffraction Ltd., Abingdon, Oxfordshire, OX, UK, 2013). Computations were performed using the SHELXTL NT ver. 5.10 program package (Bruker AXS Inc., Madison, WI, USA) on an IBM PC 586 computer. Analytic expressions of atomic scattering factors were employed, and anomalous dispersion corrections were incorporated [2,3]. Crystal drawings were produced with XP (SHELXTL. Structure Determination Programs, Version 5.10, Bruker AXS Inc., Madison, WI, USA).

Table S3-1. Details of Data Collection, Processing and Structure Refinement.

Sample code 3g Molecular formula C₁₆H₁₉NO₂ 257.32 Molecular weight Color and habit colorless block Crystal size $0.20 \times 0.25 \times 0.30$ mm Crystal system monoclinic Space group $P2_1/c$ (No. 14) Unit cell parameters a = 12.2516(4) Å $\alpha = 90.00^{\circ}$ b = 8.9803(2) Å $\beta = 107.083(3)^{\circ}$ c = 12.5810(4) Å $\gamma = 90.00^{\circ}$ $V = 1323.13(7) \text{ Å}^3 Z = 4$ F(000) = 552 1.292 g/cm^3 Density (calcd) Diffractometer SuperNova, Dual, Cu at home/near, AtlasS2 Cu K α , $\lambda = 1.54178$ Å Radiation Temperature 173±2K Scan type ω-scan Data collection range $-14 < h < 12, -10 < k < 8, -15 < l < 14; \quad \theta_{\text{max}} = 71.5^{\circ}$ Total: 4794 Unique (*n*): 2495 Observed $[I \ge 2\sigma(I)]$: 2237 **Reflections measured** Absorption coefficient 0.675 mm⁻¹ Minimum and maximum transmission 0.834, 1.000 No. of variables, p 172 $w = \frac{1}{\sigma^2 (F_o^2) + (0.001P)^2 + 1.2P} \qquad P = (F_o^2 + 2F_c^2)/3$ Weighting scheme $R1 = \frac{\sum ||F_{o}| - |F_{c}||}{\sum |F_{o}|} \text{ (for all reflections)}$ 0.0440 0.0395 (for observed data) $wR2 = \sqrt{\frac{\Sigma[w(F_o^2 - F_c^2)^2]}{\Sigma w(F_o^2)^2}}$ (for all reflections) 0.0839 0.0815 (for observed data) Goof = S = $\sqrt{\frac{\Sigma[w(F_o^2 - F_c^2)^2]}{n - p}}$ 1.017 Largest and mean Δ/σ 0.000, 0.000 Residual extrema in final difference map -0.246 to 0.236 $e^{\text{Å}^{-3}}$

Atoms	X	у	Z.	Ueq.
O(1)	0.75990(9)	0.14968(13)	0.02237(9)	0.0269(3)
O(2)	0.60713(9)	0.02934(12)	0.25157(9)	0.0251(3)
N(1)	0.74999(11)	0.16686(14)	0.20035(10)	0.0209(3)
C(1)	0.72761(12)	0.09955(17)	0.09910(12)	0.0209(3)
C(2)	0.71947(13)	0.09304(17)	0.29122(12)	0.0219(3)
C(3)	0.59691(12)	-0.06619(17)	0.16334(13)	0.0219(3)
C(4)	0.52465(13)	-0.18757(18)	0.15087(14)	0.0268(4)
C(5)	0.51384(14)	-0.28301(19)	0.06197(14)	0.0292(4)
C(6)	0.57451(14)	-0.25791(19)	-0.01406(1)	0.0297(4)
C(7)	0.64518(14)	-0.13489(18)	-0.00147(1)	0.0262(3)
C(8)	0.65738(12)	-0.03768(17)	0.08730(12)	0.0212(3)
C(9)	0.81198(13)	0.30915(17)	0.22123(12)	0.0215(3)
C(10)	0.73363(14)	0.43686(18)	0.23107(15)	0.0283(4)
C(11)	0.79679(15)	0.58592(18)	0.24525(15)	0.0309(4)
C(12)	0.90569(14)	0.58182(19)	0.34255(14)	0.0294(4)
C(13)	0.98185(14)	0.45271(19)	0.33097(14)	0.0291(4)
C(14)	0.91822(13)	0.30461(18)	0.32195(13)	0.0249(3)
C(15)	0.80351(13)	-0.02475(17)	0.34711(13)	0.0234(3)
C(16)	0.84976(19)	-0.0317(2)	0.45467(15)	0.0448(5)

Table S3-2. Atomic coordinates and equivalent isotropic temperature factors* (Å²).

 $*U_{eq.}$ defined as one third of the trace of the orthogonalized U tensor.

Table 55-5. Dolla le	inguis (A) and boild an	igics ().	
O(1)-C(1)	1.2310(18)	C(5)-C(6)	1.391(2)
O(2)-C(3)	1.3792(18)	C(6)-C(7)	1.384(2)
O(2)-C(2)	1.4377(18)	C(7)-C(8)	1.391(2)
N(1)-C(1)	1.3630(19)	C(9)-C(10)	1.524(2)
N(1)-C(2)	1.4620(19)	C(9)-C(14)	1.527(2)
N(1)-C(9)	1.4702(19)	C(10)-C(11)	1.530(2)
C(1)-C(8)	1.485(2)	C(11)-C(12)	1.523(2)
C(2)-C(15)	1.499(2)	C(12)-C(13)	1.522(2)
C(3)-C(4)	1.384(2)	C(13)-C(14)	1.529(2)
C(3)-C(8)	1.395(2)	C(15)-C(16)	1.306(2)
C(4)-C(5)	1.384(2)		
C(3)-O(2)-C(2)	112.21(11)	C(7)-C(6)-C(5)	119.56(15)
C(1)-N(1)-C(2)	120.15(12)	C(6)-C(7)-C(8)	120.61(15)
C(1)-N(1)-C(9)	120.26(12)	C(7)-C(8)-C(3)	118.82(14)
C(2)-N(1)-C(9)	119.45(12)	C(7)-C(8)-C(1)	121.58(14)
O(1)-C(1)-N(1)	123.22(14)	C(3)-C(8)-C(1)	119.51(14)
O(1)-C(1)-C(8)	122.36(14)	N(1)-C(9)-C(10)	111.34(12)
N(1)-C(1)-C(8)	114.39(13)	N(1)-C(9)-C(14)	113.25(12)
O(2)-C(2)-N(1)	110.35(12)	C(10)-C(9)-C(14)	110.88(13)
O(2)-C(2)-C(15)	109.73(12)	C(9)-C(10)-C(11)	111.03(13)
N(1)-C(2)-C(15)	112.86(12)	C(12)-C(11)-C(10)	111.48(14)
O(2)-C(3)-C(4)	119.02(14)	C(13)-C(12)-C(11)	111.00(14)
O(2)-C(3)-C(8)	119.79(13)	C(12)-C(13)-C(14)	110.87(13)
C(4)-C(3)-C(8)	121.18(15)	C(9)-C(14)-C(13)	109.28(13)
C(3)-C(4)-C(5)	119.05(15)	C(16)-C(15)-C(2)	123.29(16)
C(4)-C(5)-C(6)	120.76(15)		

Table S3-3. Bond lengths (Å) and bond angles (°).

Atoms	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O(1)	0.0328(6)	0.0274(6)	0.0221(5)	0.0002(5)	0.0106(5)	-0.0053(5)
O(2)	0.0240(5)	0.0240(6)	0.0305(6)	-0.0050(5)	0.0131(5)	-0.0030(5)
N(1)	0.0267(7)	0.0158(6)	0.0212(6)	0.0000(5)	0.0084(5)	-0.0025(5)
C(1)	0.0213(7)	0.0184(8)	0.0219(7)	0.0008(6)	0.0047(6)	0.0033(6)
C(2)	0.0268(8)	0.0180(8)	0.0227(7)	-0.0027(6)	0.0100(6)	-0.0024(6)
C(3)	0.0198(7)	0.0197(8)	0.0250(8)	-0.0010(6)	0.0046(6)	0.0024(6)
C(4)	0.0214(8)	0.0262(9)	0.0328(9)	0.0021(7)	0.0080(7)	-0.0013(7)
C(5)	0.0239(8)	0.0224(8)	0.0368(9)	-0.0008(7)	0.0020(7)	-0.0048(7)
C(6)	0.0345(9)	0.0231(9)	0.0273(8)	-0.0055(7)	0.0023(7)	-0.0017(7)
C(7)	0.0294(8)	0.0242(8)	0.0245(8)	-0.0010(7)	0.0073(7)	0.0005(7)
C(8)	0.0204(7)	0.0181(8)	0.0234(7)	0.0005(6)	0.0040(6)	0.0009(6)
C(9)	0.0271(8)	0.0162(7)	0.0217(7)	0.0001(6)	0.0076(6)	-0.0029(6)
C(10)	0.0244(8)	0.0188(8)	0.0365(9)	-0.0017(7)	0.0007(7)	0.0008(6)
C(11)	0.0345(9)	0.0172(8)	0.0386(9)	-0.0017(7)	0.0071(8)	0.0006(7)
C(12)	0.0336(9)	0.0232(8)	0.0314(9)	-0.0067(7)	0.0098(7)	-0.0085(7)
C(13)	0.0239(8)	0.0300(9)	0.0317(9)	0.0000(7)	0.0057(7)	-0.0054(7)
C(14)	0.0223(8)	0.0218(8)	0.0298(8)	0.0022(7)	0.0065(6)	0.0019(6)
C(15)	0.0282(8)	0.0175(8)	0.0257(8)	0.0000(6)	0.0097(6)	-0.0034(6)
C(16)	0.0679(14)	0.0350(11)	0.0280(9)	0.0043(8)	0.0088(9)	0.0127(10)

Table S3-4. Anisotropic thermal parameters* (Å²).

The exponent takes the form: $-2\pi^2 \Sigma \Sigma U_{ij} h_i h_j \mathbf{a}_i^ \mathbf{a}_j^*$

Atoms	X	У	Z.	$U_{\it eq.}$
H(2)	0.7181	0.1687	0.3469	0.026
H(4)	0.4839	-0.2048	0.2015	0.032
H(5)	0.4655	-0.3649	0.0530	0.035
H(6)	0.5676	-0.3234	-0.0730	0.036
H(7)	0.6849	-0.1171	-0.0529	0.031
H(9)	0.8379	0.3298	0.1561	0.026
H(10A)	0.7054	0.4198	0.2945	0.034
H(10B)	0.6685	0.4403	0.1648	0.034
H(11A)	0.8158	0.6093	0.1776	0.037
H(11B)	0.7471	0.6639	0.2576	0.037
H(12A)	0.9468	0.6747	0.3455	0.035
H(12B)	0.8861	0.5716	0.4115	0.035
H(13A)	1.0492	0.4503	0.3951	0.035
H(13B)	1.0065	0.4672	0.2652	0.035
H(14A)	0.9676	0.2237	0.3139	0.030
H(14B)	0.8963	0.2875	0.3890	0.030
H(15)	0.8237	-0.0964	0.3030	0.028
H(16A)	0.8309	0.0387	0.5006	0.054
H(16B)	0.9015	-0.1071	0.4853	0.054

Table S3-5. Coordinates and isotropic temperature factors^{*} ($Å^2$) for H atoms.

*The exponent takes the form: $-8\pi^2 U \sin^2 \theta / \lambda^2$



ORTEP drawing of $C_{16}H_{19}NO_2$ with 50% probability ellipsoids, showing the atomic numbering scheme.



6. The results from the reactions of 1a with propargyl alcohol in either KOD/D₂O/DMSO or KOD/D₂O/MeCN

The reaction of **1a** with propargyl alcohol in either KOD/D₂O/DMSO or KOD/D₂O/MeCN have been performed, and the products are called as **2a-D** and **3a-D**.

We have compared the GC-MS results of **2a-D** and **3a-D** with **2a** and **3a**, respectively. **2a-D** and **3a-D** have been isolated, and their ¹H-NMR spectra have been compared with ones of **2a** and **3a**.

On the basis of the comparison, it seems to observe the D-incorporated into **2a-D** and **3a-D** in low percentages, but these observations cannot confirm whether D is really incorporated or not.



Possible D incorporated position in 2a

Possible D incorporated position in 3a





GC-MS results

According to GC-MS charts, the peak of 218 (from one D isotope) in **2a-D** sample seems to be higher than **2a**. It may imply that one D is incorporated into **2a-D**. GC-MS of **2a**:





The similar phenomenon can be also observed, when we compare the GC-MS spectra of **3a** with **3a-D**.

GC-MS of 3a



¹H NMR results

Slight splitting peaks seem to be observed at 5.43 ppm and 1.93 ppm. We assume that it is from D-incorporated in **2a-D** into vinyl and methyl group.

¹H NMR of **2a**



¹H NMR of **2a-D**



Also, slight splitting peaks seem to be observed at 5.35 ppm, and we assume that it is from D-incorporated in **3a-D** into vinyl group.





¹H NMR of **3a-D**



References

- 1. Seth, K.; Nautiyal, M.; Purohit, P.; Parikh, N.; Chakraborti, A.K. Palladium catalyzed Csp²–H activation for direct aryl hydroxylation: The unprecedented role of 1,4-dioxane as a source of hydroxyl radicals. *Chem. Commun.* **2015**, *51*, 191–194.
- Creagh, D.C. Tables 4.2.6.8. In *International Tables for Crystallography*; Wilson, A.J.C., Prince, E., Eds.; Kluwer Academic Publisher: Dordrecht, the Netherlands, 1999; Volume C, pp. 255–257.
- Maslen, E.N.; Fox, A.G.; O'Keefe, M.A. Tables 6.1.1.4. In *International Tables for Crystallography*; Wilson, A.J.C., Prince, E., Eds.; Kluwer Academic Publisher: Dordrecht, the Netherlands, 1999; Volume C, pp. 572–574.