

Supporting Information

Title: Photosensitized 2+2 Cycloaddition Reaction Using Homochirality Generated by Spontaneous Crystallization

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Experimental

General. NMR spectra were recorded on CDCl₃ solutions on a BRUKER 300 operating 300 MHz, respectively, for ¹H- and ¹³C-NMR spectroscopy. Chemical shifts are reported in parts per million (ppm) relative to TMS as internal standards. IR spectra were recorded on a JASCO FT/IR-230 spectrometers.

General procedure for the preparation of *N,N*-Diethyl-4-ethylcoumarin-3-carboxamide **1**.

To a THF solution containing 1.51 g (5.5 mmol) of 4-ethylcoumarin-3-carboxylic acid and triethylamine 0.67g (6.6 mmol) was added 0.79 g (6.6 mmol) of thionyl chloride at 0°C. The reaction mixture was stirred for 0.5 h, and then a THF solution containing 0.95 g of diethylamine (13.0 mmol) was added dropwise. After the reaction mixture was stirred for 2 h, water and ethyl acetate were added, and the organic layer was extracted in the usual manner. After the organic solvent was evaporated in *vacuo*, the residual mixture was subjected to chromatography on silica gel and the amide **1** was separated. The structure of **1** was determined on the basis of spectral data, mass spectroscopy, and unequivocally X-ray single crystallographic analyses.

N,N-Diethyl-4-ethyl-3-coumarincarboxamide **1** was obtained as colorless crystals from hexane-chloroform: m.p.114 °C; IR (cm⁻¹, KBr) 1718, 1610; ¹H NMR (CDCl₃) δ 1.15-1.20 (m, 3H), 1.26-1.36 (m, 6H), 2.68-2.74 (m, 1H), 2.86-2.92 (m, 1H), 3.23-3.35 (m, 2H), 3.44-3.51 (m, 1H), 3.70-3.77 (m, 1H), 7.32-7.38 (m, 2H), 7.66 (ddd, *J*=1.5, 5.9 and 8.2 Hz, 1H), 7.67 (d, *J*=7.9 Hz, 1H); ¹³C NMR (CDCl₃) δ 13.1, 14.1, 14.4, 23.7, 39.3, 43.5, 117.8, 118.8, 123.7, 125.0, 125.4, 132.4, 153.8, 154.0, 158.9, 164.7; HRMS (FAB-MS) *m/z* calcd for C₁₆H₁₉NO₃ + H 274.1443, found 274.1442.

X-Ray single crystal analysis of *N,N*-Diethyl-4-ethyl-3-coumarincarboxamide **1**

Crystal data of **1**: Orthorhombic space group $P2_12_12_1$, $a = 9.228(2)$ Å, $b = 11.560(3)$ Å, $c = 14.204(4)$ Å, $V = 1515.1(6)$ Å³, $Z = 4$, $\rho = 1.198$ Mg/m³, in the final least-squares refinement cycles on F^2 , the model converged at $R_1 = 0.0445$, $wR_2 = 0.1157$, and $GOF = 1.073$ for 1656 reflections (CCDC 661727).

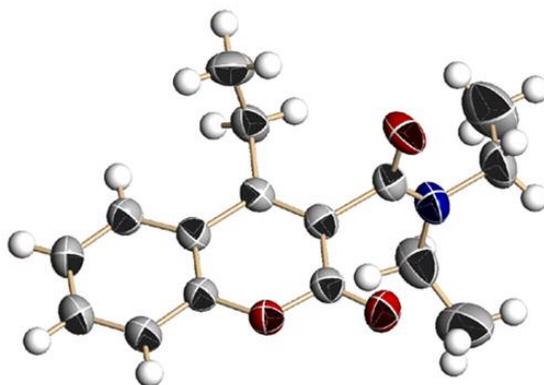


Fig. S1. Ortep view of **1** showing the atoms and thermal ellipsoids at 50% probability.

Preparation of chiral crystals for asymmetric photochemical reactions.

The crystals of **1** used for the asymmetric synthesis were prepared by stirred crystallization at high temperature, by which the completely melted sample of **1** at 120°C (mp: 114°C) was cooled and solidified by lowering the temperature to 110°C with stirring. A high level of reproducibility of both chiral crystallization and asymmetric photoreaction was achieved by this method. The use of crystals generated in this fashion in the photocycloaddition reaction can lead to isolation of either of the enantiomers of the cycloadduct. Of course, the desired crystals of **1** could be selectively prepared in large quantities by the addition of a corresponding seed crystal during the crystallization process.

Kinetic studies for racemization of **1**

Cryostat apparatus was used for measuring CD spectra at low temperature. The powdered crystals of **1**

were dissolved into cooled THF, MeOH, or DMF in a cryostat apparatus and the CD spectra were monitored. The rate for enantiomerization was determined on the basis of the attenuation of the CD spectra. The activation parameters were obtained from the Eyring equation and Arrhenius plots. When a single crystal of **1** selected randomly was dissolved in MeOH at 20 °C using a cryostat apparatus, a strong Cotton effect was observed at below 350 nm (**Fig. S2**). The Cotton effect gradually decreased with racemization as a result of the rotation about the coumarin-C(=O) bond. The first-order kinetic plots of the decay profile of CD intensity was shown as a plot of $\ln(ee)$ versus time (eq. 1 and Fig. S3), and the rate of racemization (k_{rac}) was calculated from the slope of the line. Furthermore, the rate of racemization at 15 and 25°C was also determined. The free energy barrier (ΔG^\ddagger) for racemization is calculated according to the Eyring equation (eq 2). The value of $\ln(k_{rac})$ versus $1/T$ was plotted (Arrhenius plots) (Fig S4), and then E_a was determined. From the value of k_{rac} and E_a , ΔH^\ddagger , ΔS^\ddagger , and half-life were calculated according to equations (4)-(6).

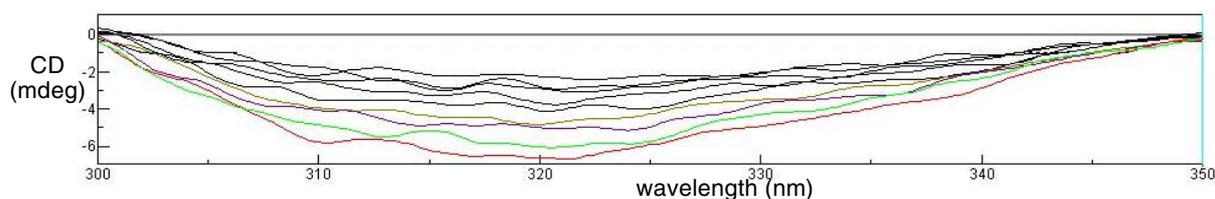


Fig. S2. Changes of CD spectra of a MeOH solution provided by dissolving enantiomeric crystal of **1** to MeOH at 20°C using cryostat apparatus. CD spectra of a solution of (-)-crystal measured every 10 min.

$$\ln(ee) = k_{rac}t \quad (\text{eq. 1})$$

$$k_{rac} = \frac{kT}{h} \exp(-\Delta G^\ddagger/RT) \quad (\text{eq. 2})$$

$$k_{rac} = A \exp(-E_{rac}/RT) \quad (\text{eq. 3})$$

$$\Delta H^\ddagger = E_{rac} - RT \quad (\text{eq. 4})$$

$$k_{rac} = \frac{kT}{h} \exp(-\Delta H^\ddagger/RT) \exp(\Delta S^\ddagger/R) \quad (\text{eq. 5})$$

$$t_{1/2} = \ln 2 / k_{rac} \quad (\text{eq. 6})$$

k_{rac} : rate of racemization, h : Planck constant, k : Boltzmann constant, R : gas constant, T : temperature

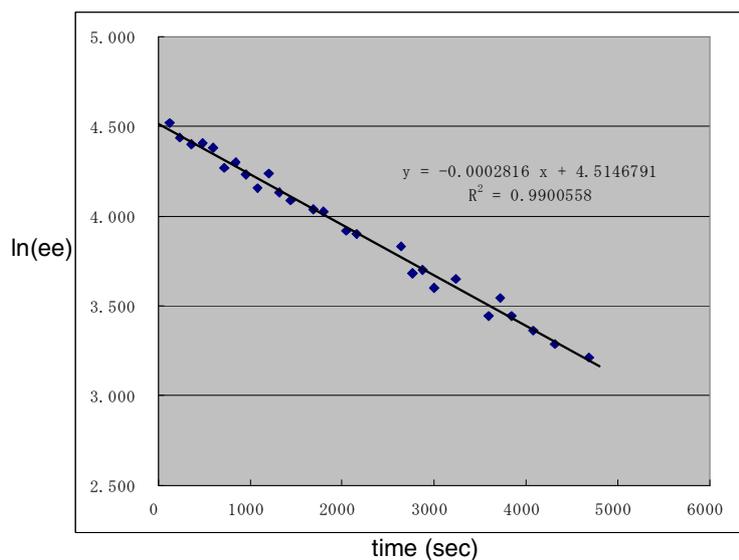


Fig S3. Plot of $\ln(ee)$ versus time (sec) obtained for racemization of amide **1** in MeOH at 20°C.

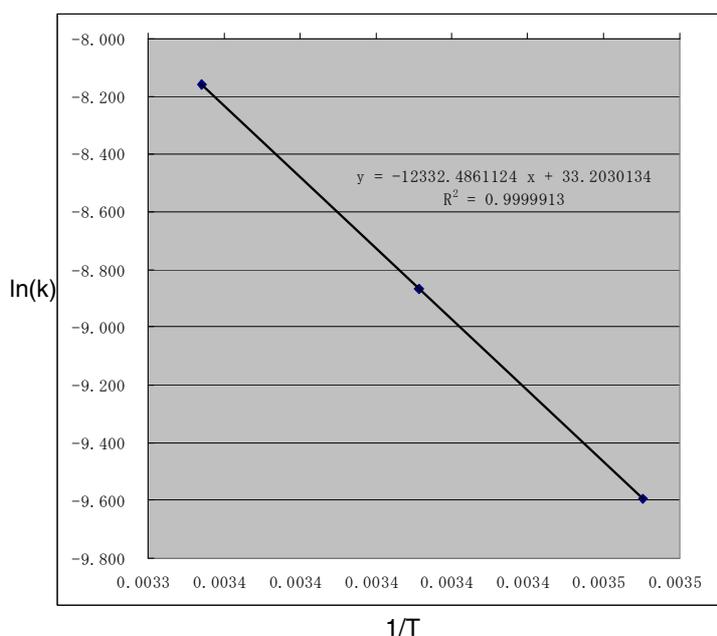


Fig S4. Arrhenius plots of racemization rate constants of the amide **1** in MeOH at 15, 20, and 25°C.

Table S1. Kinetic parameters for racemization of the coumarincarboxamide **1** in various conditions^a

Solvent	Temp (°C)	$t_{1/2}$ (min)	$k \times 10^{-4}$ (S ⁻¹)	ΔG^\ddagger (kcal mol ⁻¹)	ΔH^\ddagger (kcal mol ⁻¹)	ΔS^\ddagger (cal mol ⁻¹ deg ⁻¹)
THF	-5	82.0	0.704	20.7	28.1	27.3
	0	30.5	1.89	20.6	28.1	27.3
	5	11.9	4.85	20.5	28.0	27.2
MeOH	15	84.8	0.681	22.3	23.9	5.53
	20	41.0	1.41	22.3	23.9	5.48
	25	20.2	2.86	22.3	23.9	5.46
DMF	15	92.7	0.623	22.4	22.8	1.30
	20	45.5	1.27	22.4	22.8	1.29
	25	23.6	2.44	22.4	22.8	1.23

^a Arrhenius parameter E value was 28.6, 24.5, and 23.3 kcal mol⁻¹, for THF, MeOH, and DMF, respectively.

General procedure for photochemical cycloaddition reaction of coumarincarboxamides **1 with ethyl vinyl ether or 2-methoxypropene.**

The photochemical reaction of coumarincarboxamide **1** in the presence of alkenes was exemplified. Crystals of **1** were added to a cooled and deoxygenated (by bubbling argon) MeOH solution containing ethyl vinyl ether (0.1 mol/L), and the solution was irradiated with a 365 nm line using a 350-W ultra-high pressure mercury lamp for 0.5–6 h at the same temperature. After removing the solvent in vacuo, the crude photolysate was subjected to chromatography on silica gel. The 2+2 cycloadduct **2** was isolated. The chemical yield of **2** was determined on the basis of the consumed coumarincarboxamide **1**.

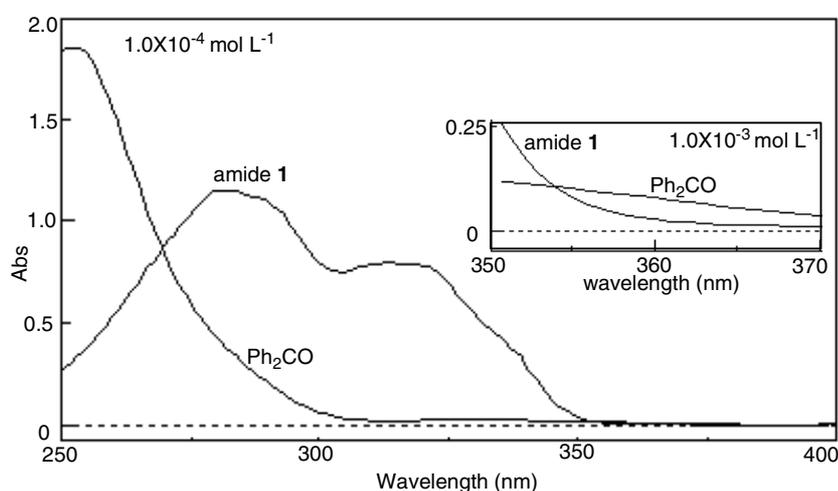


Fig. S5. UV spectra of coumarincarboxamide **1** and benzophenone in MeOH. Absorption coefficients of the amide **1** and BP at 365 nm in the MeOH were 20 and 60 mol⁻¹ cm⁻¹ dm³, respectively.

Photoadduct with ethyl vinyl ether *endo*-2a**** was obtained as colorless crystals from hexane-chloroform: m.p. 83.5–84.5 °C; IR (cm⁻¹, KBr) 1740, 1639; ¹H NMR (CDCl₃) δ 0.88–1.01 (m, 6H), 1.08–1.20 (m, 6H), 1.94 (ddd, *J*=7.4, 7.5 and 7.2 Hz, 2H), 2.12–2.23 (m, 1H), 2.92–3.05 (m, 2H), 3.20–3.43 (m, 3H), 3.49–3.61 (m, 2H), 3.89 (dd, *J*=6.43 and 5.9 Hz, 1H), 7.08–7.22 (m, 3H), 7.31 (ddd, *J*=7.6, 6.4 and 7.6 Hz, 1H); ¹³C NMR (CDCl₃) δ 9.8, 12.1, 12.4, 15.6, 28.8, 39.5, 40.7, 41.3, 43.1, 54.3, 65.4, 78.1 (d, *J*=22.0 Hz) 117.6, 118.0, 124.5, 125.7, 126.1, 129.2, 151.5, 167.1, 169.6; HRMS (FAB-MS) *m/z* calcd for C₂₀H₂₇NO₄ + H 346.1995, found 346.2018.

Photoadduct with *endo-2b* was obtained as colorless crystals from hexane-chloroform: m.p. 115-116°C; IR (cm⁻¹, KBr) 1737, 1630; ¹H NMR (CDCl₃) δ 0.78 (dd, *J*=7.2 and 7.1 Hz, 3H), 1.03-1.15 (m, 9H), 2.03-2.15 (m, 2H), 2.66-2.77 (m, 2H), 2.92 (s, 3H), 3.05-3.18 (m, 2H), 3.40-3.53 (m, 2H), 7.05-7.21 (m, 3H), 7.29-7.34 (m, 1H); ¹³C NMR (CDCl₃) δ 7.4, 10.3, 10.6, 15.7, 21.2, 40.0, 41.0, 48.9, 50.6, 54.4, 76.1, 80.5, 115.5, 119.0, 123.3, 125.5, 127.7, 152.1, 165.7, 167.8; HRMS (FAB-MS) *m/z* calcd for C₂₀H₂₇NO₄ + H 346.2018, found 346.2010.

X-Ray crystallographic analysis of *exo-2a*

Crystal data of *exo-2a*: Monoclinic space group *Cc*, *a* = 9.914(2) Å, *b* = 13.460(3) Å, *c* = 14.925(4) Å, β = 108.382(2), *V* = 108.382(2) Å³, *Z* = 4, ρ = 1.214 Mg/m³, in the final least-squares refinement cycles on F², the model converged at *R*₁ = 0.063, *wR*₂ = 0.122, and GOF = 0.997 for 3643 reflections (CCDC 661728).

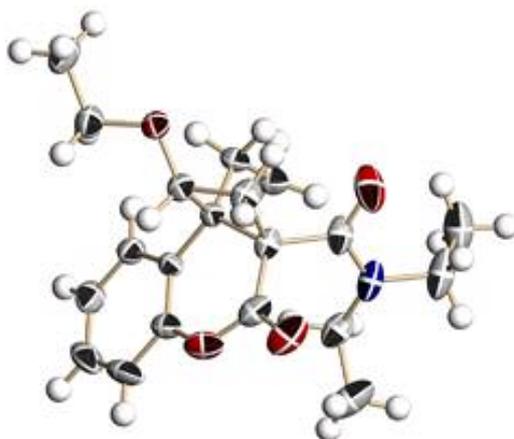


Fig. S6. Ortep view of *exo-2a* showing the atoms and thermal ellipsoids at 50% probability.

X-Ray crystallographic analyses of *endo-2b*

Crystal data of *endo-2b*: Monoclinic space group $C2/c$, $a = 14.1721(17)$ Å, $b = 14.2071(17)$ Å, $c = 19.191(2)$ Å, $\beta = 106.0940(10)$, $V = 3712.5(8)$ Å³, $Z = 8$, $\rho = 1.236$ Mg/m³, in the final least-squares refinement cycles on F^2 , the model converged at $R_1 = 0.0469$, $wR_2 = 0.1539$, and GOF = 1.151 for 4256 reflections (CCDC 661729).

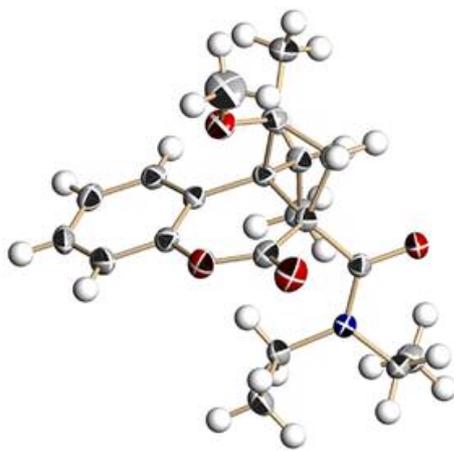


Fig. S7. Ortep view of *endo-2b* showing the atoms and thermal ellipsoids at 50% probability.

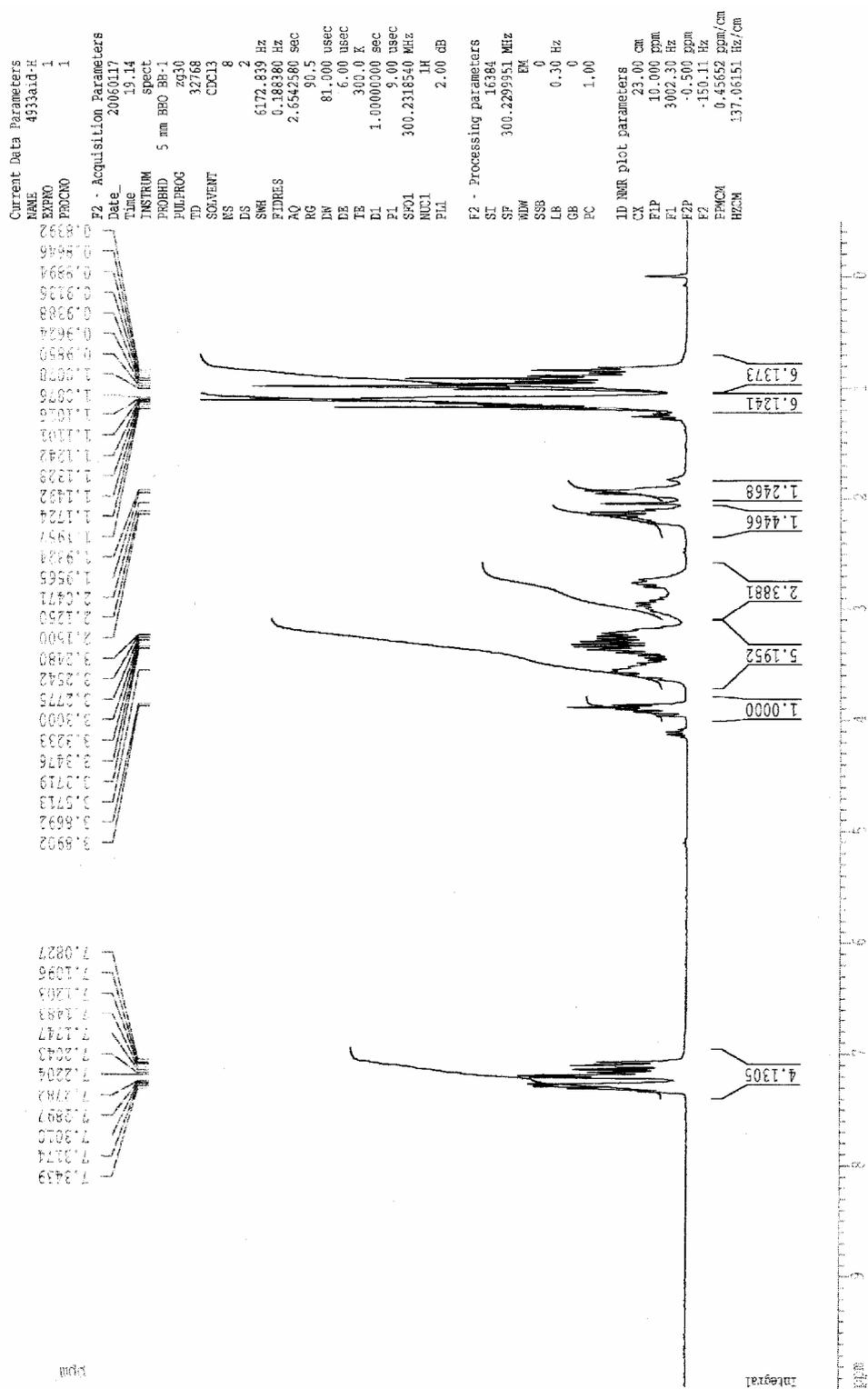
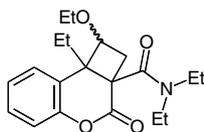
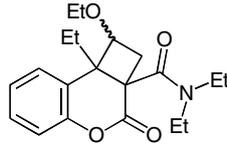


Fig. S8. ¹H NMR spectrum of adduct-2a



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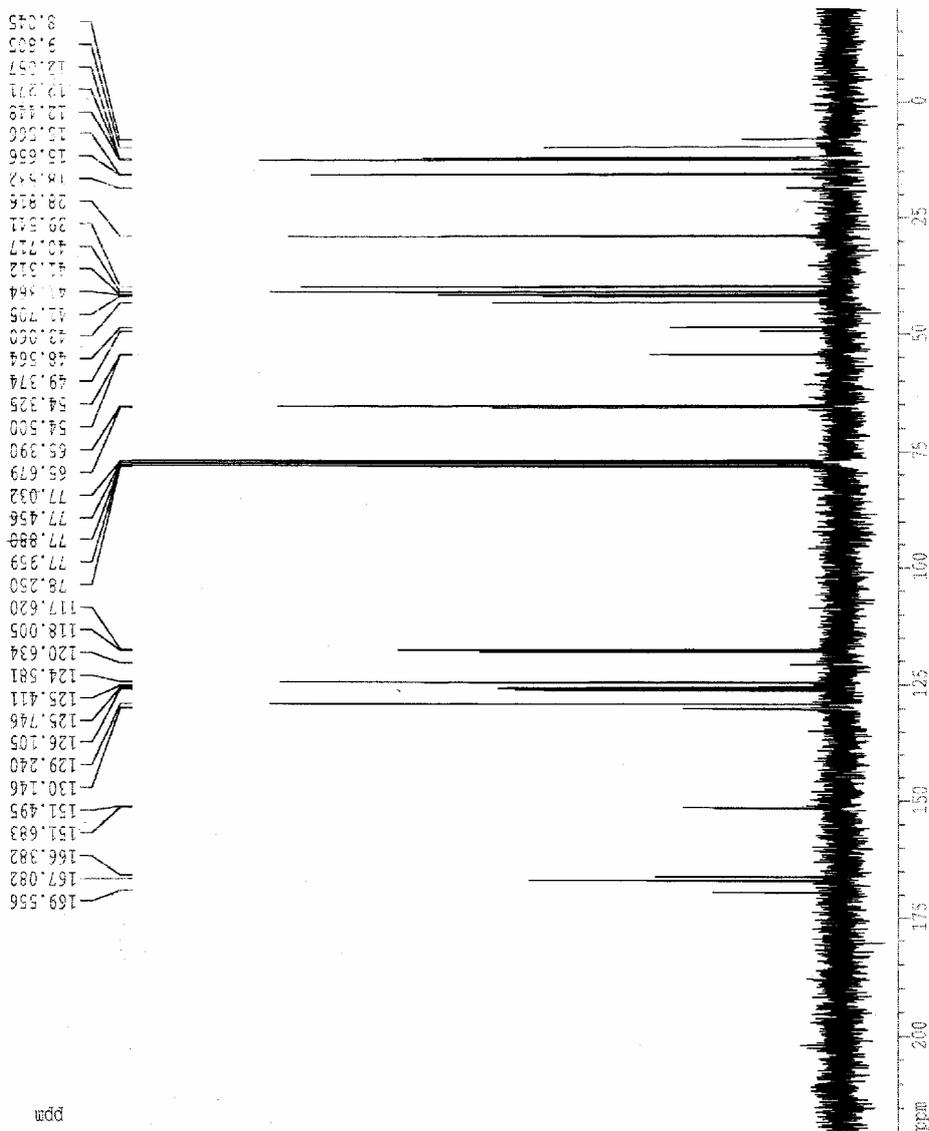


Fig. S9. ¹³C NMR spectrum of adduct-2b

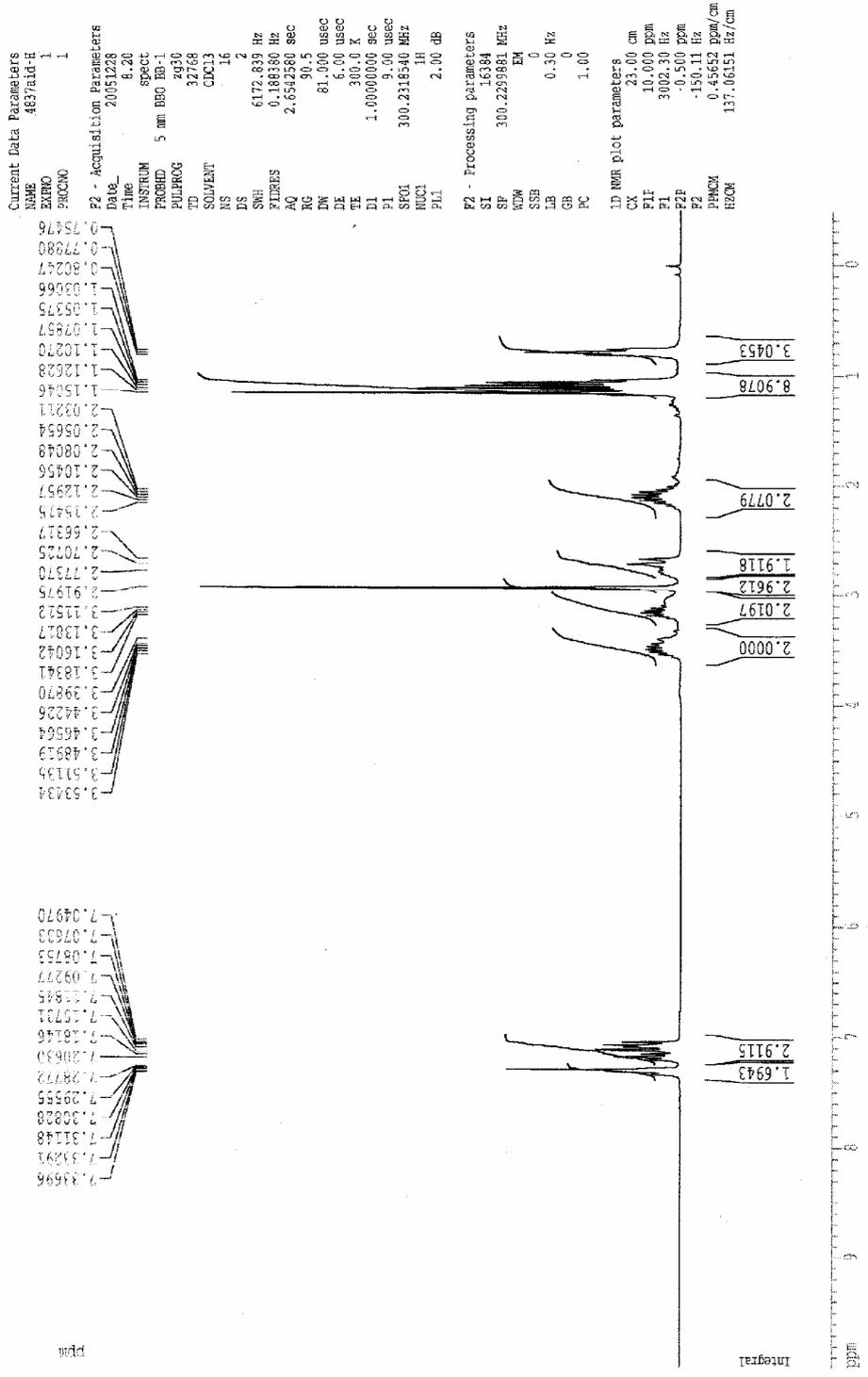
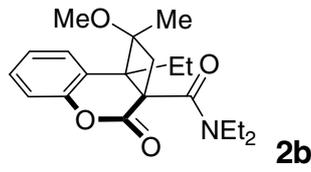
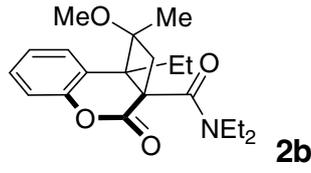


Fig. S10. ¹H NMR spectrum of adduct-2b



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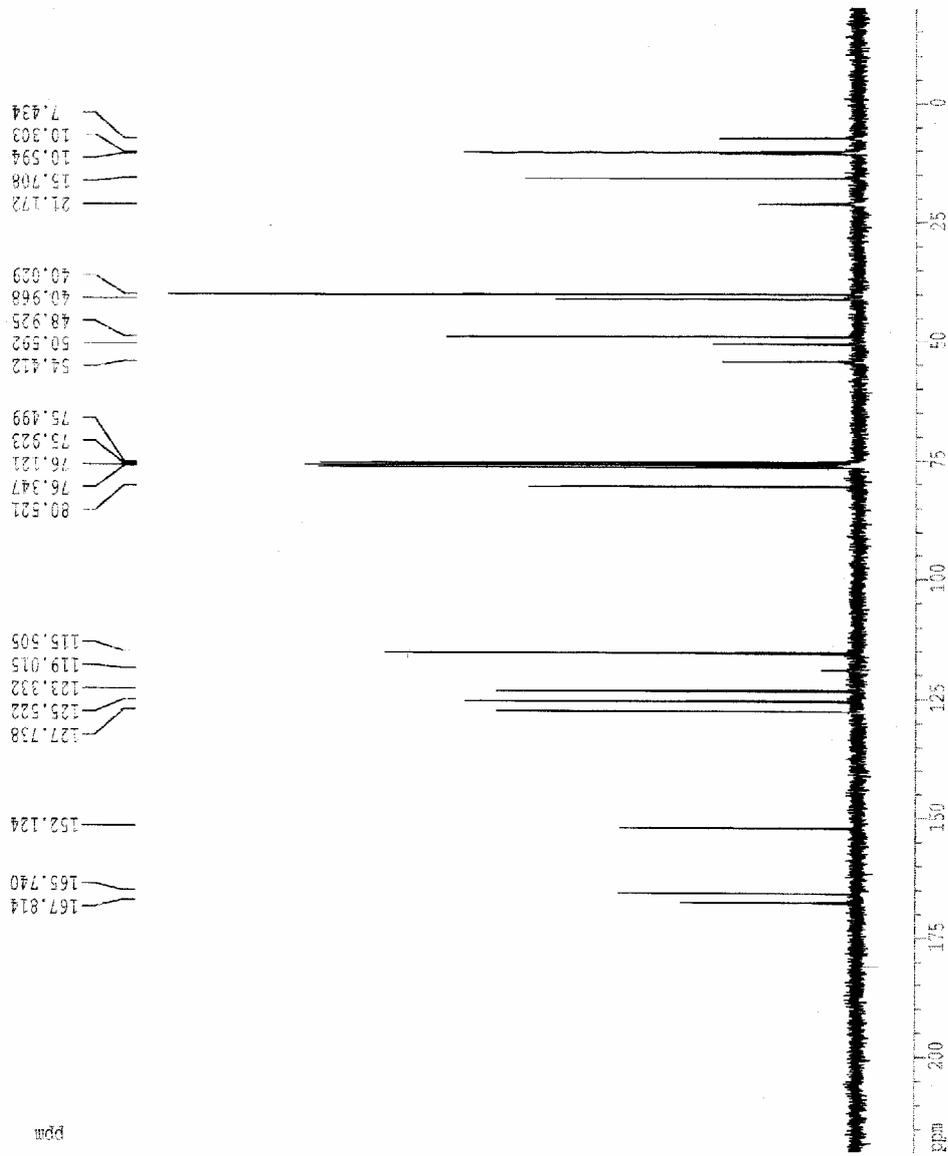


Fig. S11. ¹³C NMR spectrum of *adduct-2b*