Supporting Information

Cage-Catalyzed Knoevenagel Condensation under Neutral Conditions in Water

Takashi Murase, Yuki Nishijima, and Makoto Fujita*

Department of Applied Chemistry, School of Engineering, The University of Tokyo, CREST, Japan Science and Technology Agency (JST), 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan.
E-mail: mfujita@appchem.t.u-tokyo.ac.jp

Contents

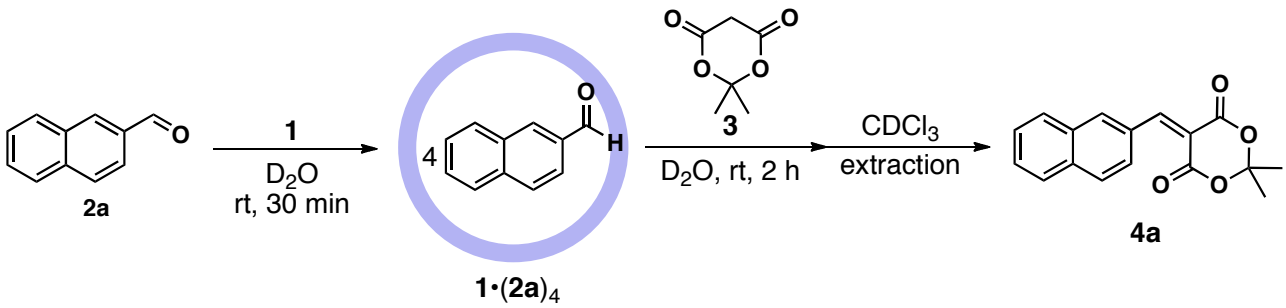
Materials and instrumentations: ^{1}H, ^{13}C, and other 2D NMR spectra were recorded on a Bruker DRX-500 (500 MHz) or Bruker AV-500 (500 MHz) spectrometer. TMS ($CDCl_3$ solution) in a capillary served as an external standard (δ = 0 ppm). IR measurements were carried out using a DIGILAB Scimitar FTS-2000 instrument. GC-MS spectra were measured on Agilent Technologies 5973N spectrometer. Melting points were determined with a Yanaco MF-500 V micro melting point apparatus.

Solvents and reagents were purchased from TCI Co., Ltd., WAKO Pure Chemical Industries Ltd., KANTO Chemical Co. and Sigma-Aldrich Co. All the chemicals were of reagent grade and used without any further purification. Deuterated H_2O (D_2O) was acquired from Cambridge Isotope Laboratories, Inc. and used as supplied for the complexation reactions and NMR measurements. 6-Dimethylamino-2-naphthaldehyde (**2f**) was prepared according to the previously established method.[1]

Reference

(1) Okamoto, A.; Tainaka, K.; Saito. I.; Takahashi, N. Preparation, fluorescence analysis, and detection of gene polymorphism of PRODAN-containing DNA. U.S. Patent 20,060,142, 311, Jun 29, 2006.

Reaction procedure for the Knoevenagel condensation of aldehyde 2a in cage 1 with Meldrum's Acid 3



1•(2a)$_4$

An excess amount of 2-naphthaldehyde (**2a**, 6.25 mg; 0.040 mmol) was suspended in a D_2O solution (1.0 mL) of cage **1** (5.0×10^{-3} mmol; 5.0 mM), and the solution was stirred at room temperature for 30 min. After filtration, the quantitative formation of inclusion complex **1•(2a)$_4$** was confirmed by ^{1}H NMR. Meldrum's acid **3** (2.88 mg, 0.020 mmol) was added to the solution, and the resulting solution was stirred for 2 h. After extraction with $CDCl_3$, condensation product **4a** was obtained in 92% yield, as determined by NMR analysis.

Physical data of 1•(2a)$_4$: 9.34 (d, 24H, J = 6.5 Hz, PyH_b, **1**), 8.56 (d, 24H, J = 6.5 Hz, PyH_a, **1**), 8.36 (s, 1H, C*H*O, **2a**), 6.38 (d, 24H, J = 8.0 Hz, Ar, **2a**), 6.31 (d, 1H, J = 7.5 Hz, Ar, **2a**), 5.80 (br, 1H, Ar, **2a**), 5.34 (br, 1H, Ar, **2a**), 5.23 (br, 1H, Ar, **2a**), 5.16 (br, 1H, Ar, **2a**), 5.00 (br, 1H, Ar, **2a**), 3.01 (s, 24H, **1**).

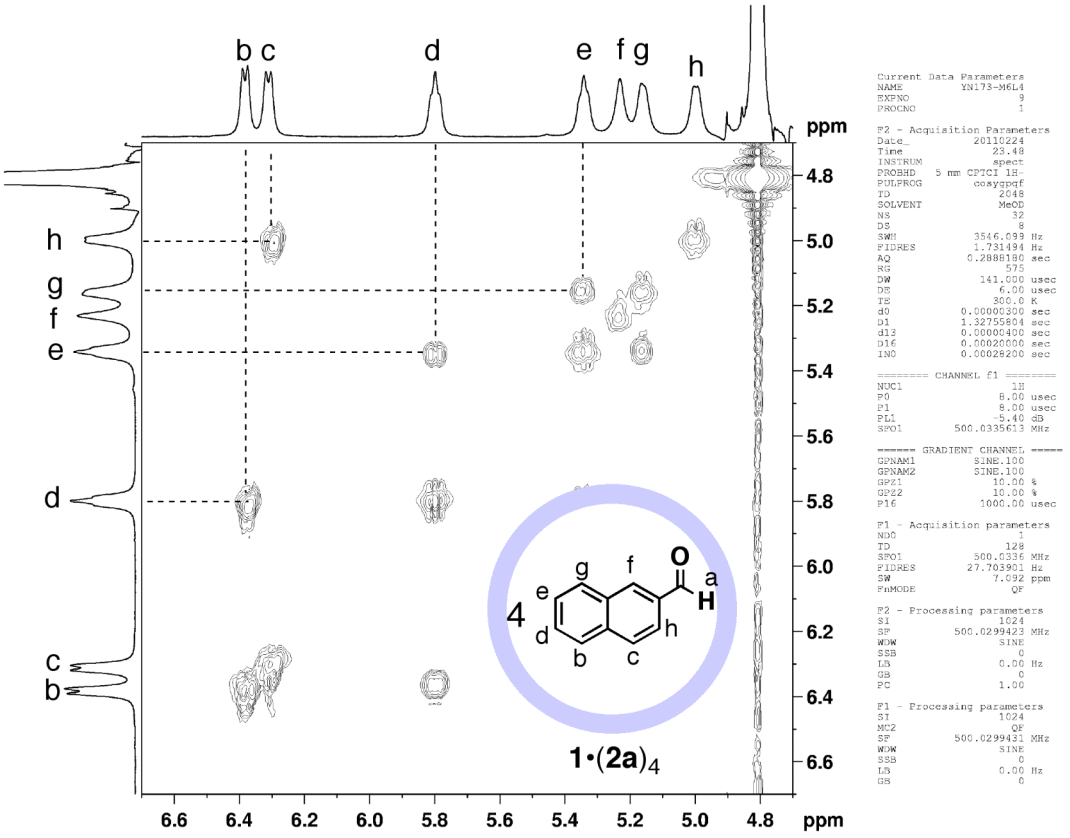
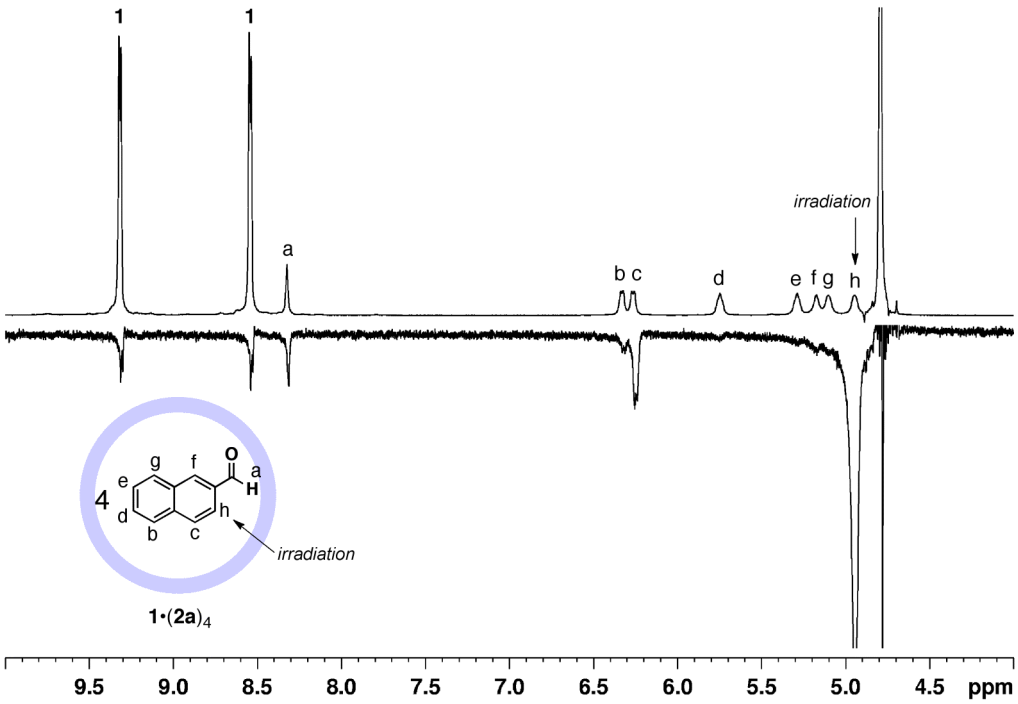
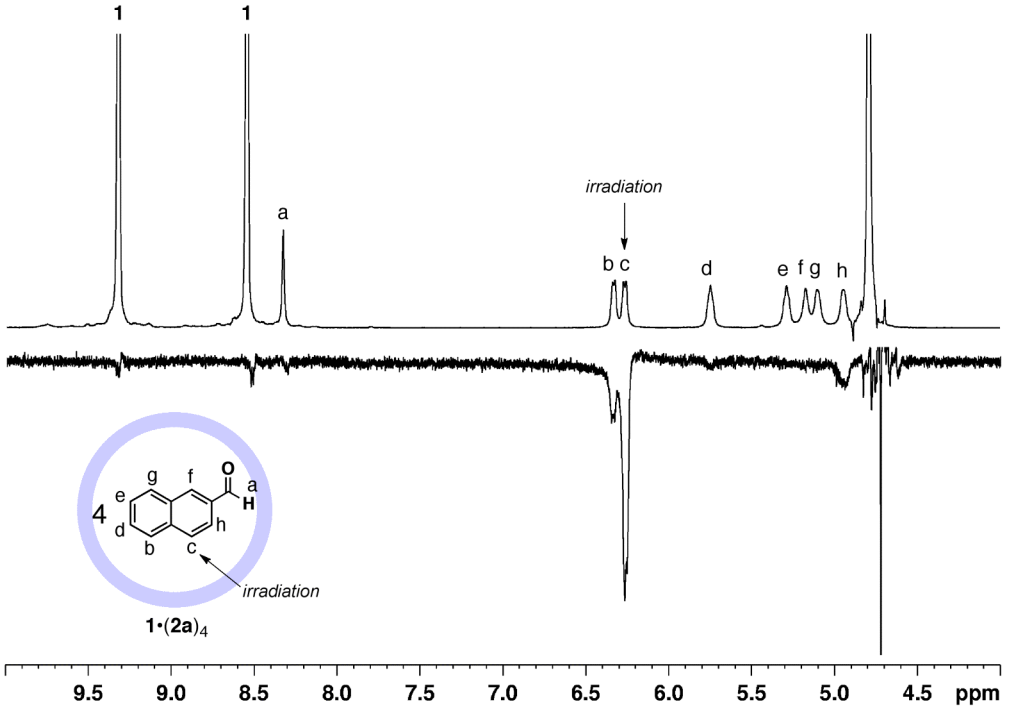


Figure S1. H–H COSY spectrum of **1•(2a)$_4$**.




```
Current Data Parameters
NAME                  YN173-M6L4
EXPNO                          3
PROCNO                         1

F2 - Acquisition Parameters
Date_                   20110217
Time                       19.32
INSTRUM                    spect
PROBHD     5 mm CPTCI 1H-
PULPROG                selnogp.3
TD                         65536
SOLVENT                    CDCl3
NS                            36
DS                             1
SWH                     7500.000 Hz
FIDRES                  0.114441 Hz
AQ                      4.3691168 sec
RG                            57
DW                         66.667 usec
DE                          6.00 usec
TE                         300.0 K
D1                    10.00000000 sec
D8                     0.80000001 sec
D16                    0.00020000 sec
d20                    0.39880002 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                          1H
P1                          8.00 usec
P2                         16.00 usec
P12                     25000.00 usec
PL0                       120.00 dB
PL1                        -5.40 dB
SFO1                  500.0330879 MHz
SF2                        50.77 dB
SPNAM2                 Gaus1.1000
SPOAL2                      0.500
SPOFFS2                  -662.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1                 sine.100
GPNAM2                 sine.100
GPNAM3                 sine.100
GPNAM4                 sine.100
GPZ1                       11.00 %
GPZ2                       17.00 %
GPZ3                       40.00 %
GPZ4                      -40.00 %
P16                     1000.00 usec

F2 - Processing parameters
SI                         131072
SF                    500.0299583 MHz
WDW                            EM
SSB                             0
LB                          0.30 Hz
GB                              0
PC                           1.00
```

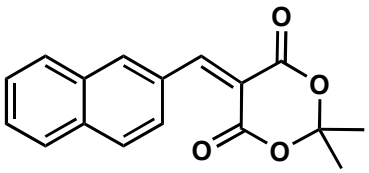
Figure S2. ^{1}H nOe NMR spectrum of **1•(2a)**$_4$.




```
Current Data Parameters
NAME                  YN173-M6L4
EXPNO                          6
PROCNO                         1

F2 - Acquisition Parameters
Date_                   20110217
Time                       20.26
INSTRUM                    spect
PROBHD     5 mm CPTCI 1H-
PULPROG                selnogp.3
TD                         65536
SOLVENT                    CDCl3
NS                            16
DS                             1
SWH                     7500.000 Hz
FIDRES                  0.114441 Hz
AQ                      4.3691168 sec
RG                          90.5
DW                         66.667 usec
DE                          6.00 usec
TE                         300.0 K
D1                    10.00000000 sec
D8                     0.80000001 sec
D16                    0.00020000 sec
d20                    0.39880002 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                          1H
P1                          8.00 usec
P2                         16.00 usec
P12                     50000.00 usec
PL0                       120.00 dB
PL1                        -5.40 dB
SFO1                  500.0330879 MHz
SF2                        56.79 dB
SPNAM2                 Gaus1.1000
SPOAL2                      0.500
SPOFFS2                  -8.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1                 sine.100
GPNAM2                 sine.100
GPNAM3                 sine.100
GPNAM4                 sine.100
GPZ1                       11.00 %
GPZ2                       17.00 %
GPZ3                       40.00 %
GPZ4                      -40.00 %
P16                     1000.00 usec

F2 - Processing parameters
SI                         131072
SF                    500.0299501 MHz
WDW                            EM
SSB                             0
LB                          0.30 Hz
GB                              0
PC                           1.00
```

Figure S3. ^{1}H nOe NMR spectrum of **1•(2a)**$_4$.

2,2-Dimethyl-5-(naphthalene-2-ylmethylene)-1,3,-dioxane-4,6-dione (4a).



4a

Physical data: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.60 (1H, s, H_a), 8.56 (1H, s, H_b), 8.14 (1H, d, *J* = 8.5 Hz, H_c), 7.96 (1H, d, *J* = 8 Hz, H_d), 7.89 (1H, d, *J* = 8.5 Hz, H_e), 7.88 (1H, d, *J* = 6.5 Hz, H_f), 7.64 (1H, dd, *J* = 7.5, 7.0 Hz, H_g), 7. 57 (1H, dd, *J* = 7.5, 8.0 Hz, H_h), 1.85 (6H, s, H_i); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 163.9 (C), 160.4 (C), 158.6 (CH), 137.5 (CH), 136.0 (C), 133.0 (C), 130.2 (CH), 129.9 (CH), 129.8 (C), 128.7 (CH), 128.5 (CH), 128.2 (CH), 127.4 (CH), 114.8 (C), 105.0 (C), 28.1 (CH_3); GC-MS: *m/z* = 282 $[M]^+$; IR (ATR, cm^{-1}): 3016, 2999, 2976, 1767, 1737, 1606, 1390, 1379, 1294, 1273, 1205, 1172, 1139, 1027; m.p. 150.8–151.5 ºC; E.A. Calcd. for $C_{17}H_{14}O_4$ C, 72.33; H, 5.00; Found: C, 72.05; H, 5.05.

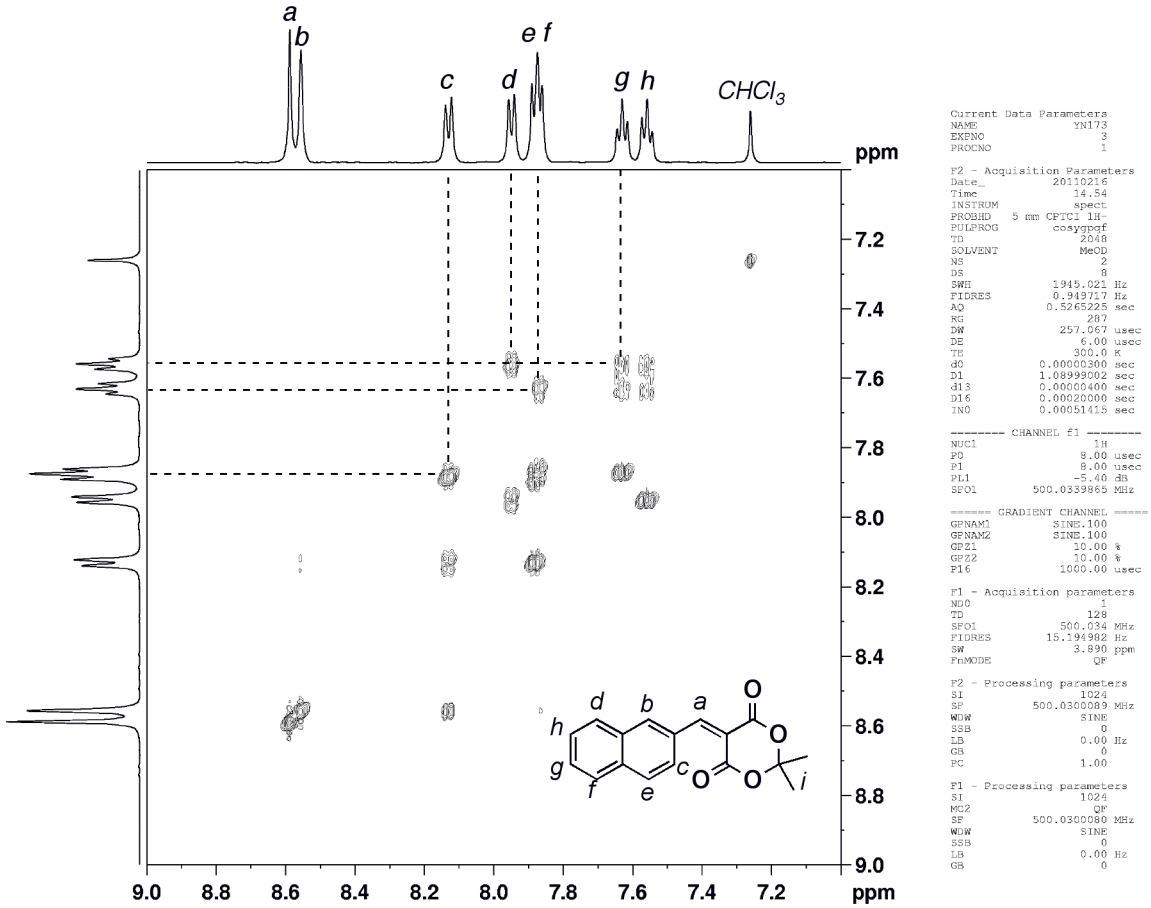
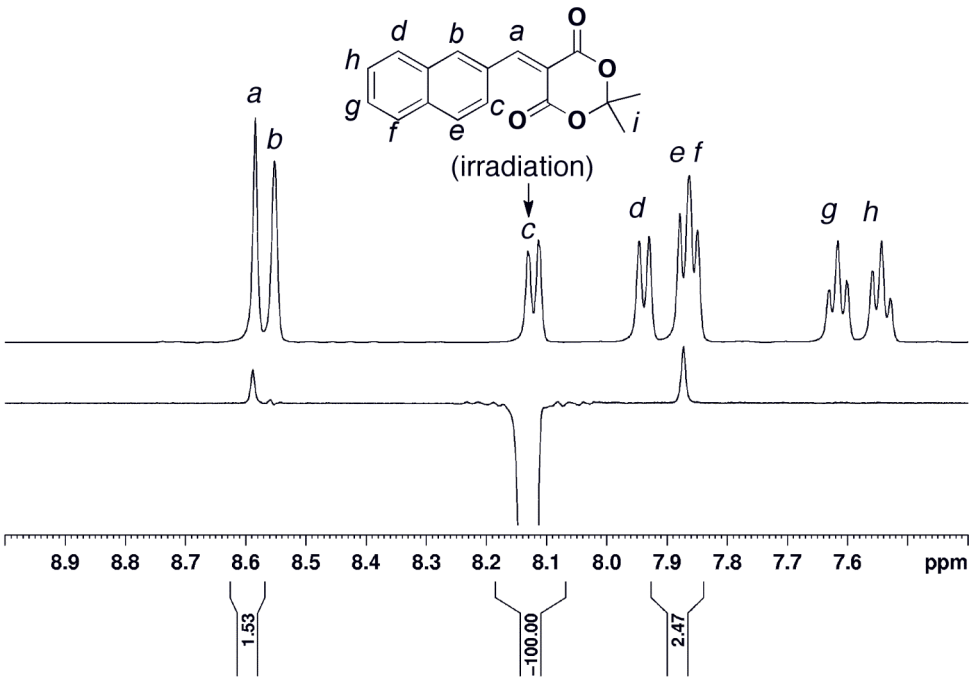
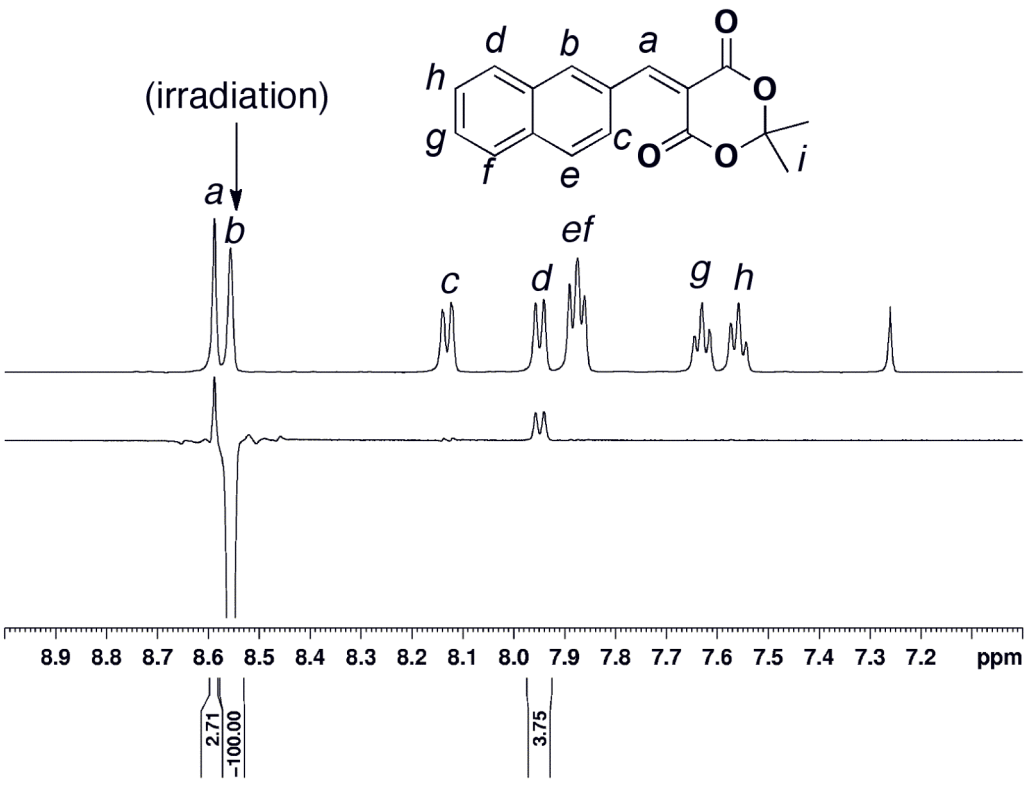


Figure S4. H–H COSY spectrum of **4a**.



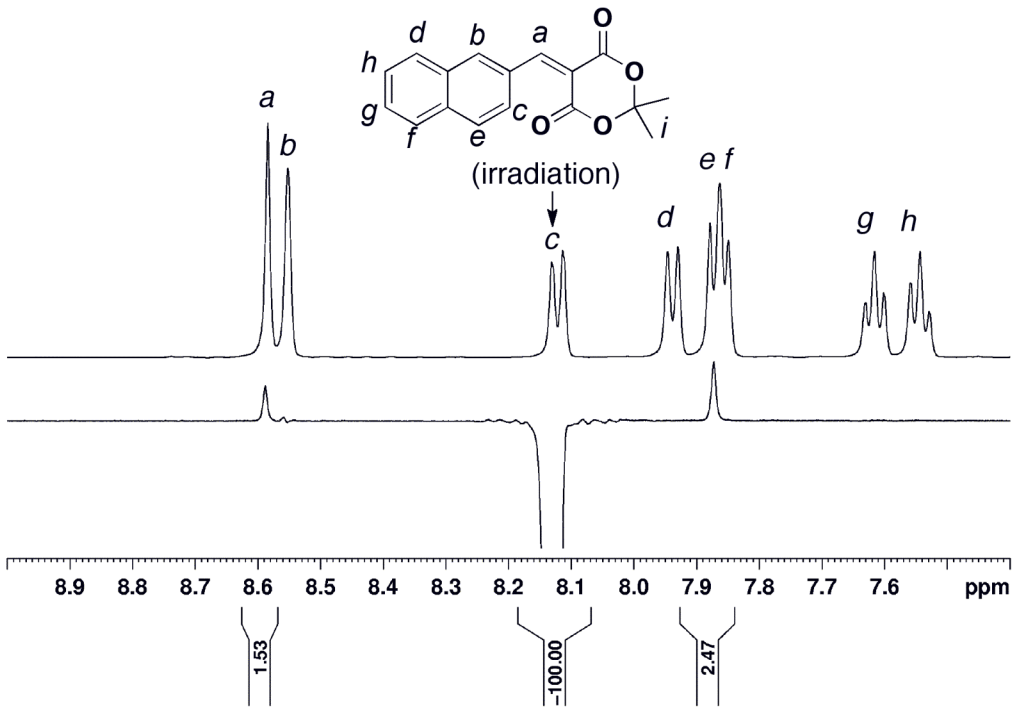

```
Current Data Parameters
NAME                  YN173
EXPNO                     7
PROCNO                    1

F2 - Acquisition Parameters
Date_              20110217
Time                   0.07
INSTRUM                spect
PROBHD   5 mm CPTCI 1H-
PULPROG          selnogp.3
TD                     65536
SOLVENT                CDCl3
NS                         4
DS                         1
SWH                7500.000 Hz
FIDRES             0.114441 Hz
AQ                 4.3691168 sec
RG                      50.8
DW                    66.667 usec
DE                     6.00 usec
TE                    300.0 K
D1                10.00000000 sec
D8                 0.80000001 sec
D16                0.00020000 sec
d20                0.39880002 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                      8.00 usec
P2                     16.00 usec
P12                50000.00 usec
PL0                  120.00 dB
PL1                   -5.40 dB
SFO1           500.0330879 MHz
SP2                   56.79 dB
SPNAM2           Gaus1.1000
SPOAL2                0.500
SPOFFS2             982.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1             sine.100
GPNAM2             sine.100
GPNAM3             sine.100
GPNAM4             sine.100
GPZ1                 11.00 %
GPZ2                 17.00 %
GPZ3                 40.00 %
GPZ4                -40.00 %
P16                1000.00 usec

F2 - Processing parameters
SI                    131072
SF               500.0300101 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

Figure S5. ^{1}H nOe NMR spectrum of **4a**.



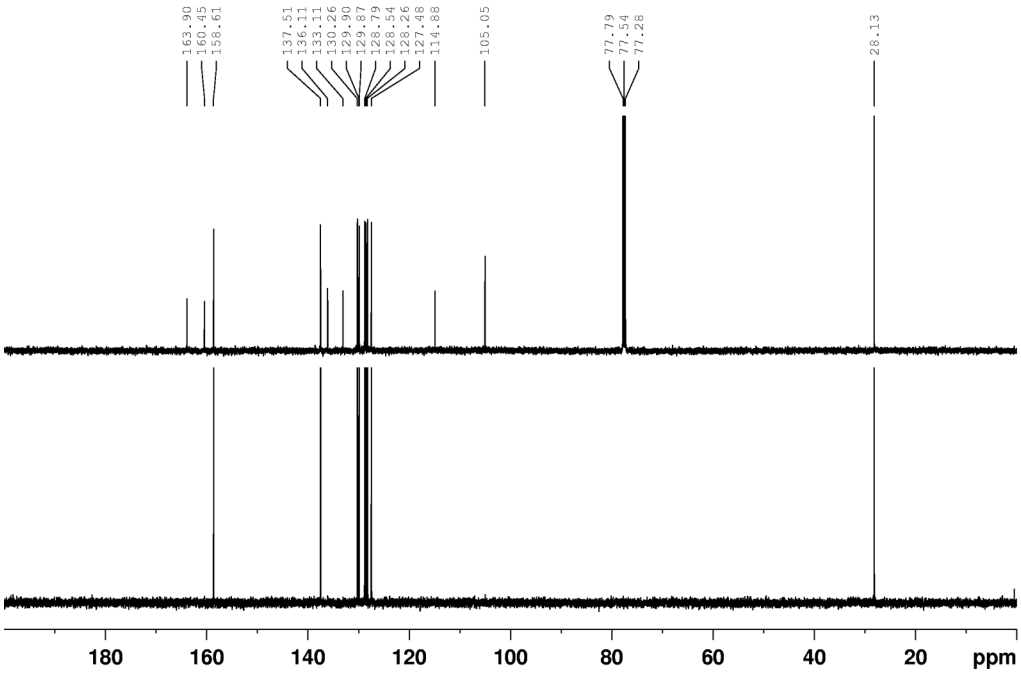

```
Current Data Parameters
NAME                  YN173
EXPNO                     8
PROCNO                    1

F2 - Acquisition Parameters
Date_              20110217
Time                   0.19
INSTRUM                spect
PROBHD   5 mm CPTCI 1H-
PULPROG          selnogp.3
TD                     65536
SOLVENT                CDCl3
NS                         4
DS                         1
SWH                7500.000 Hz
FIDRES             0.114441 Hz
AQ                 4.3691168 sec
RG                        57
DW                    66.667 usec
DE                     6.00 usec
TE                    300.0 K
D1                10.00000000 sec
D8                 0.80000001 sec
D16                0.00020000 sec
d20                0.39880002 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                      8.00 usec
P2                     16.00 usec
P12                100000.00 usec
PL0                  120.00 dB
PL1                   -5.40 dB
SFO1           500.0330879 MHz
SP2                   62.81 dB
SPNAM2           Gaus1.1000
SPOAL2                0.500
SPOFFS2            1200.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1             sine.100
GPNAM2             sine.100
GPNAM3             sine.100
GPNAM4             sine.100
GPZ1                 11.00 %
GPZ2                 17.00 %
GPZ3                 40.00 %
GPZ4                -40.00 %
P16                1000.00 usec

F2 - Processing parameters
SI                    131072
SF               500.0300100 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

Figure S6. ^{1}H nOe NMR spectrum of **4a**.



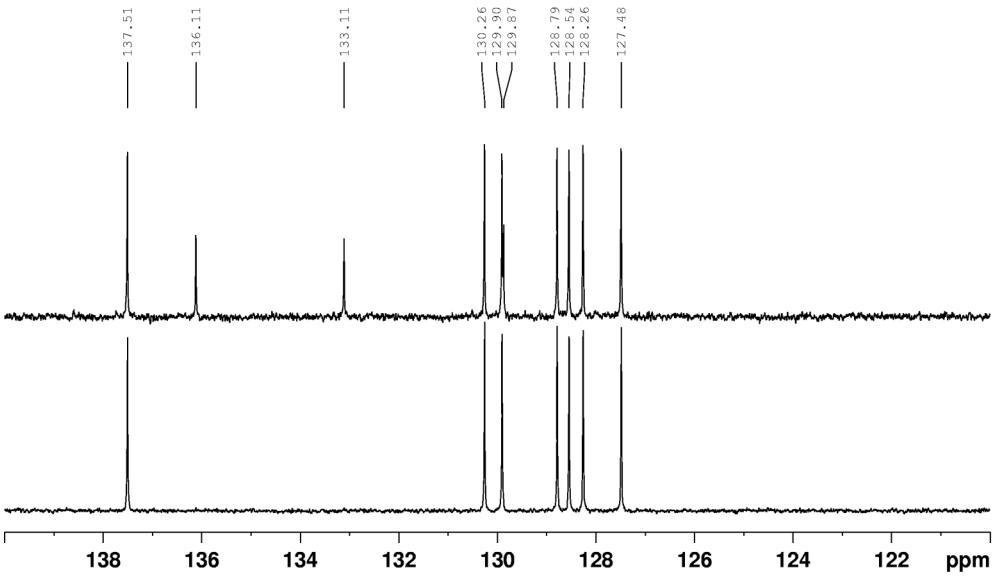

```
Current Data Parameters
NAME                  YN173
EXPNO                     7
PROCNO                    1

F2 - Acquisition Parameters
Date_              20110217
Time                  0.07
INSTRUM              spect
PROBHD    5 mm CPTCI 1H-
PULPROG          selnogp.3
TD                    65536
SOLVENT               CDCl3
NS                        4
DS                        1
SWH                7500.000 Hz
FIDRES             0.114441 Hz
AQ                 4.3691168 sec
RG                     50.8
DW                   66.667 usec
DE                    6.00 usec
TE                   300.0 K
D1              10.00000000 sec
D8               0.80000001 sec
D16              0.00020000 sec
d20              0.39880002 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                     8.00 usec
P2                    16.00 usec
P12                50000.00 usec
PL0                  120.00 dB
PL1                   -5.40 dB
SFO1           500.0330879 MHz
SP2                   56.79 dB
SPNAM2          Gaus1.1000
SPOAL2               0.500
SPOFFS2            982.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1              sine.100
GPNAM2              sine.100
GPNAM3              sine.100
GPNAM4              sine.100
GPZ1                 11.00 %
GPZ2                 17.00 %
GPZ3                 40.00 %
GPZ4                -40.00 %
P16                1000.00 usec

F2 - Processing parameters
SI                    131072
SF             500.0300101 MHz
WDW                       EM
SSB                        0
LB                    0.30 Hz
GB                         0
PC                    1.00
```

Figure S7. ^{1}H nOe NMR spectrum of **4a**.




```
Current Data Parameters
NAME              YN177-13C
EXPNO                     2
PROCNO                    1

F2 - Acquisition Parameters
Date_              20110303
Time                 21.07
INSTRUM              spect
PROBHD    5 mm CPTCI 1H-
PULPROG            zgpg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        4
SWH               29761.904 Hz
FIDRES             0.454131 Hz
AQ                 1.1010548 sec
RG                     2050
DW                   16.800 usec
DE                    6.00 usec
TE                   300.0 K
D1              2.00000000 sec
d11             0.03000000 sec
DELTA           1.89999998 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                    12.00 usec
PL1                   -6.00 dB
SFO1          125.7452168 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                     1H
PCPD2                80.00 usec
PL2                  -1.00 dB
PL12                 14.00 dB
PL13                 14.00 dB
SFO2           500.0320001 MHz

F2 - Processing parameters
SI                    131072
SF             125.7325849 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                    1.40
```

Figure S8. ^{13}C and DEPT NMR spectra of **4a**.




```
Current Data Parameters
NAME                  YN177-13C
EXPNO                         4
PROCNO                        1

F2 - Acquisition Parameters
Date_                  20110303
Time                      21.15
INSTRUM                   spect
PROBHD    5 mm CPTCI 1H-
PULPROG                dept45
TD                      65536
SOLVENT                 CDCl3
NS                         32
DS                          4
SWH                 29761.904 Hz
FIDRES                0.454131 Hz
AQ                    1.1010548 sec
RG                         2050
DW                       16.800 usec
DE                        6.00 usec
TE                       300.0 K
CNST2               145.0000000
D1                    2.00000000 sec
d2                    0.00344828 sec
d12                   0.00002000 sec
DELTA                 0.00001528 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                        13C
P1                        12.00 usec
p2                        24.00 usec
PL1                       -6.00 dB
SFO1                125.7452168 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                        1H
P3                        15.00 usec
p4                        30.00 usec
PCPD2                     80.00 usec
PL2                       -1.00 dB
PL12                      14.00 dB
SFO2                500.0320001 MHz

F2 - Processing parameters
SI                         131072
SF                  125.7325852 MHz
WDW                           EM
SSB                            0
LB                          1.00 Hz
GB                             0
PC                          1.40
```

Figure S9. ^{13}C and DEPT NMR spectra of **4a**.

Knoevenagel condensation in the absence of cage 1

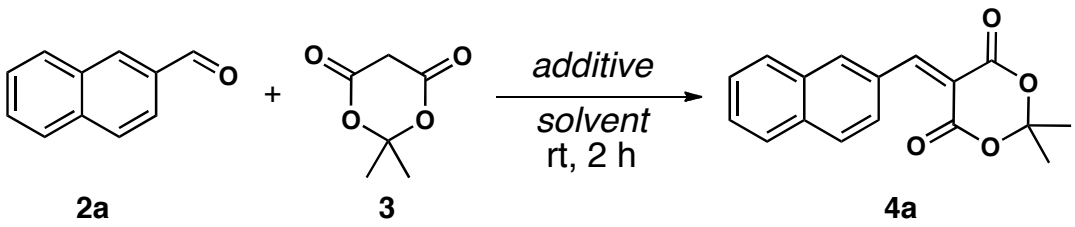


Table S1. Yields of Condensation Product **4a**.

Entry	Cage	Additive	Solvent	Yield[a] (%)
1	**1**	–	D_2O	92
2	–	–	D_2O	2
3	–	–	MeOH	8
4	–	–	DMSO	1
5	–	$(en)Pd(NO_3)_2$	D_2O	3
6	–	TPT[b]	D_2O	8

[a] Determined by ^1H NMR

[b] TPT:2,4,6-tri(4-pyridyl)-1,3,5-triazine

Encapsulation of Knoevenagel condensation product 4a within cage 1

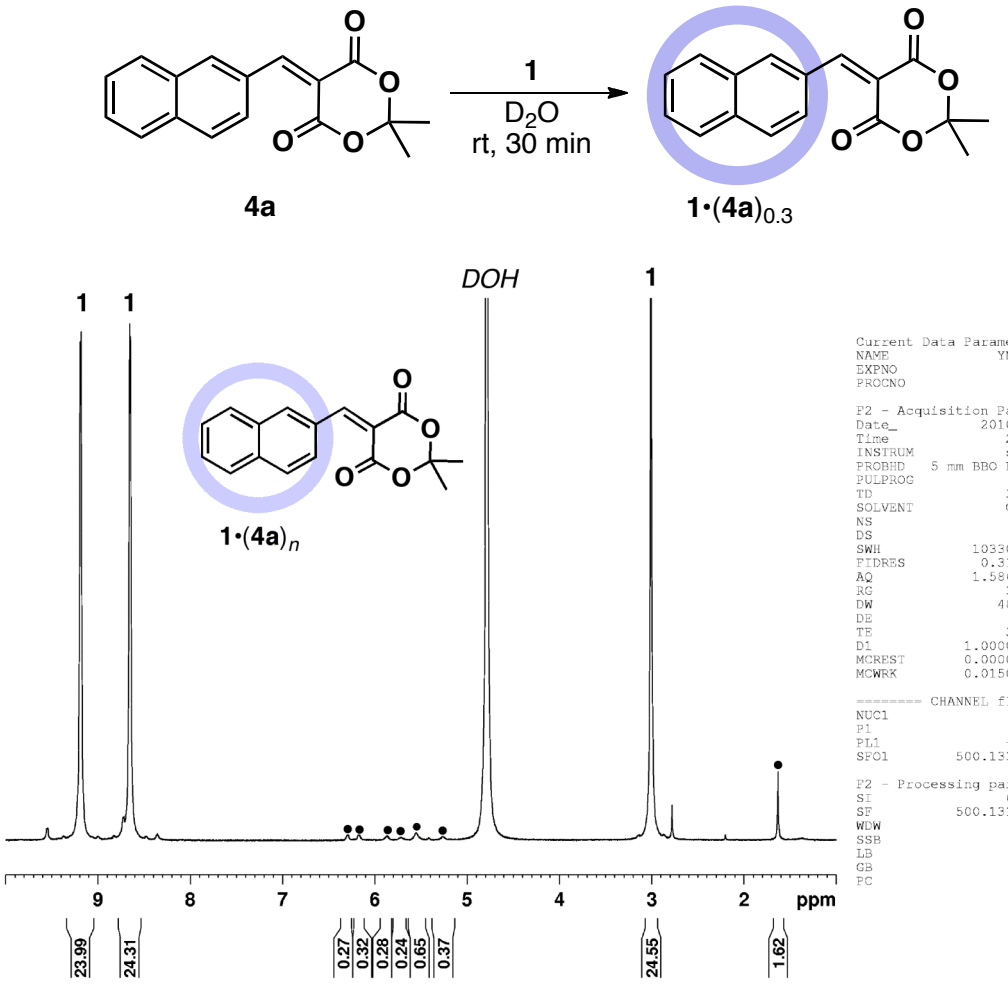
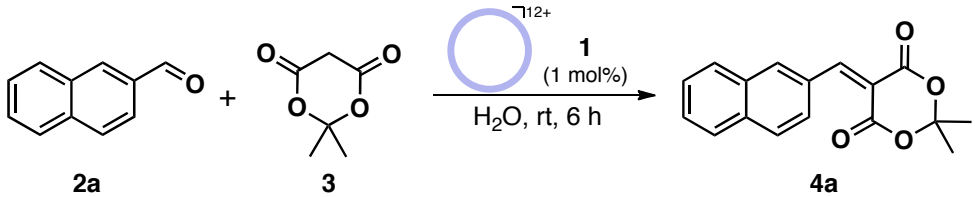


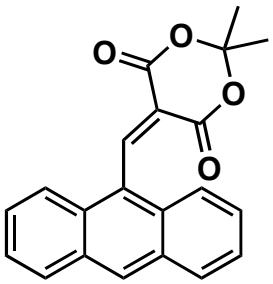
Figure S10. Encapsulation of condensation product **4a** within cage **1**. Only 0.3 molecule of product **4a** was encapsulated in cage **1** on average. Compared with aldehyde **2a** (encapsulation number: 4 molecules), product **4a** was a poor guest for cage **1**.

Typical procedure for the Knoevenagel condensation of aldehyde 2 with Meldrum's Acid 3 in the presence of a catalytic amount of cage 1



Aldehyde **2a** (0.500 mmol, 78.1 mg) and compound **3** (0.500 mmol, 72.1 mg) were added to an aqueous solution (5 mL) of cage **1** (15.0 mg, 5.00×10^{-3} mmol; 1 mol%), and the reaction mixture was stirred at room temperature for 6 h. The product was extracted with $CHCl_3$ (2 × 5 mL), and the organic layer was evaporated *in vacuo* to give condensation product **4a** in 96% NMR yield. The obtained product **4a** was purified by recrystallization from refluxing ethanol to afford a pale yellow solid (121 mg, 86%).

5-(anthracen-9-ylmethylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (4b)



4b

Reaction condition: Reaction time 96 h

Yield: 63% (NMR)

Physical data: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.47 (1H, s, H_a), 8.55 (1H, s, H_b), 8.06 (2H, d, J = 8.8 Hz, H_c), 7.84 (2H, d, J = 9.1 Hz, H_d), 7.52 (1H, t, J = 9.1, H_e), 7.50 (1H, t, J = 8.8 Hz, H_f), 1.90 (6H, s, H_g); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 161.91 (C), 157.89 (C), 157.75 (CH), 130.94 (C), 130.29 (CH), 129.34 (CH), 128.63 (C), 127.09 (CH), 126.80 (C), 125.58 (CH), 124.52 (CH), 121.02 (C), 104.97 (C), 28.17 (CH_3); GC-MS (EI): m/z = 332 $[M]^+$; IR (ATR, cm^{-1}): 3049, 3031, 3013, 2925, 2854, 1764, 1737, 1631, 1446, 1396, 1385, 1365, 1334, 1292, 1218, 1202, 1123, 1067, 1028; m.p. 193.6–194.3 ºC; E.A. Calcd. for $C_{21}H_{16}O_4$: C, 75.89; H, 4.85; Found: C, 75.66; H, 5.03.

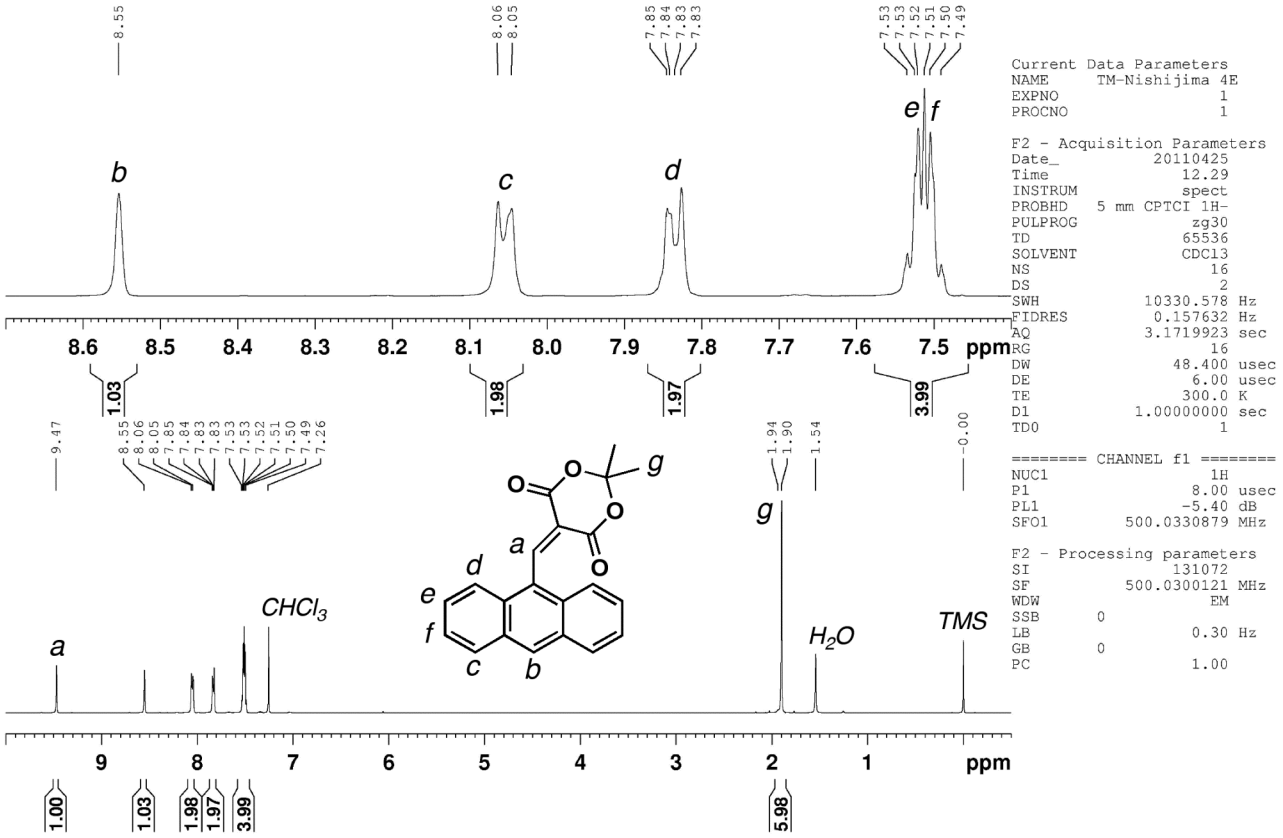


Figure S11. ^{1}H NMR spectrum of **4b**.

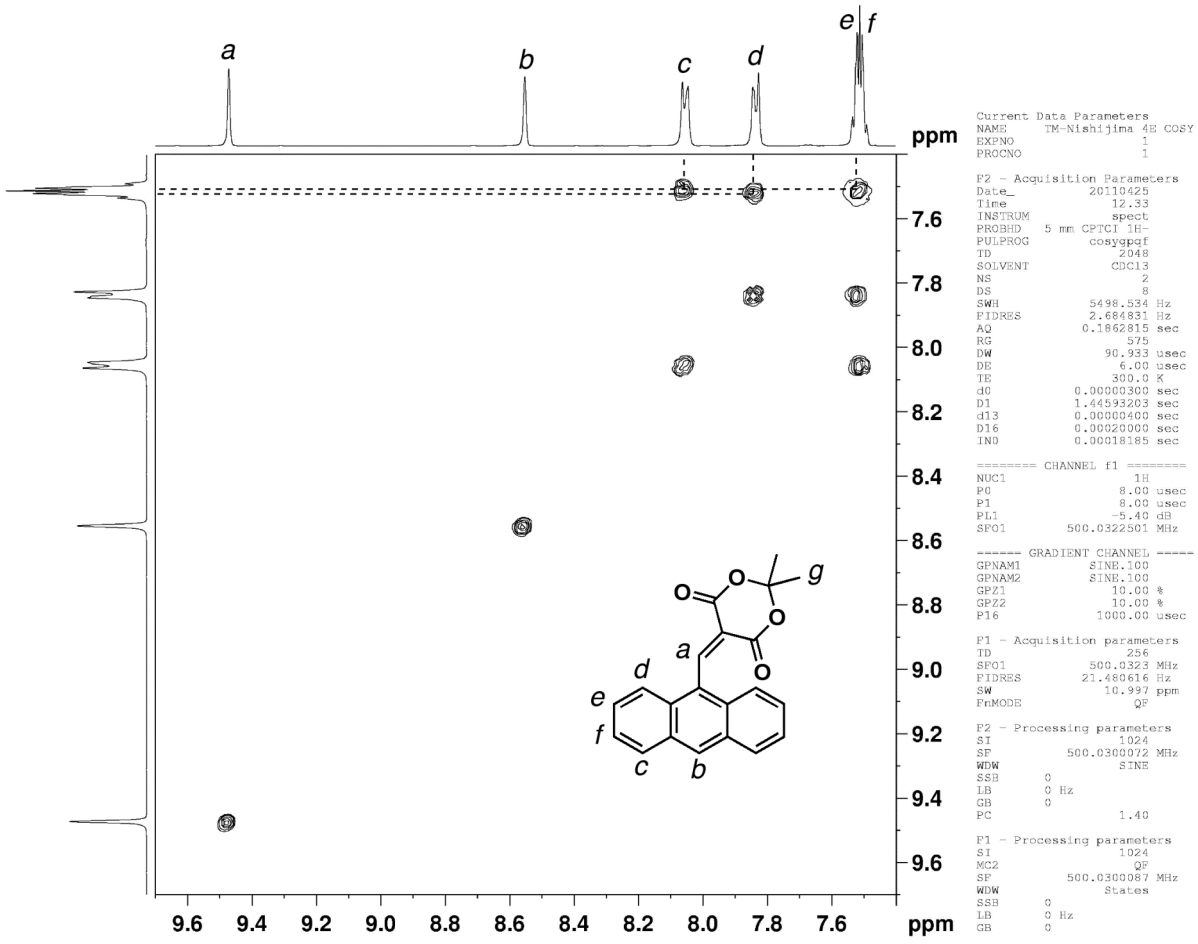


Figure S12. H–H COSY spectrum of **4b**.

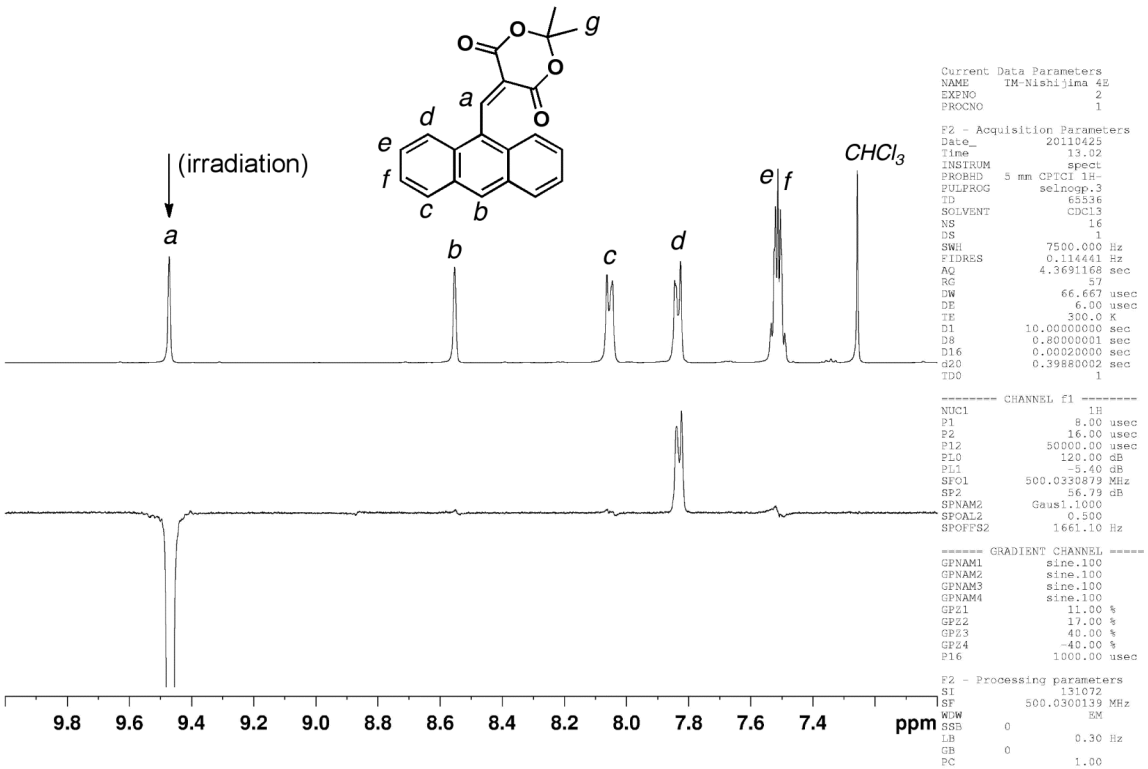


Figure S13. ^{1}H nOe NMR spectrum of **4b**.

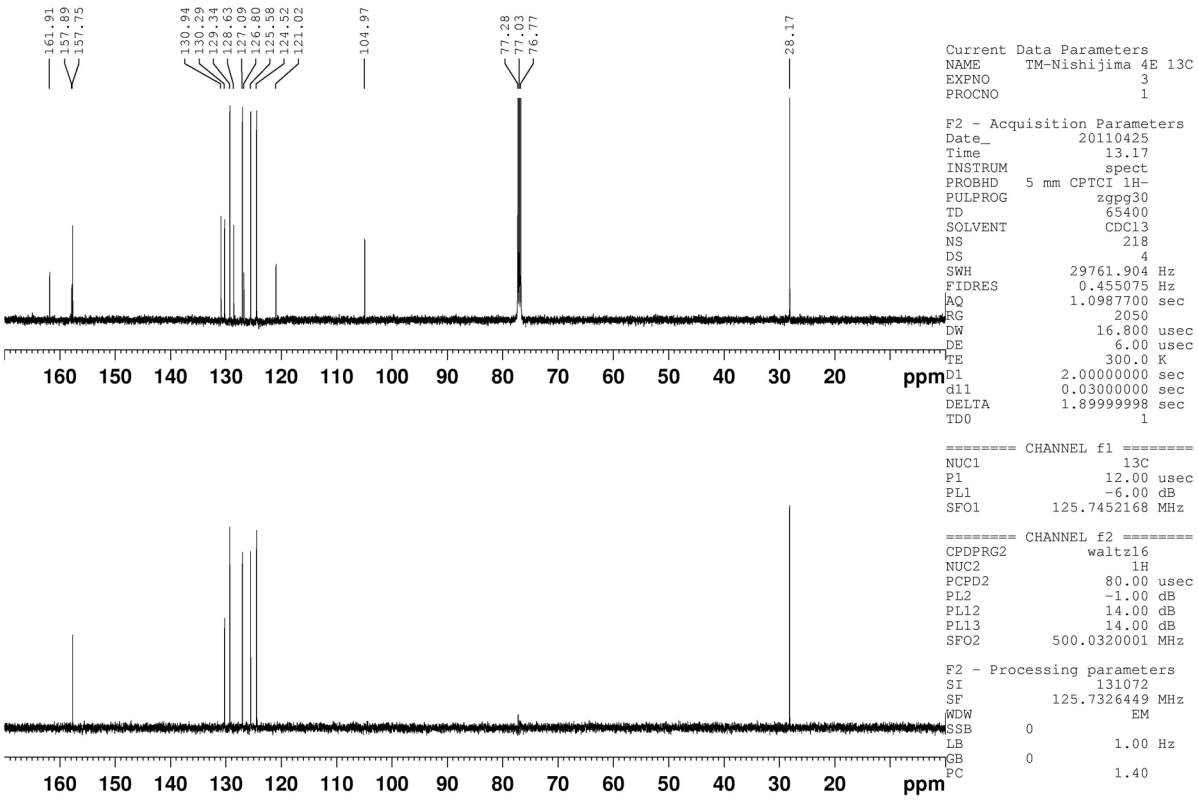


Figure S14. ^{13}C and DEPT NMR spectra of **4b**.

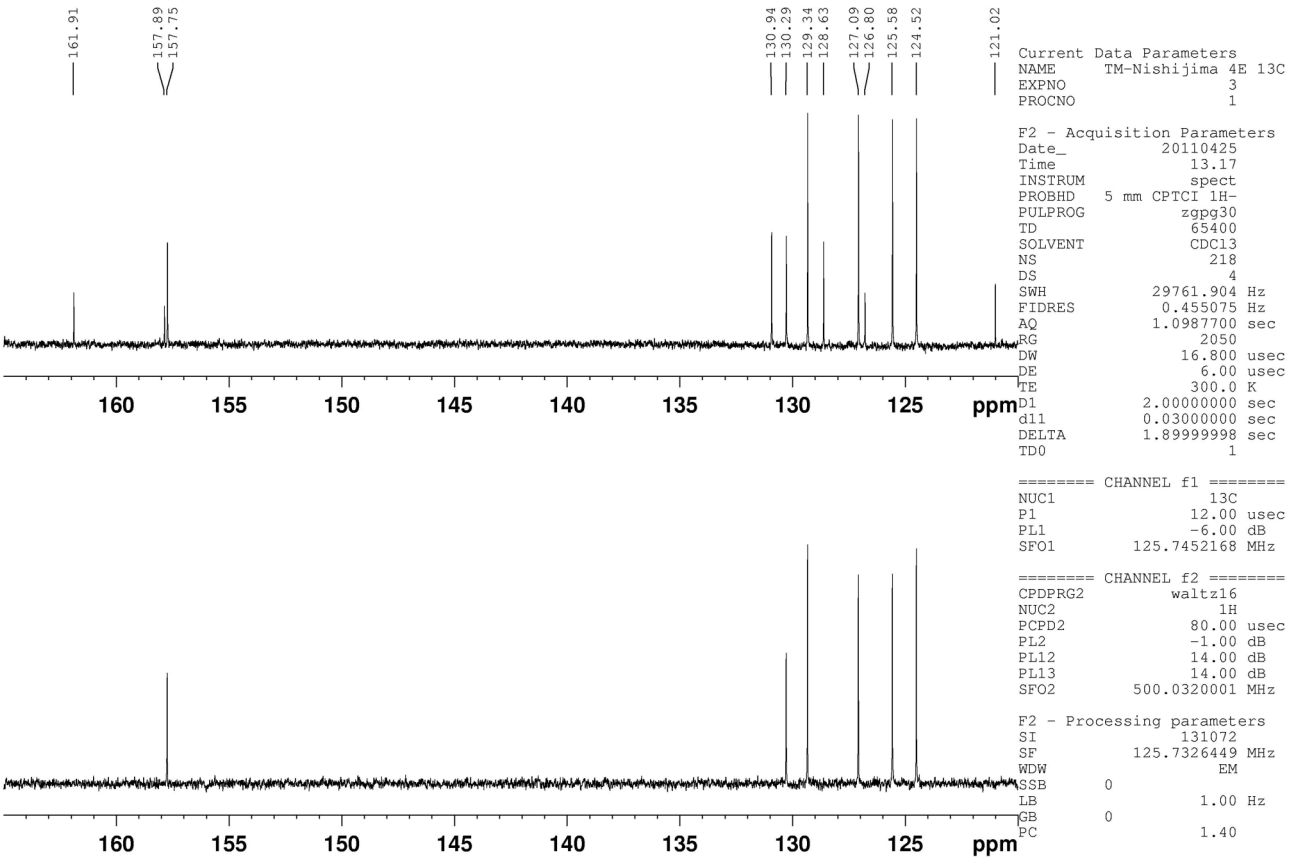
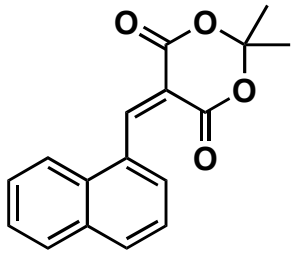


Figure S15. ^{13}C and DEPT NMR spectra of **4b**.

2,2-Dimethyl-5-(naphthalen-1-ylmethylene)-1,3-dioxane-4,6-dione (4c)



4c

Reaction condition: 24 h

Yield: 67% (NMR)

Physical data: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.22 (1H, s, H_a), 8.02 (2H, d, J = 7.8 Hz, H_b and H_c), 7.98 (1H, d, J = 8.3 Hz, H_d), 7.92 (1H, d, J = 7.8, H_e), 7.62 (1H, t, J = 8.3 Hz, H_f), 7.58 (1H, t, J = 7.8 Hz, H_g), 7.54 (1H, t, J = 7.8 Hz, H_h), 1.87 (6H, s, H_i); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 162.78 (C), 159.41 (C), 156.48 (CH), 133.32 (C), 133.23 (CH), 131.75 (C), 129.97 (CH), 129.17 (CH), 129.02 (C), 127.80 (CH), 126.68 (CH), 124.94 (CH), 123.60 (CH), 117.01 (C), 104.81 (C), 27.84 (CH_3); GC-MS (EI): m/z = 282 $[M]^+$; IR (ATR, cm^{-1}): 3016, 2997, 2989, 1762, 1732, 1624, 1394, 1381, 1358, 1284, 1212, 1198, 1118, 1025; m.p. 144.9–145.4 ºC; E.A. Calcd. for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00; Found: C, 72.26; H, 5.09.

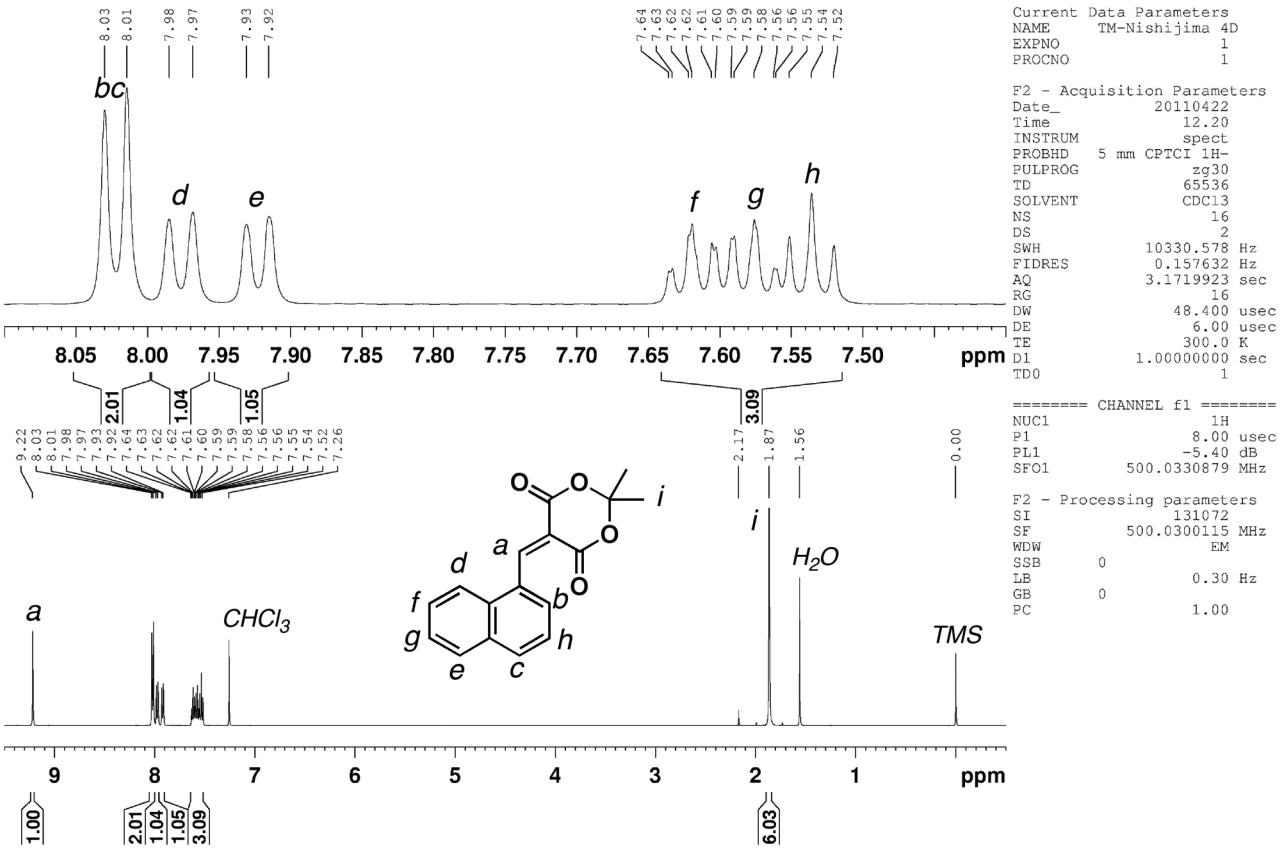


Figure S16. ^{1}H NMR spectrum of **4c**.

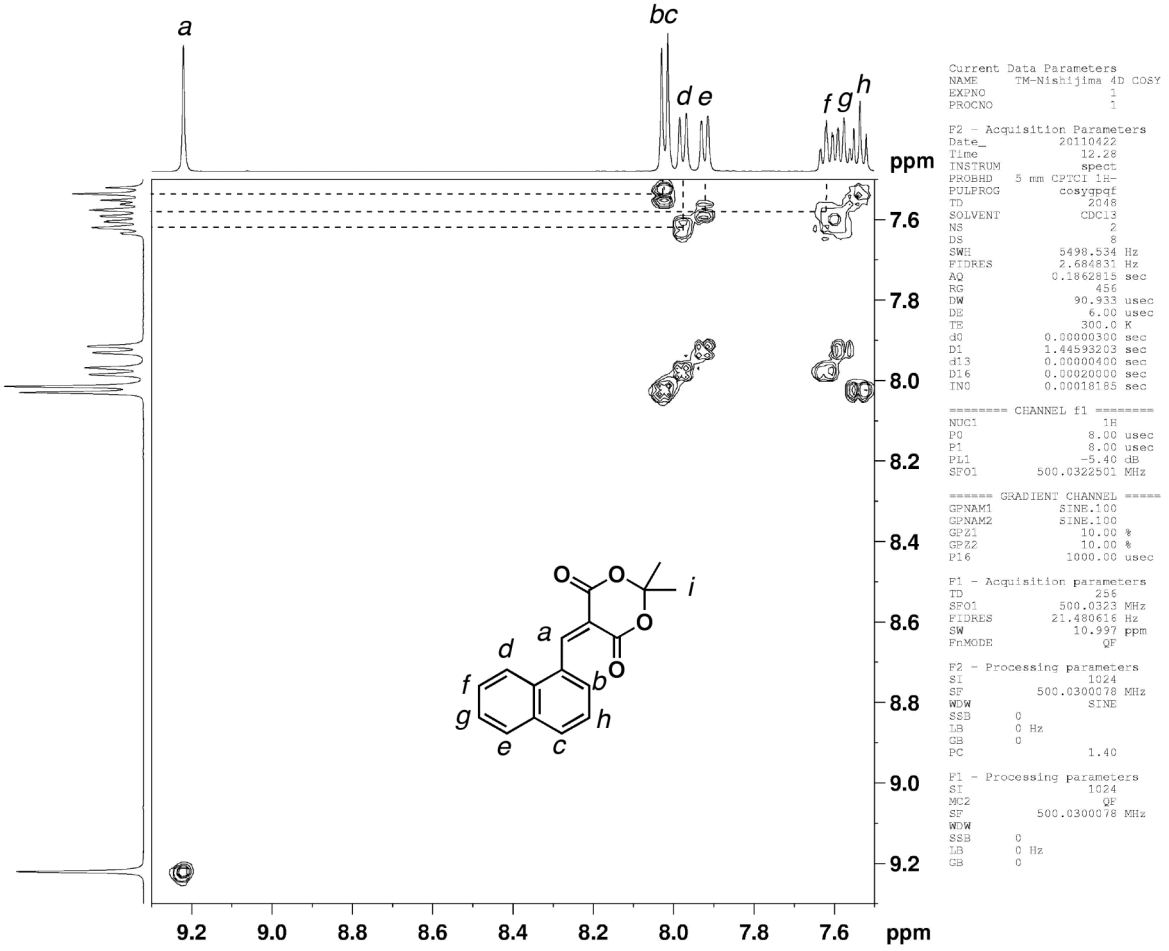


Figure S17. H–H COSY spectrum of **4c**.

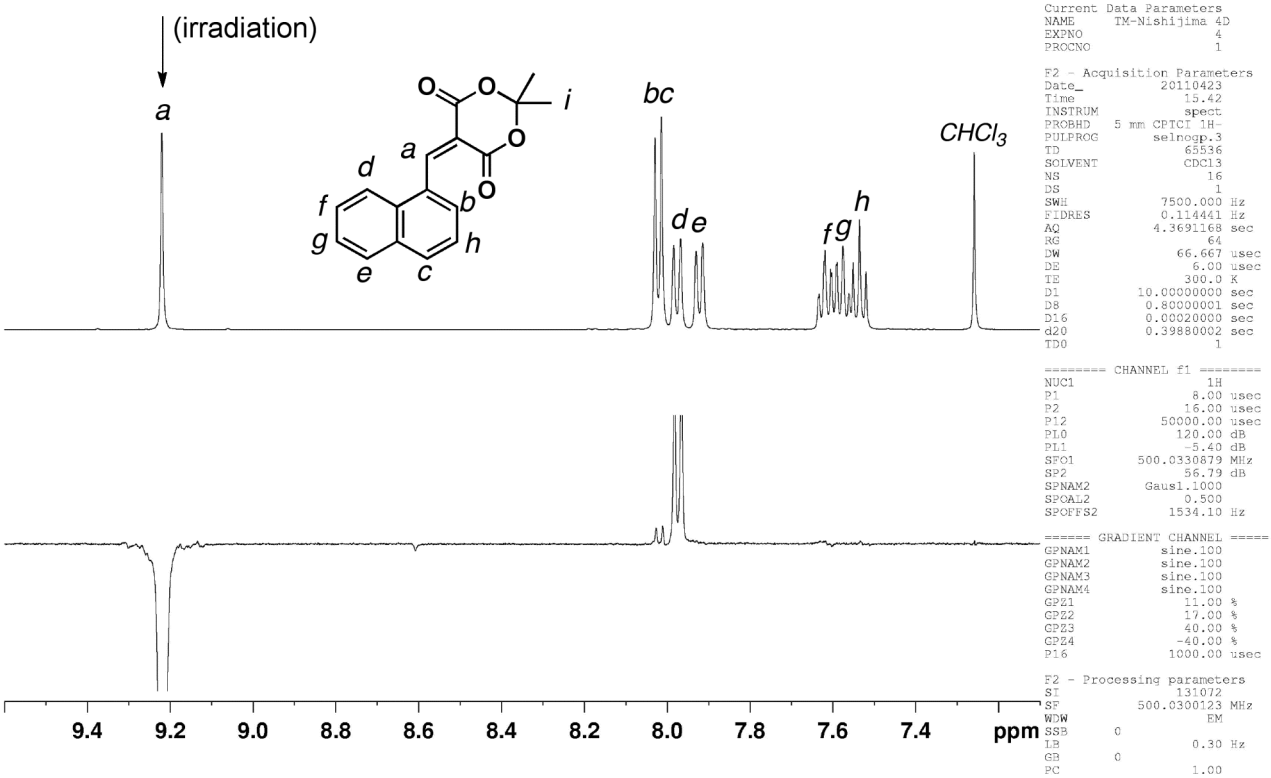


Figure S18. ^{1}H nOe NMR spectrum of **4c**.

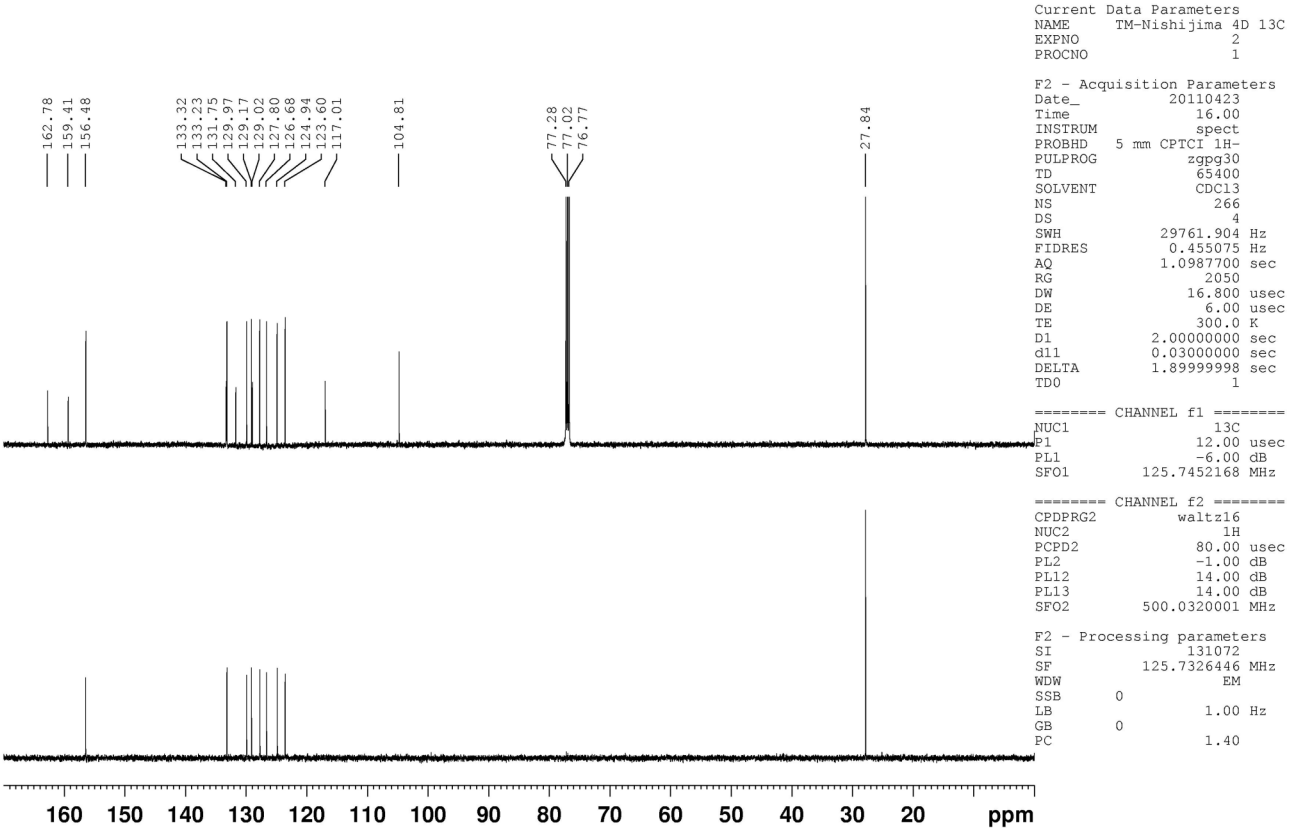


Figure S19. ^{13}C and DEPT NMR spectra of **4c**.

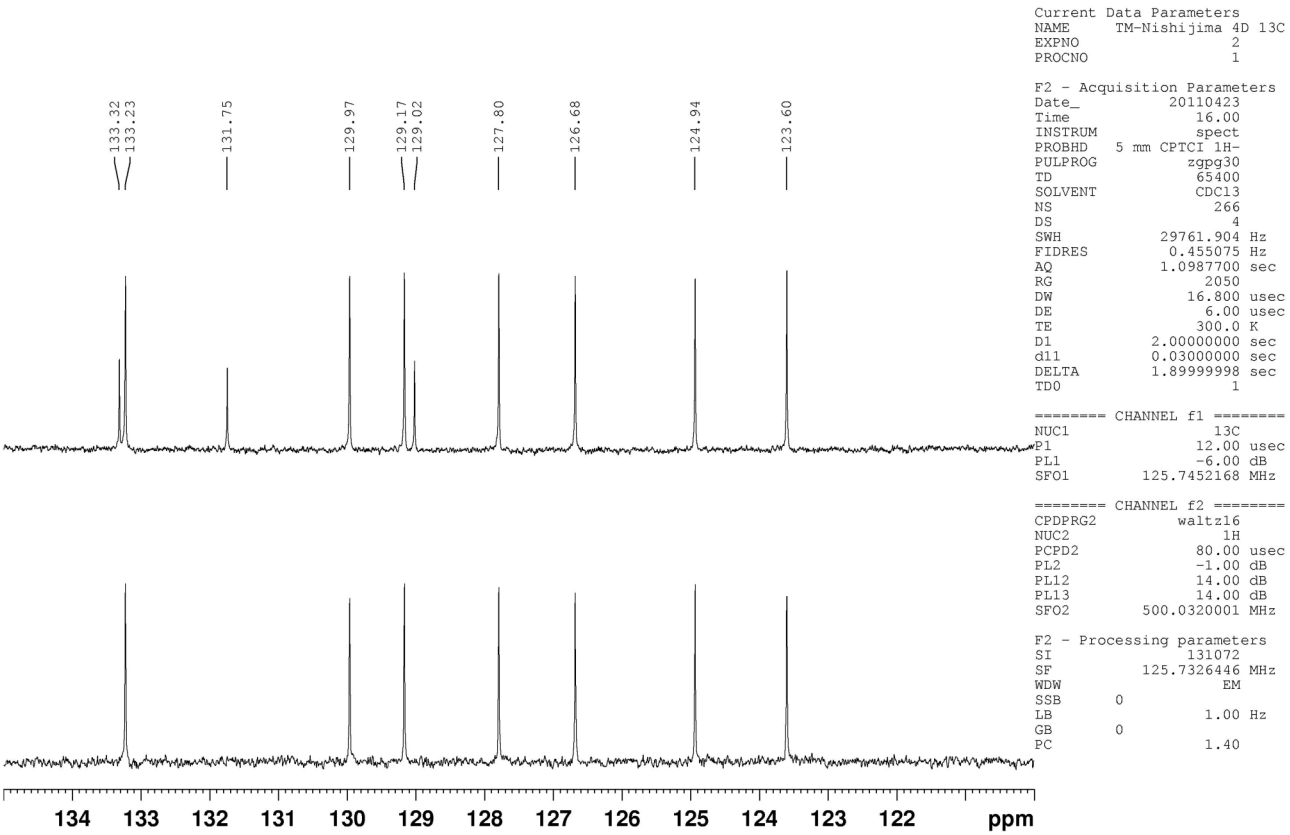
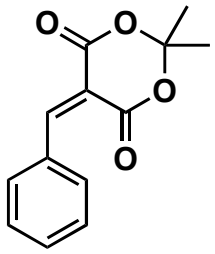


Figure S20. ^{13}C and DEPT NMR spectra of **4c**.

5-benzylidene-2,2-dimethyl-1,3-dioxane-4,6-dione (4d)



4d

Yield : 38% (NMR)

Physical data: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.43 (1H, s, H_a), 8.05 (2H, d, J = 7.5 Hz, H_b), 7.57 (1H, t, J = 7.4 Hz, H_c), 7.49 (2H, t, J = 7.4, H_d), 1.81 (6H, s, H_e); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 161.30 (C), 159.76 (C), 158.15 (CH), 133.71 (CH), 133.62 (CH), 131.71 (C), 128.75 (CH), 114.84 (C), 104.60 (C), 27.64 (CH_3); GC-MS (EI): m/z = 232 $[M]^+$, 174 $[M–(CH_3)_2CO]^+$; IR (ATR, cm^{-1}): 2999, 2923, 2852, 1767, 1732, 1621, 1394, 1283, 1363, 1299, 1222, 1202, 1029; m.p. 74.5–75.5 ºC; E.A. Calcd. for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21; Found: C, 66.96; H, 5.32.

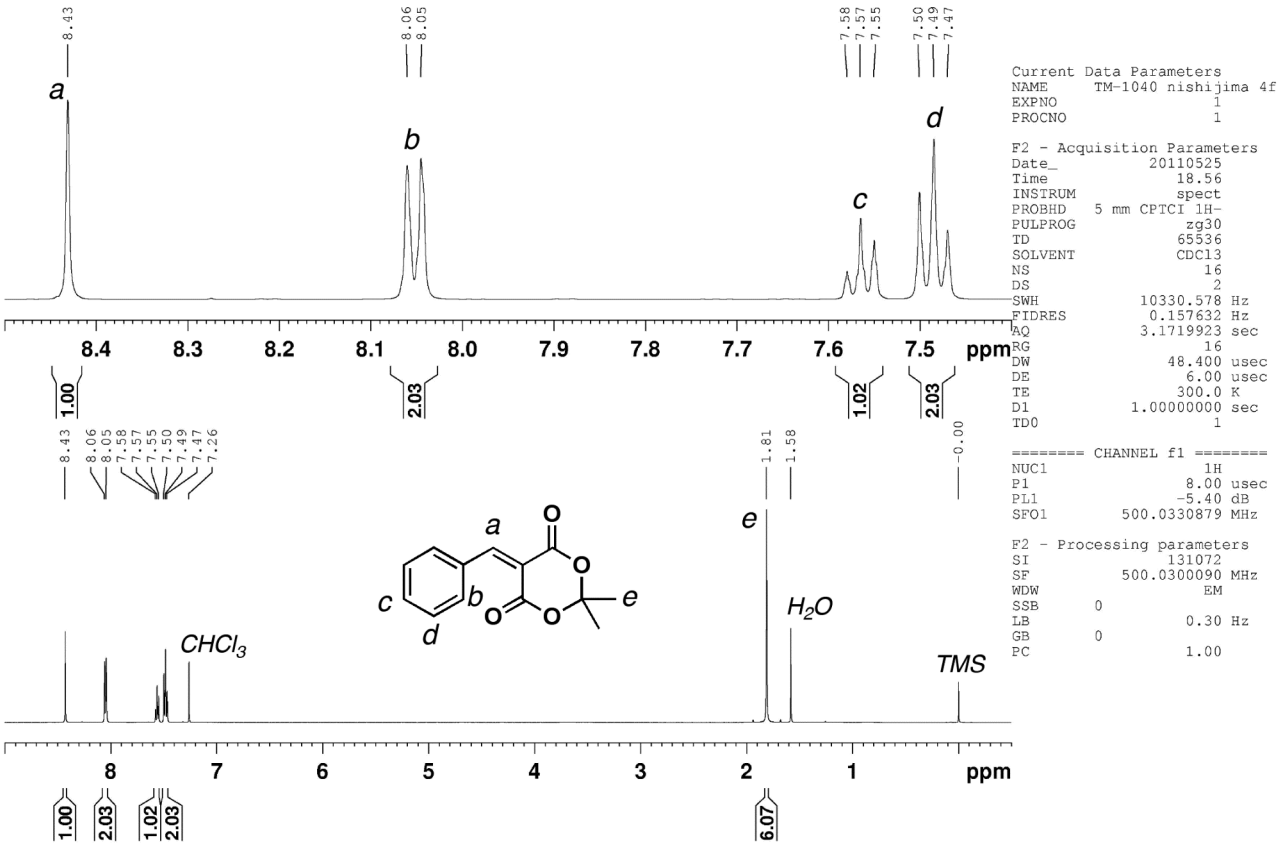


Figure S21. ^{1}H NMR spectrum of **4d**.

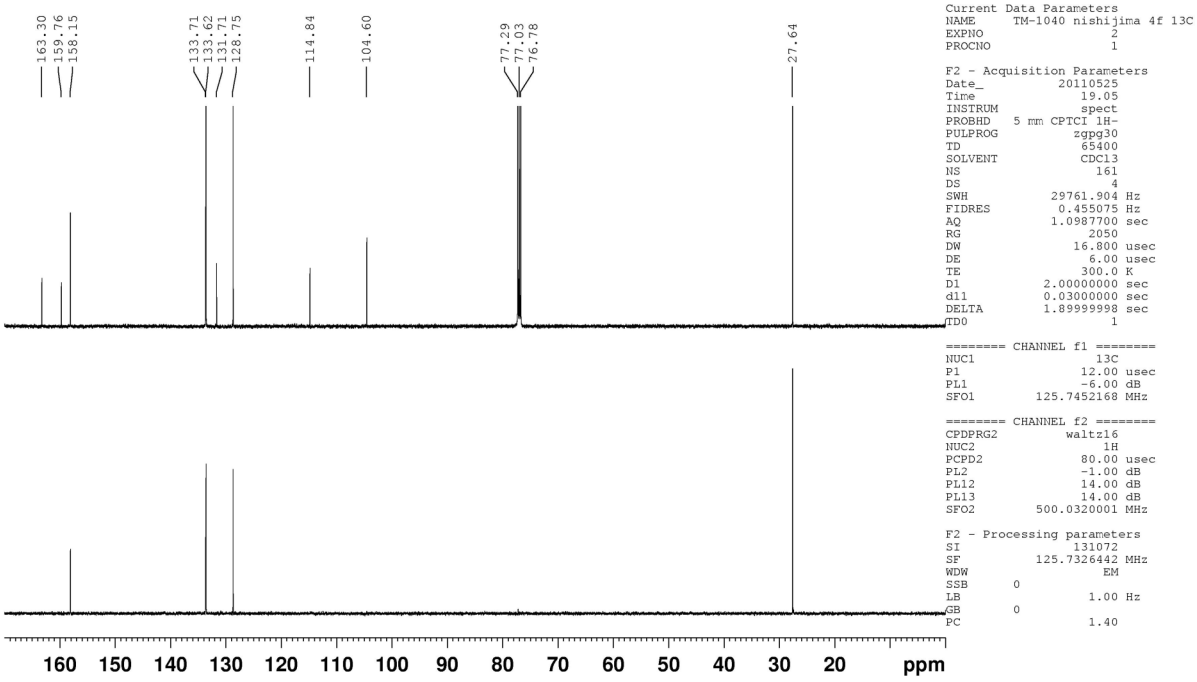


Figure S22. ^{13}C and DEPT NMR spectra of **4d**.

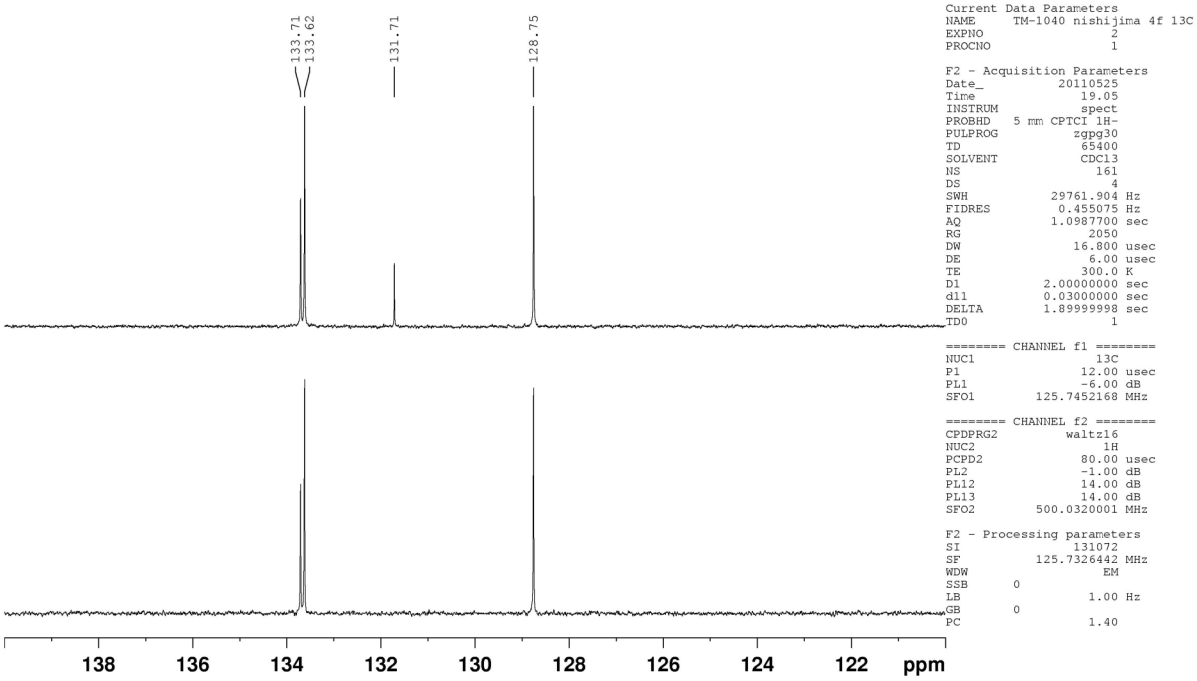
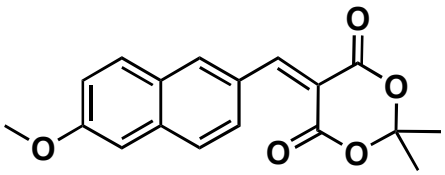


Figure S23. ^{13}C and DEPT NMR spectra of **4d**.

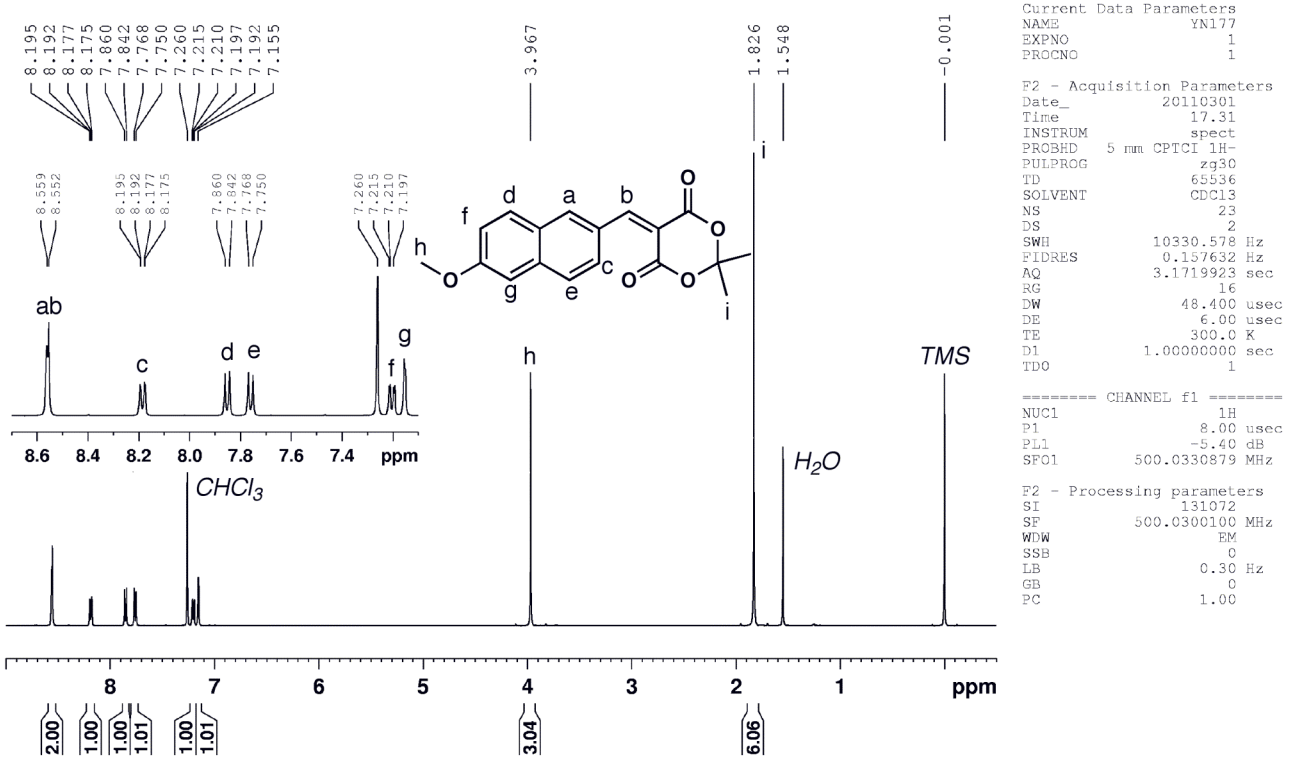
5-((6-Methoxynaphthalen-2-yl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (4e)



4e

Yield: 96% (NMR), 88% (isolated)

Physical data: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.56 (1H, br s, H_a), 8.55 (1H, s, H_b), 8.18 (1H, dd, *J* = 8.8, 1.7 Hz, H_c), 7.85 (1H, d, *J* = 9.0 Hz, H_d), 7.76 (1H, d, *J* = 8.8 Hz, H_e), 7.21 (1H, dd, *J* = 9.0, 2.4 Hz, H_f), 7.16 (1H, d, *J* = 2.4 Hz, H_g), 3.97 (3H, s, H_h), 1.83 (6H, s, H_i); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.8 (C), 160.9 (C), 160.3 (C), 158.5 (CH), 137.8 (C), 137.7 (CH), 131.7 (CH), 129.4 (CH), 128.1 (C), 127.3 (C), 127.1 (CH), 120.0 (CH), 112.7 (C), 106.0 (CH), 104.4 (C), 55.6 (CH_3), 27.6 (CH_3); GC-MS (EI): *m/z* = 312 $[M]^+$; IR (ATR, cm^{-1}): 2992, 2946, 1756, 1725, 1587, 1402, 1341, 1291, 1222, 1158, 1023, 1010; m.p. 191.2–192.2 ºC; E.A. Calcd. for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16. Found: C, 69.11; H, 5.32.




```
Current Data Parameters
NAME                  YN177
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20110301
Time                 17.31
INSTRUM              spect
PROBHD    5 mm CPTCI 1H-
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      23
DS                       2
SWH              10330.578 Hz
FIDRES           0.157632 Hz
AQ               3.1719923 sec
RG                      16
DW                 48.400 usec
DE                  6.00 usec
TE                 300.0 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   8.00 usec
PL1                 -5.40 dB
SFO1          500.0330879 MHz

F2 - Processing parameters
SI                  131072
SF            500.0300100 MHz
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                  1.00
```

Figure S24. ^{1}H NMR spectrum of **4e**.

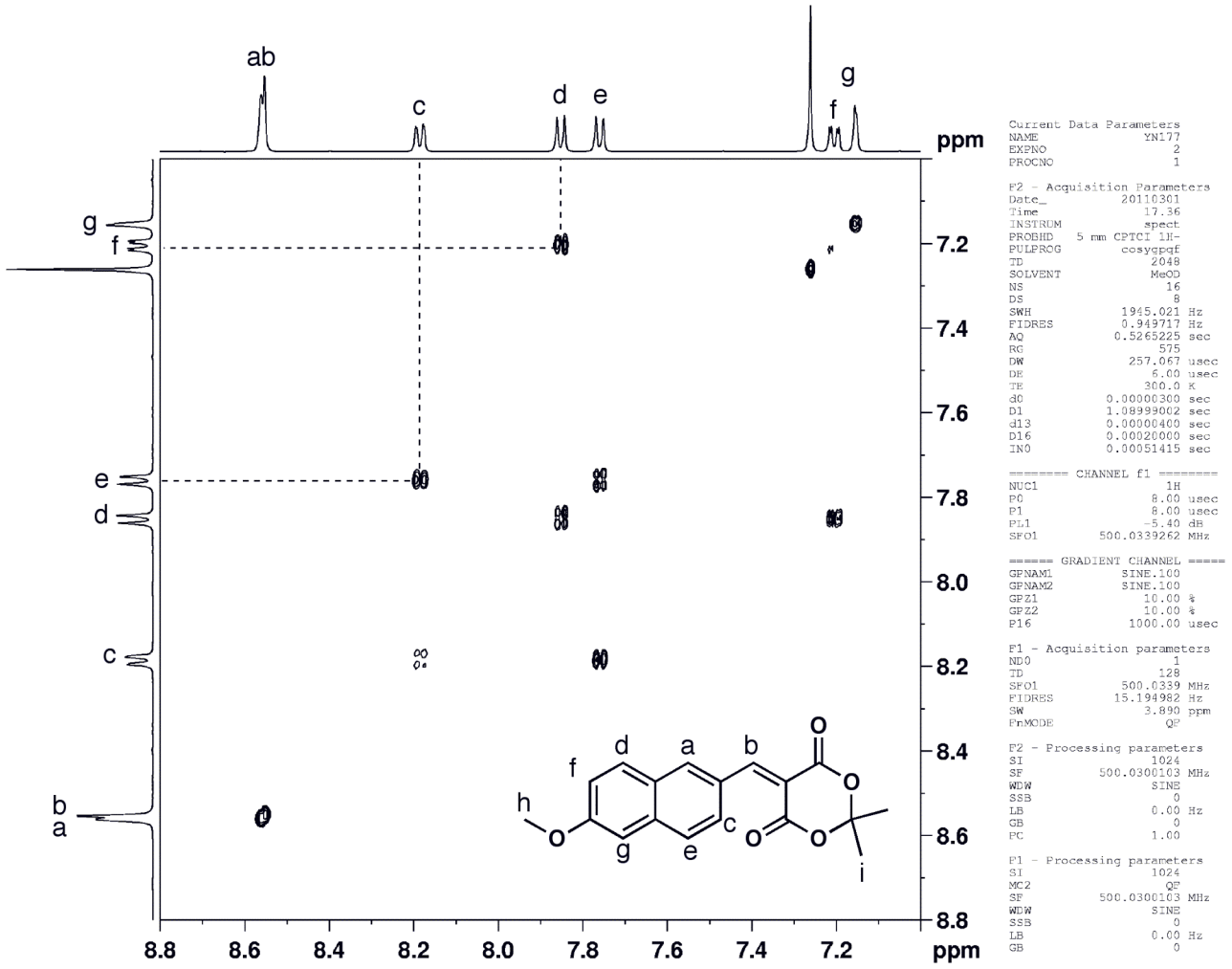


Figure S25. H–H COSY spectrum of **4e**.

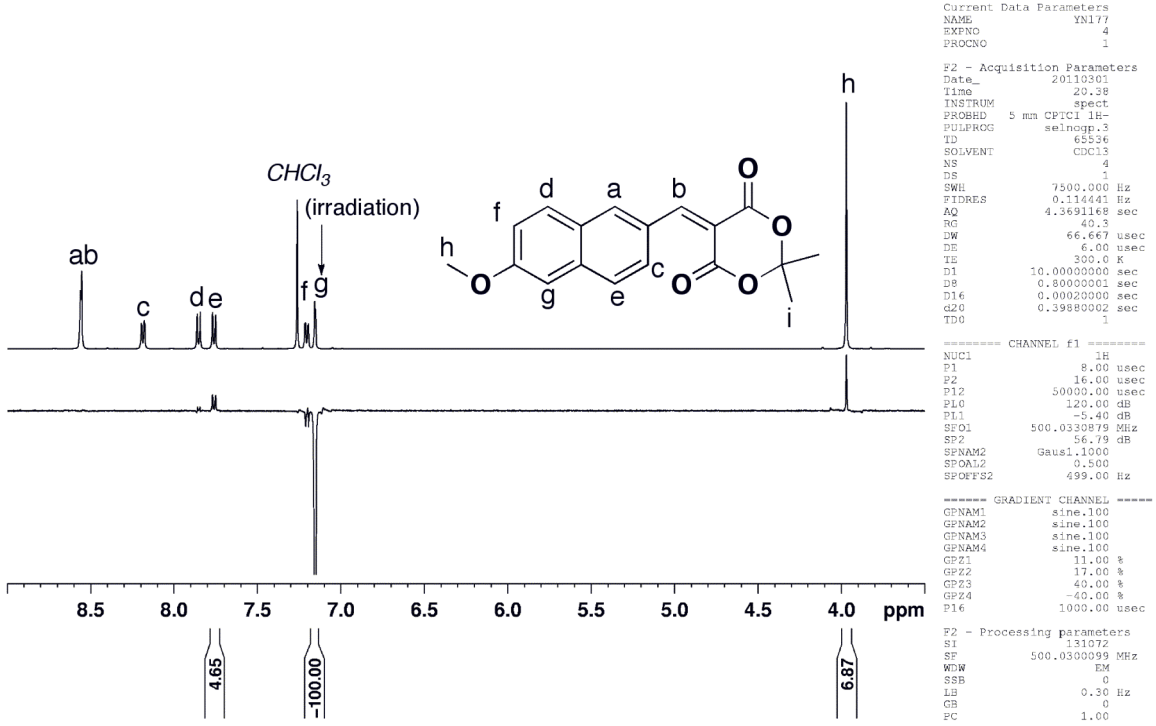


Figure S26. ^{1}H nOe NMR spectrum of **4e**.

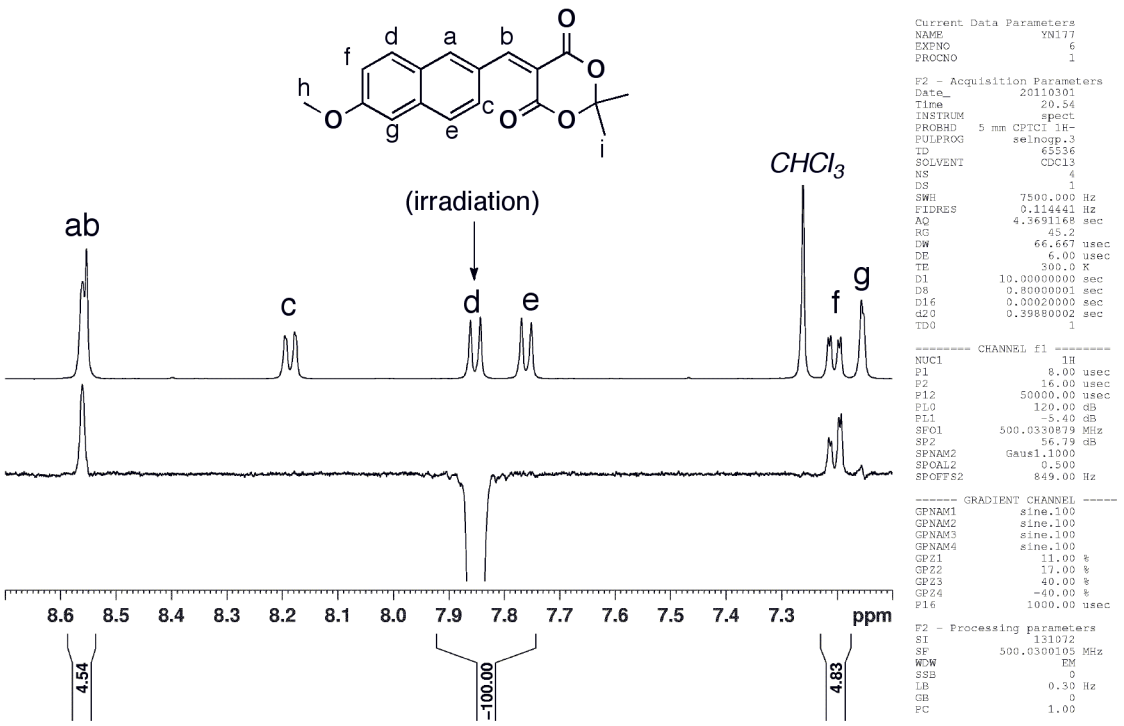


Figure S27. ^{1}H nOe NMR spectrum of **4e**.

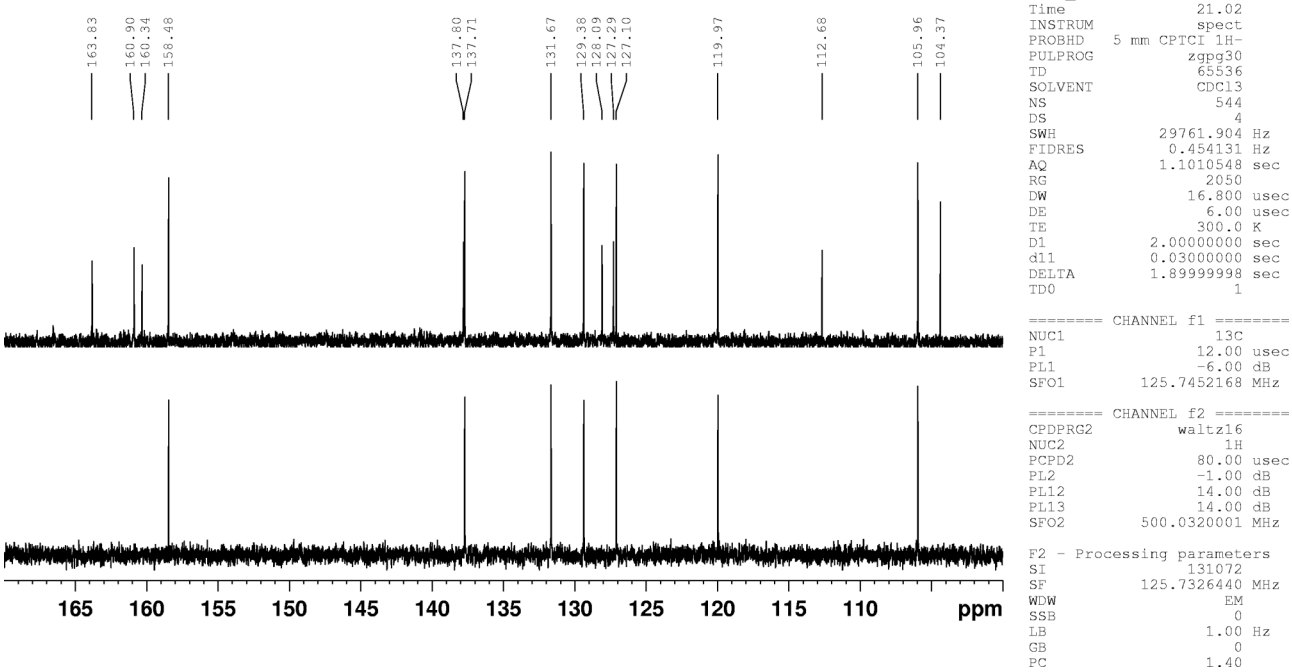
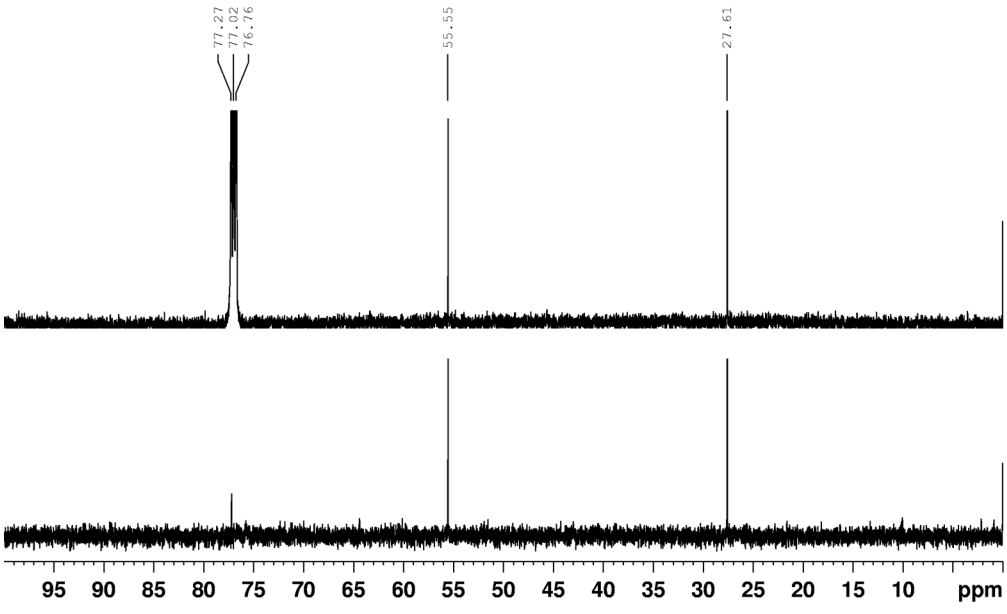


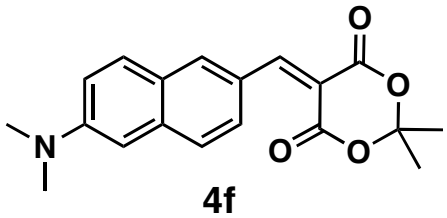
Figure S28. ^{13}C and DEPT NMR spectra of **4e**.




```
Current Data Parameters
NAME                  YN177
EXPNO                     7
PROCNO                    1

F2 - Acquisition Parameters
Date_              20110301
Time                 21.02
INSTRUM              spect
PROBHD    5 mm CPTCI 1H-
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      544
DS                        4
SWH              29761.904 Hz
FIDRES            0.454131 Hz
AQ                1.1010548 sec
RG                     2050
DW                  16.800 usec
DE                   6.00 usec
TE                  300.0 K
D1               2.00000000 sec
d11              0.03000000 sec
DELTA            1.89999998 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                    12.00 usec
PL1                   -6.00 dB
SFO1           125.7452168 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                    1H
PCPD2                 80.00 usec
PL2                   -1.00 dB
PL12                  14.00 dB
PL13                  14.00 dB
SFO2           500.0320001 MHz

F2 - Processing parameters
SI                    131072
SF             125.7326440 MHz
WDW                       EM
SSB                        0
LB                    1.00 Hz
GB                         0
PC                    1.40
```

Figure S29. ^{13}C and DEPT NMR spectra of **4e**.

5-((6-(Dimethylamino)naphthalen-2-yl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (4f)



4f

Yield: 82% (NMR)**,** 73% (isolated)

Physical data: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.53 (1H, d, *J* = 1.6 Hz, H_a), 8.50 (1H, s, H_b), 8.16 (1H, dd, *J* = 8.9, 1.6 Hz, H_c), 7.79 (1H, d, *J* = 9.2 Hz, H_d), 7.59 (1H, d, *J* = 8.9 Hz, H_e), 7.13 (1H, dd, *J* = 9.2, 2.4 Hz, H_f), 6.84 (1H, d, *J* = 2.4 Hz, H_g), 3.16 (6H, s, H_h), 1.81 (6H, s, H_i); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.49 (C), 160.86 (C), 158.77 (CH), 151.32 (CH), 139.40 (CH), 138.51 (C), 131.80 (CH), 129.87 (CH), 126.10 (CH), 125.40 (C), 125.23 (C), 115.93 (CH), 109.73 (C), 105.18 (CH), 103.97 (C), 40.32 (CH_3), 27.50 (CH_3); GC-MS (EI): *m/z* = 325 $[M]^+$; IR (ATR, cm^{-1}): 3002, 2976, 2925, 1739, 1712, 1630, 1574, 1432, 1402, 1387, 1308, 1273, 1225, 1205, 1175, 1138, 1025, 1004; m.p. 209.5–210.3 ºC; E.A. Calcd. for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31; Found: C, 69.75; H, 5.97; N, 4.16.

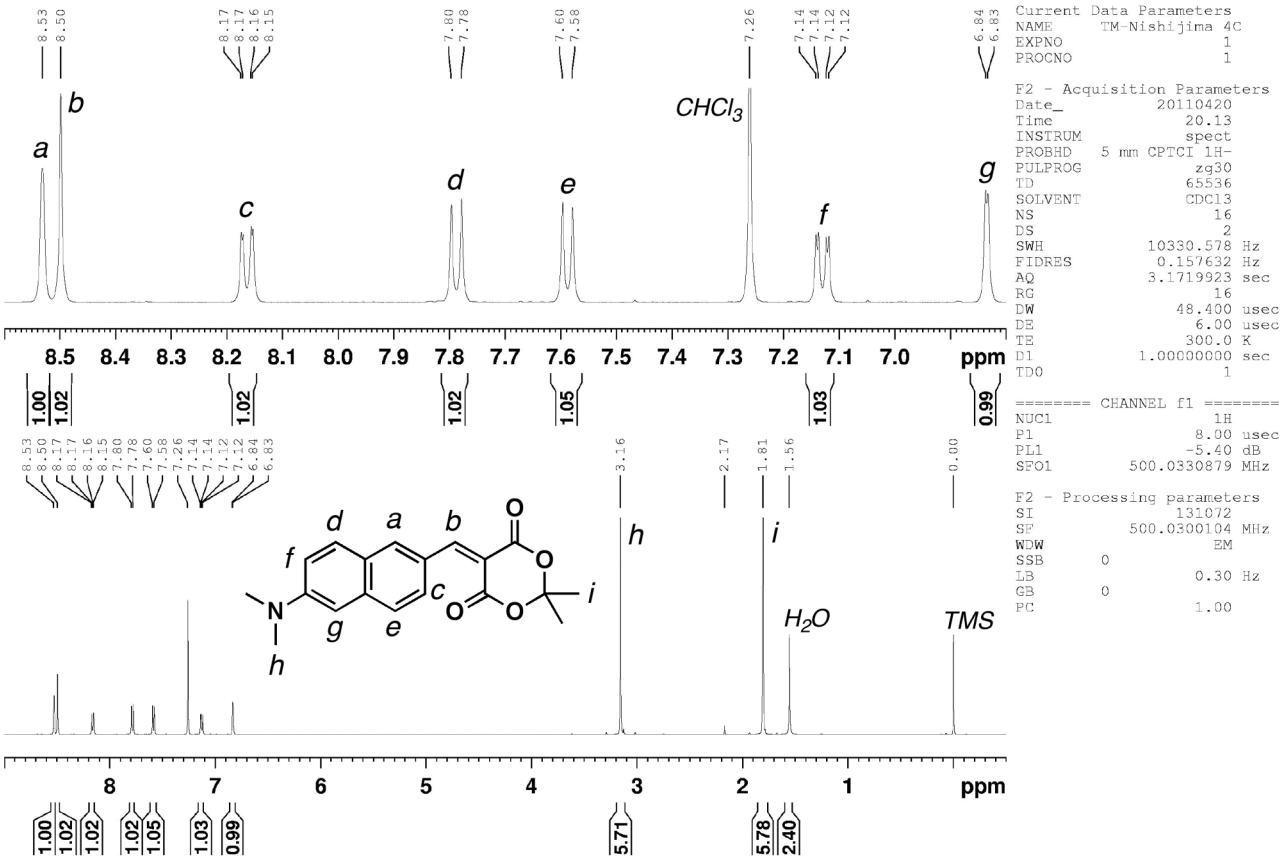


Figure S30. ^{1}H NMR spectrum of **4f**.

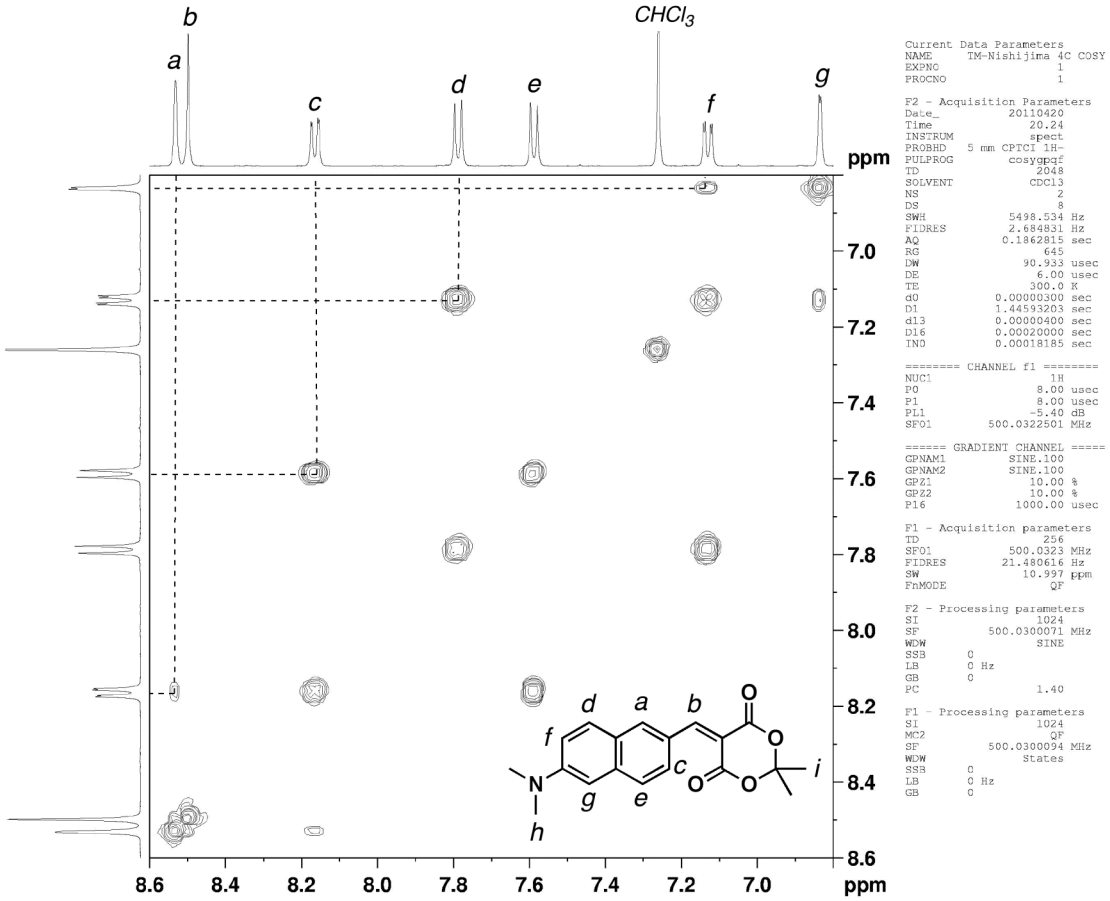


Figure S31. H–H COSY spectrum of **4f**.

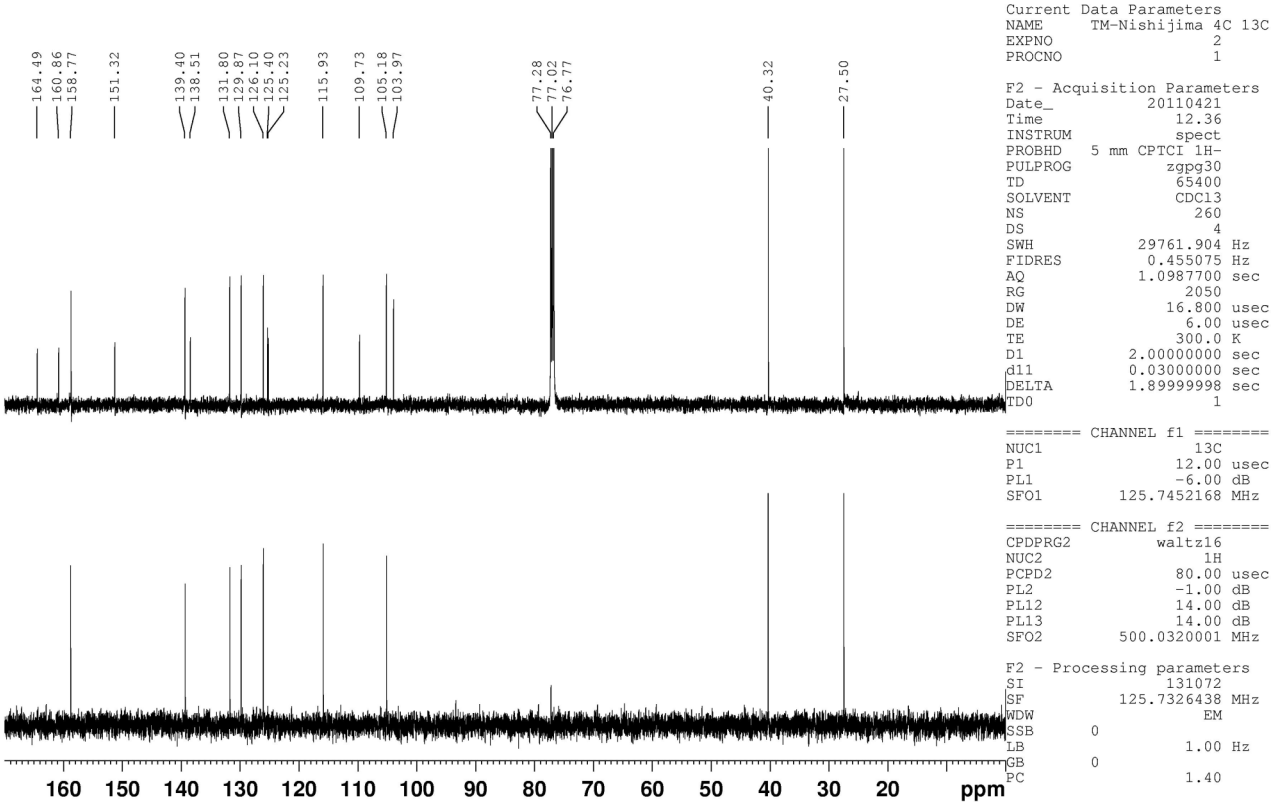


Figure S32. ^{13}C and DEPT NMR spectra of **4f**.

Molecular modeling of inclusion complex 1•(2a)$_4$

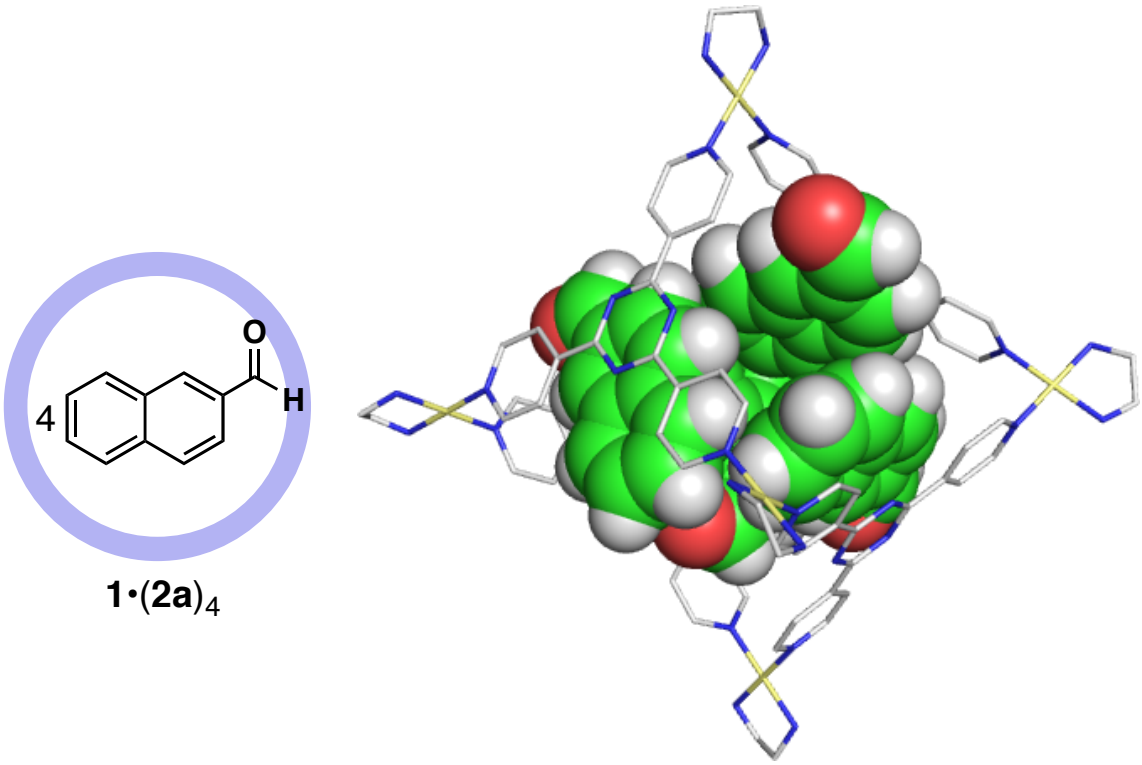
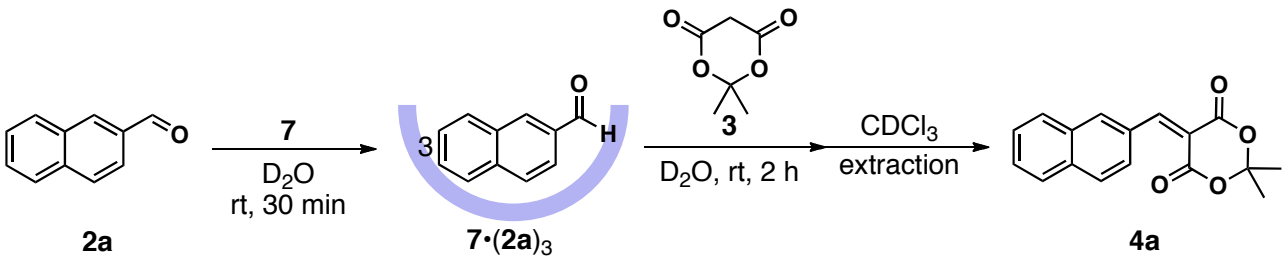


Figure S33. Molecular modeling of inclusion complex **1•(2a)**$_4$ optimized by a force-field calculation on MS Modeling 4.4 program. The four molecules of naphthaldehyde **2a** completely occupy the vacant space of cage **1** but freely rotate within the cage. Aldehyde **2a** is shown in the Corey–Pauling–Kolton (CPK) representation (cage **1**: C gray, N blue, Pd yellow; aldehyde **2a**: C green, H gray, O red).

Reaction Procedure for the Knoevenagel condensation of aldehyde 2a in bowl-shaped cage 7



2-Naphthaldehyde (**2a**, 6.25 mg; 0.040 mmol) was suspended in a D_2O solution (1.0 mL) of cage **7** (5.0×10^{-3} mmol; 5.0 mM), and the solution was stirred at room temperature for 30 min. After filtration, inclusion complex **7•(2a)**$_3$ was obtained in a quantitative yield. Meldrum's acid **3** (2.16mg, 0.015 mmol) was added to the solution, and the resulting solution was stirred for 2 h. After extraction with $CDCl_3$, condensation product **4a** was obtained in 17% yield, as determined by NMR analysis.