CONFORMATIONAL EXCHANGE OF 1,8-DIBENZOYL-2,7-DIMETHOXYNAPHTHALENE ANALOGUES IN SOLUTION

Akiko Okamoto,[a]* Shinji Ohisa,[a] Sayaka Yoshiwaka,[a] and Noriyuki Yonezawa[a]

Keywords: *peri*-Aroylated naphthalene, Solution structure, Cooperative bond rotation, interconversion behaviour, ^{1}H NMR study.

Dynamic feature of 1,8-dibenzoyl-2,7-dimethoxynaphthalene in solution is revealed through systematic comparison with the analogues bearing *p*-carboxy group or *p*-amino one. (Carbonyl)C–C(naphthalene) bond rotation of aroyl group in amino group-bearing analogue is slower than that of aroyl group in no substituent-bearing (*i.e.*, benzoyl group or carboxy group) analogues. NMR study of unsymmetrically substituted 1,8-dibenzoylnaphthalene analogues shows that (carbonyl)C–C(naphthalene) bond rotation of one benzoyl group is retarded by the other aroyl group bearing *p*-amino group. These results strongly indicate that the bond rotation behaviour of two aroyl groups in the 1,8-diaroylnaphthalene analogue does not occur independently with each other but cooperatively.

*Corresponding Author
Phone: +81-42-388-7601
E-Mail: aokamoto@cc.tuat.ac.jp
[a] Department of Organic and Polymer Materials Chemistry, Tokyo University of Agriculture and Technology, 2–24–16 Naka-machi, Koganei, Tokyo 184–8588, Japan

Introduction

1,2-Disubstituted polyaromatic compounds (e.g., naphthalene, phenanthrene, and anthracene) have been recognized as important building blocks because of their great number of chemical properties, including stereoselectivity in organic reactions, molecular recognitions, axial chilarity, and so on.[1-5] These unique chemical properties are originated from configurationally stable isomers and the transformation. Therefore, conformational studies of this type of the polyaromatic frameworks in crystal and in solution have been actively performed.[6-8] We have found that *peri* (1,8)-selective diaroylation of naphthalene ring core readily proceeds by employing suitable acidic mediator.[9,10] The naphthalene ring bearing two identical α-substituted benzoyl groups in *peri*-positions is expected to involve two types of conformers, because the *peri*-substituted benzoyl groups can adopt either an *anti*-disposition (with the two benzoyl groups oriented in an opposite direction) or a *syn*-disposition (with the two benzoyl groups oriented in same direction). In crystalline form, almost all *peri*-aroylnaphthalene derivatives reported by us have two common structural features, viz., two benzoyl groups are attached almost perpendicularly to the naphthalene ring and oriented in an opposite direction (*anti*-conformer).[11-13] Several examples have proved the existence of *peri*-aroylnaphthalene compounds in which the two aroyl groups are oriented in same direction (*syn*-conformer).[14,15] To clarify the structure determining factors of the *anti*-conformer and *syn*-one, we have investigated the spatial organizations and the molecular accumulation structures of the *syn*-conformer and the designed *syn*-candidates in their crystals. Comparison of *syn*-conformer with the *syn*-candidate analogues has revealed that selection of *anti*- or *syn*-conformer in crystal state is mainly determined by the balance between strong molecular interaction and molecular packing density.[16] In solution, both conformers are unlikely to be configurationally stable and would rapidly interconvert at ambient temperature. In fact, by using variable temperature NMR, we have reported that the two aroyl groups in 1,8-dibenzoylated naphthalene compounds rotate freely.[17] Recently, we have found that bridged *peri*-aroylnaphthalene can be easily prepared by a reaction of 1,8-bis(4-fluorobenzoyl)naphthalene derivatives and catechol without high dilution conditions.[18] The susceptibility of the intramolecularly connection indicates that *peri*-aroylnaphthalene analogues partially take *syn*-conformation in solution. However, the detailed bond rotation behaviour of the two aroyl groups in *peri*-aroylnaphthalene derivatives and the conformational exchange has not been revealed yet.

Herein, we will discuss the rotation behaviour of the neighbouring two aroyl groups in 1,8-diaroylnaphthalene analogues in solution and estimate the interconversion behaviour including plausible intermediates through systematic comparison of ^{1}H NMR spectra of symmetrically substituted 1,8-diaroylnaphthalene analogues and the unsymmetrically substituted ones.

Experimental

All reagents were of commercial quality and were used as received. Solvents were dried and purified using standard techniques.[19] 2,7-dimethoxynaphthalene (**1**) was prepared according to literature method.[20]

Measurements

^{1}H NMR spectra were recorded on a JEOL JNM-AL300 spectrometer (300 MHz) and a JEOL ECX400 spectrometer (400 MHz). Chemical shifts are expressed in ppm relative to internal standard of TMS (δ 0.00). ^{13}C NMR spectra were recorded on a JEOL JNM-AL300 spectrometer (75 MHz). Chemical shifts are expressed in ppm relative to $CDCl_3$ (δ 77.0). IR spectra were recorded on a JASCO FT/IR-4100 spectrometer. Elemental analyses were performed on a SUMIKA CHEMICAL ANALYSIS SERVICE Sumigraph NHC-22F analyzer. High-resolution FAB mass spectra were recorded on a JEOL MStation (MS700) ion trap mass spectrometer in positive ion mode.

Synthesis of 1,8-dibenzoyl-2,7-dimethoxynaphthalene (2)

The title compound was synthesized by a direct condensation of 2,7-dimethoxynaphthalene (**1**) with benzoic acid, mediated by P_2O_5–MsOH. To a mixture of 2,7-dimethoxynaphthalene (0.200 mmol, 37.6 mg) and benzoic acid (0.440 mmol, 174 mg), P_2O_5–MsOH (0.88 mL) was added by portions at room temperature. After the reaction mixture was stirred at 60 ˚C for 3 h, it was poured into iced water (20 mL) and the mixture was extracted with $CHCl_3$ (15 mL × 3). The combined extract was washed successively with 2 M aqueous NaOH and brine. The organic layer thus obtained was dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to give a powdery product. Isolation of the title compound was carried out by column chromatography [hexane : AcOEt = 2 : 1] (1,8-diaroylnaphthalene 63 %; 3-monoaroylnaphthalene 19 %; 1-monoaroylnaphthalene 3 %). Colorless single crystals suitable for X-ray diffraction were obtained by recrystallization from ethanol as colorless needles, m.p.: 530 K. IR (KBr): 1665, 1626 cm^{-1}. ^1H NMR δ (300 MHz, DMSO-d_6): 3.61 (6H, s), 7.35 (4H, t, *J* = 7.4 Hz), 7.41 (2H, d, *J* = 9.0 Hz), 7.47 (4H, d, *J* = 7.8 Hz), 7.50 (2H, t, *J* = 6.9 Hz), 8.16 (2H, d, *J* = 9.0 Hz) ppm. ^1H NMR δ (400 MHz, $CDCl_3$): 3.68 (6H, s), 7.21 (2H, d, *J* = 9.2 Hz), 7.34 (4H, dd, *J* = 7.6, 7.6 Hz), 7.49 (2H, t, *J* = 7.4 Hz), 7.70 (4H, d, *J* = 7.4 Hz), 7.95 (2H, d, *J* = 9.2 Hz) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$): 56.40, 111.24, 121.47, 125.55, 127.95, 129.09, 129.84, 132.03, 132.64, 138.61, 156.28, 196.875 ppm. The recorded m.p. and spectral data are compatible with the literature values.[21]

Synthesis of 1,8-bis(4-carboxymethylbenzoyl)-2,7-dimethoxy-naphthalene (3)

In a 10 mL-flask, substrate **1** (1.0 mmol, 188 mg), terephthaloyl chloride (4.0 mmol, 208 mg) and dichloromethane (2.5 mL) were placed. The reaction mixture was heated with stirring up to 60 ˚C, and then $TiCl_4$ (4.4 mmol, 0.48 mL) was added. After stirring at 60 ˚C for 6 h, the reaction mixture was poured into methanol (30 mL), and stirred at room temperature overnight. The reaction mixture was added to water (20 mL), and extracted with chloroform (20 mL × 3). The combined extract was washed successively with water (20 mL × 3) and brine (20 mL × 3). The organic layer thus obtained was dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give a cake. Compound (**3**) was isolated by silica gel column chromatography (hexane: AcOEt = 5 : 4) as pale white yellow powder, Yield: 23%, m.p.: 467–468 K. IR (KBr): 1724, 1670, 1609, 1511, 1270 cm^{-1}. ^1H NMR δ (300 MHz, $CDCl_3$): 3.66 (6H, s), 3.93(6H, s), 7.20 (2H, d, *J* = 9.0 Hz), 7.76 (4H, d, *J* = 8.4 Hz), 7.97 (2H, d, *J* = 9.0 Hz), 8.03 (4H, d, *J* = 8.4 Hz) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$): 52.33, 56.27, 111.13, 120.49, 125.52, 128.87, 129.43, 133.35, 141.90, 156.66, 166.57, 196.90, 196.95 ppm. Calcd for $C_{30}H_{24}O_8$: C, 70.31; H, 4.72; found C, 70.19; H, 4.74.

Synthesis of 1,8-bis(4-carboxybenzoyl)-2,7-dimethoxynaphtha-lene (4)

In a 50 mL flask, the methyl ester (**3**) (0.23 mmol, 118 mg), acetone (2.5 mL), and 2 M aqueous NaOH (2.5 mL) were placed. After stirring at room temperature for 3 h, conc. HCl was added to the reaction mixture until the pH is 2. The precipitates were collected by filtration with suction and washed with water followed by drying in vacuo. Colour: yellow powdery solid, Yield: 99 %, m.p.: 612 K. IR (KBr): 1698, 1673, 1268 cm^{-1}. ^1H NMR δ (300 MHz, DMSO-d_6): 3.62 (6H, s), 7.46 (2H, d, *J* = 9.0 Hz), 7.59 (4H, d, *J* = 8.1 Hz), 7.91 (4H, d, *J* = 8.7 Hz), 8.20 (2H, d, *J* = 9.0 Hz) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$): 56.910, 112.352, 119.972, 125.470, 129.170, 129.466, 129.733, 133.434, 134.715, 141.732, 156.876, 167.297, 196.687 ppm. Calcd. for $C_{28}H_{20}O_8$: C, 69.42 %, H, 4.16%, found C, 69.32 %, H, 4.01 %.

Synthesis of 2,7-dimethoxy-1,8-bis(4-nitrobenzoyl)naphthalene (5)

In a 10 mL flask, 4-nitrobenzoyl chloride (1.2 mmol, 222 mg) and 1,2-dichloroethane (1.0 mL) were placed. The reaction mixture was stirred at 70 ˚C, and $TiCl_4$ (1.2 mmol, 0.13 mL) was added. After stirring for 0.5 h, substrate **1** (0.2 mmol, 37.6 mg) was added to the reaction mixture and further stirred for 3 h. Then the mixture was poured into iced water (30 mL) and extracted with chloroform (15 mL × 3). The combined extract was washed successively with 2 M aqueous NaOH solution (15 mL × 3) and brine (15 mL × 3). The organic layer thus obtained was dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give a cake. The crude product was purified by re-precipitation with chloroform/hexane. The precipitate was collected with suction filtration and dissolved in acetone. After decolorization by activated charcoal powder, acetone solution was evaporated (81% isolated yield). The product was further washed with ethanol–ethyl acetate solution and dried in vacuo. Yield: 25 %, m.p.: 567–574 K. IR (KBr): 1657, 1604, 1519 cm^{-1}. ^1H NMR δ (300 MHz, $CDCl_3$): 3.69 (6H, s), 7.24 (2H, d, *J* = 12.0 Hz), 7.90 (2H, d, *J* = 11.6 Hz), 8.04 (2H, d, *J* = 11.6 Hz), 8.27 (2H, d, *J* = 11.6 Hz) ppm. ^{13}C NMR δ (125 MHz, $CDCl_3$): 56.35, 111.11, 119.58, 123.63, 125.61, 129.86, 130.54, 133.48, 143.47, 150.22, 157.14, 196.84 ppm; HRMS (FAB; *m*-NBA) m/z: $[M + H]^+$, Calc. for $C_{26}H_{19}N_2O_8$, 487.1141; found, 487.1197.

Reduction of 2,7-dimethoxy-1,8-bis(4-nitrobenzoyl)naphtha-lene (5)

In a 10 mL flask, (**5**) (0.2 mmol, 97.3 mg), stannous chloride dihydrate (2.0 mmol, 431 mg), and ethanol (1.6 mL) were placed. The reaction mixture was stirred at 70 ˚C for 2 h. After the reaction is over, the mixture was poured into 2 M aqueous HCl (15 mL) and stirred at room temperature for 15 min. The solution mixture was washed with chloroform (15 mL ×3) and poured into 4 M aqueous NaOH solution (40 mL). The precipitate was collected with suction filtration, and dried under reduced pressure. The collected precipitate was dissolved in acetone, filtered and solvent was removed to get the product, 1,8-bis(4-aminobenzoyl)-2,7-dimethoxynaphthalene (**6**).[13] The product was further purified for X-ray crystallography by recrystallization from methanol as yellow needles. Yield: 93 %, m.p. = 580.5–583 K (decomp.). IR (KBr): 3455, 3374, 1660, 1625 cm^{-1}. ^1H NMR δ (300 MHz, DMSO-d_6): 3.62 (6H, s), 5.89 (4H, s), 6.40 [4H, d (broad), *J* = 8.4 Hz], 7.15 [4H, d(br), *J* = 7.5 Hz], 7.35 (2H, d, *J* = 9.0 Hz), 8.02 (2H, d,

J = 9.0 Hz) ppm. ^{13}C NMR δ (75 MHz, DMSO-d_6); 56.37, 111.59. 112.22, 122.11, 125.06. 127.41, 128.86, 131.15, 131.29, 153.09, 155.06, 192.49 ppm. HRMS (FAB; *m*-NBA) m/z: $[M+H]^+$: Calc. for $C_{26}H_{23}O_4N_2$, 427.1658; found, 427.1633.

Synthesis of methyl 4-(2,7-dimethoxy-1-naphthoyl)benzoate (7)

Terephthaloyl chloride (0.60 mmol, 122 mg) and dichloromethane (1.0 mL), and $TiCl_4$ (0.66 mmol, 0.072 mL) stirred in a 10 mL flask to give a clear yellow solution. Then substrate **1** (0.4 mmol, 75.2 mg) was added to the reaction solution and stirred at room temperature for 3 h. After the reaction is over, the mixture was poured into methanol (30 mL) and stirred for 1 h. The mixture was added to water (20 mL) and extracted with chloroform (20 mL × 3). The combined extract was washed successively with water (20 mL × 3), 2 M NaOH aqueous (20 mL × 3) and brine (20 mL × 3). The organic layer thus obtained was dried over anhydrous $MgSO_4$.[22] The solvent was removed under reduced pressure to give cake. Compound (**7**) was isolated by silica gel column chromatography (hexane: AcOEt = 4 : 1; 66% isolated yield; pale yellow powder). The product was further purified for X-ray crystallography by recrystallization from methanol. Colour: pale yellow, yield: 66 %, m.p. = 428–430 K. IR (KBr): 1674, 1625, 1511 cm^{-1}. ^{1}H NMR δ (300 MHz, $CDCl_3$): 3.73 (3H, s), 3.76 (3H, s), 3.94 (3H, s), 6.83 (1H, s), 7.01 (1H, d, *J* = 9.0 Hz), 7.14 (1H, d, *J* = 9.0 Hz), 7.71 (1H, d, *J* = 9.0 Hz), 7.87–7.90 (3H, m), 8.07 (2H, d, *J* = 8.1 Hz) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$): 52.4, 55.2, 56.2, 101.9, 110.1, 117.2, 121.0, 124.4, 129.2, 129.7, 129.8, 131.6, 133.0, 133.9, 141.6, 155.4, 159.1, 166.4, 197.5 ppm. Calc. For $C_{21}H_{18}O_5$: C, 71.99; H, 5.18; found C, 72.05; H, 5.25.

Synthesis of unsymmetric 1,8-diaroylated analogue (8)

Benzoyl chloride (0.60 mmol, 0.070 mL), methylene chloride (0.5 mL), and $TiCl_4$ (0.9 mmol, 0.099 mL) were placed in a 10 mL flask and stirred to give a clear yellow solution. Compound (**7**) (0.15 mmol, 52 mg) was added to the this mixture. After stirring at room temperature for 20 h, the mixture was poured into iced water (30 mL), and extracted with chloroform (15 mL × 3). The combined extract was washed with water (20 mL × 3), 2 M NaOH aq. (20 mL × 3) and brine (20 mL × 3). The organic layers thus obtained were dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give a cake. 1-Benzoyl-8-(4-carboxymethylbenzoyl)-2,7-dimethoxynaphthalene (**8)** was isolated by preparative TLC (PTLC; toluene: AcOEt = 15 : 1) as a yellow powdery solid, Yield: 46 %, m.p.: 450–451 K. IR (KBr): 1725, 1664, 1650, 1608, 1510, 1458 (Ar, naphthalene), 1268 cm^{-1}. ^{1}H NMR δ (300 MHz, DMSO-d_6): 3.65 (3H, s), 3.67 (3H, s), 3.92 (3H, s), 7.19 (1H, d, *J* = 9.0 Hz), 7.21 (1H, d, 9.0 Hz), 7.35 (2H, t, *J* = 8.4, 8.5 Hz), 7.50 (1H, t, *J* = 2.4 Hz), 7.71 (2H, d, *J* = 8.4 Hz), 7.77 (2H, d, *J* = 8.4 Hz), 7.95 (1H, d, *J* = 9.3 Hz), 7.96 (1H, d, *J* = 9.3Hz), 8.02 (2H, d, *J* = 8.7 Hz) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$): 52.417, 56.413, 56.490, 111.157, 111.396, 120.842, 121.282, 125.651, 128.156, 128.969, 129.227, 129.456, 130.126, 132.363, 132.621, 132.946, 133.328, 138.673, 142.086, 156.589 (overlap), 166.752, 196.620, 197.432 ppm. HRMS (FAB; *m*-NBA) m/z: $[M+H]^+$: Calc. for $C_{28}H_{22}O_6$, 454.1416, found, 454.1425.

Synthesis of unsymmetric 1,8-diaroylated analogue 9

The unsymmetric methyl ester (**8**) (0.06 mmol, 27.2 mg), methanol (1.0 mL), and 2 M aqueous NaOH (1.0 mL) were refluxed in a 10 mL flask with a Dimorth condenser for 3 h. The reaction mixture was cooled to room temperature and then HCl was added till pH becomes 2. The precipitate was collected by filtration with suction and washed with water, followed by drying in vacuo. The yield of 1-benzoyl-8-(4-carboxybenzoyl)-2,7-dimethoxynaphthalene (**9**) was 98 %. Colour: pale yellow solid, m.p. = 510–511 K. IR (KBr): 3448(COO–H), 1697 (C=OOH), 1664 (C=O), 1610, 1512 (Ar, naphthalene), 1268 (O-Me) cm^{-1}. ^{1}H NMR δ (300 MHz, DMSO-d_6): 3.61 (3H, s), 3.62 (3H, s), 7.33-7.378 (2H, m), 7.44-7.49 (5H, m), 7.55 (2H, d, *J* = 8.1 Hz), 7.90 (2H, d, *J* = 8.1 Hz), 8.18 (1H, d, *J* = 9.0 Hz), 8.18 (1H, d, *J* = 9.3 Hz) ppm. ^{13}C NMR δ (75 MHz, DMSO-d_6): 56.868, 56.887, 112.257, 112.324, 120.145, 120.460, 125.448, 128.701, 129.130 (overlap), 129.397, 129.712, 133.079, 133.270, 133.356, 134.615, 138.678, 141.787, 156.639, 156.705, 167.369, 196.270, 196.938 ppm. HRMS (FAB; *m*-NBA) m/z: $[M+H]^+$:calcd for $C_{27}H_{21}O_6$, 441.1338 ; found, 441.1384.

Synthesis of 1-(4-nitrobenzoyl)-2,7-dimethoxynaphthalene (10)

4-Nitrobenzoyl chloride (6.6 mmol, 1.21 g), dichloromethane (15 mL), and $AlCl_3$ (7.26 mmol, 968 mg) were placed in a 10 mL flask and stirred at 0 ˚C. Substrate **1** (6.0 mmol, 1.13 g) was added to the mixture and further stirred at 0˚C.[23] After stirring for 24 h, the mixture was poured into iced water (40 mL) and extracted with chloroform (20 mL × 3). The combined extract was washed successively with 2 M aqueous NaOH solution (30 mL × 3) and brine (20 mL × 3). The organic layer thus obtained was dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give the cake. Compound (**10**) was isolated by preparative crystallization (chloroform/hexane) as yellow cubic crystals. Yield: 45 %, m.p.: 440 K. IR (KBr): 1357, 1594, 1267 cm^{-1}. ^{1}H NMR δ (300 MHz, $CDCl_3$): 3.76 (3H, s), 3.76 (3H, s), 6.87 (1H, d, *J* = 2.3 Hz), 7.05 (1H, dd, *J* = 9.0, 2.3 Hz), 7.16 (1H, d, *J* = 9.01 Hz), 7.75 (1H, d, *J* = 8.71 Hz), 7.93 (1H, d, *J* = 9.01 Hz), 7.98 (2H, d, *J* = 9.01 Hz), 8.27 (2H, d, *J* = 8.71 Hz) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$): 21.790, 22.730, 68.346, 76.447, 82.545, 83.897, 90.317, 91.026, 95.666, 96.490, 96.704, 98.822, 99.605, 109.643, 122.302, 125.961, 162.866 ppm. Calc. For $C_{19}H_{15}O_5N$, C, 67.65; H, 4.48; N, 4.15; Found C, 67.52 ; H, 4.51 ; N, 4.06.

Synthesis of unsymmetric 1,8-diaroylated analogue 11

Benzoyl chloride (1.4 mmol, 0.16 mL), methylene chloride (2.5 mL), and $TiCl_4$ (1.1 mmol, 1.21 mL) were placed in a 10 mL flask and heated with stirring to 30 ˚C. Compound (**10**) (1.00 mmol, 337 mg) was added to the reaction mixture. After stirring at 30 ˚C for 5 h, the mixture was poured into iced water (30 mL), and extracted with chloroform (15 mL × 3). The combined extract was successively washed successively with water (20 mL × 3), 2 M aqueous NaOH (20 mL × 3) and brine (20 mL × 3). The organic layer thus obtained was dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give the cake. 1-Benzoyl-8-(4-nitrobenzoyl)-2,7-

dimethoxynaphthalene (**11**) was isolated by preparative crystallization (chloroform/hexane) as a yellow powdery solid. Yield: 44 %, m.p.: 509–510 K. IR (KBr): 1663(C=O), 1608, 1513, 1454 (Ar, naphthalene), 1346 (C–NO_2), 1268 (O–Me) cm^{-1}. ^1H NMR δ (300 MHz, DMSO-d_6): 3.67 (3H, s), 3.69 (3H, s), 7.21 (1H, d, *J* = 9.0 Hz), 7.24 (1H, d, *J* = 9.3 Hz), 7.87 (2H, d, *J* = 8.7 Hz), 7.984 (2H, d, *J* = 9.0 Hz), 8.00 (2H, d, *J* = 9.3 Hz), 7.70 (2H, dd, *J* = 1.5, 7.65 Hz), 7.53 (1H, t, *J* = 1.5, 7.2 Hz), 7.37 (2H, t, *J* = 7.2, 7.4 Hz) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$); 56.413, 56.470, 110.966, 111.501, 120.010, 120.995, 123.500, 125.613, 128.242, 129.217, 129.925, 130.202, 132.592, 133.089, 133.128, 138.682, 143.405, 150.021, 156.714, 156.800, 195.702, 197.901 ppm. HRMS (FAB; *m*-NBA) m/z: $[M+H]^+$: Calc. for $C_{26}H_{20}NO_6$, 442.1291, found, 442.1311.

Reduction of Compound 11

Compound (**11**) (0.4 mmol, 176 mg), stannous chloride dihydrate (2.0 mmol, 431 mg), and ethanol (2.0 mL) were placed in a 10 mL flask with a Dimorth condenser. The reaction mixture was stirred at 70˚C for 2.5 h. After the completion of reaction, the mixture was poured into iced water (20 mL), and 2 M aqueous NaOH (20 mL) was added. The basic solution was extracted with chloroform (10 mL ×3). The combined extract was successively washed with water (20 mL × 3), 2 M aqueous NaOH (20 mL × 3) and brine (20 mL × 3), and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give the cake (58%). 1-(4-Aminobenzoyl)-8-benzoyl-2,7-dimeth-oxynaphthalene (**12**) was isolated by silica gel column chromatography (Toluene : AcOEt = 2 : 1) as a pale yellow powder. Yield: 48%, m.p.: 537 K. IR (KBr): 3467 (N–H), 3378 (N–H), 1663, 1646 (C=O), 1597, 1510, 1450 (Ar, naphthalene), 1271 (O-Me) cm-1. ^1H NMR δ (300 MHz, DMSO-d_6): 3.59 (3H, s), 3.65 (3H, s), 5.92 (2H, broad), 6.34 (2H, broad), 7.12 (2H, broad), 7.31 (2H, m), 7.39 (2H, d, *J* = 9.0 Hz), 7.40-7.50 (3H, m), 8.07 (1H, d, *J* = 9.0 Hz), 8.09 (1H, d, *J* = 9.0 Hz) ppm. ^{13}C NMR δ (75 MHz, DMSO-d_6): 56.786, 56.882, 112.027, 112.266, 112.677, 121.234, 122.133, 125.422, 127.257, 128.366, 128.586, 128.959, 129.294, 131.225, 131.933, 132.506, 132.707, 153.922, 155.777, 156.083, 193.197, 195.406 ppm. HRMS (FAB; *m*-NBA) m/z: $[M+H]^+$: Calc. for $C_{26}H_{22}NO_4$, 412.1549 ; found, 412.1595.

Synthesis of unsymmetric 1,8-diaroylated analogue 13

Terephthaloyl chloride (1.0 mmol, 203 mg) and dichloromethane (0.7 mL), and $TiCl_4$ (1.1 mmol, 0.21 mL) were placed in a 10 mL flask and stirred with heating at 30˚C. Compound **10** (0.2 mmol, 67.4 mg) was added to the reaction mixture and stirred at 30˚C for another 24 h. After the reaction is over, the mixture was poured into methanol (30 mL) and water (20 mL) was added. The reaction mixture was extracted with chloroform (15 mL × 3). The combined extract was washed successively with water (20 mL × 3) and brine (20 mL × 3), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give the cake. The product, 1-(4-carboxymethyl)-8-(4-nitrobenzoyl)-2,7-dimethoxynaphthalene (**13**) was isolated by silica gel column chromatography (hexane: AcOEt = 5 : 4) as a yellow powdery solid. Yield: 61 %, m.p.: 468–469 K. IR (KBr): 1722, 1679, 1608, 1513, 1345 cm^{-1}. ^1H NMR δ (300 MHz, $CDCl_3$): 3.668 (3H, s), 3.673 (3H, s), 3.932 (3H, s), 7.21-7.25 (2H, m), 7.78 (2H, d, *J* = 8.1 Hz), 7.88 (2H, d, *J* = 8.4 Hz), 7.99-8.03 (2H, m), 8.05 (2H, d, *J* = 7.8 Hz), 8.23 (2H, d, *J* = 9.0 Hz) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$): 52.33, 56.23, 110.88, 111.22, 119.70, 120.27, 123.39, 125.49, 128.82, 129.42, 129.75, 130.25, 132.87, 133.55, 141.92, 143.26, 149.97, 156.78, 156.89, 196.04, 197.43, 221.54 ppm. HRMS (FAB; *m*-NBA) m/z: $[M+H]^+$: Calc. for $C_{28}H_{22}NO_8$, 500.1345, found 500.1361.

Reduction of Compound 13

Compound (**13**) (0.165 mmol, 82.5 mg), stannous chloride dihydrate (0.825 mmol, 186 mg), and ethanol (2.0 mL) were placed in a 50 mL flask with a Dimorth condenser. The reaction mixture was stirred at 70˚C for 2 h. After the completion of the reaction, the mixture was poured into iced water (20 mL) and 2 M aqueous NaOH (20 mL) was added. The basic reaction solution was extracted with chloroform (10 mL × 3). The combined extract was washed successively with 2 M aqueous NaOH (20 mL × 3) and brine (20 mL × 3). The organic layer was dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give the cake (58%). 1-(4-Aminobenzoyl)-8-(4-carboxymethyl)-2,7-dimethoxynaphthalene (**14**) was isolated by silica gel column chromatography (Toluene : AcOEt = 2: 1) as a pale yellow powder. Yield: 69 %, m.p.: 507-508 K. IR (KBr): 3463 (N–H), 3370 (N-H), 2935 (O–C), 2849 (Ar–OMe), 1720 (MeOC=O), 1664 (C=O), 1610, 1511, (Ar, naphthalene), 1277 (O-Me) cm^{-1}. ^1H NMR δ (300 MHz, DMSO-d_6): 3.59 (3H, s), 3.66 (3H, s), 3.84 (3H, s), 5.98 (2H, s), 6.32 (2H, broad), 7.18 (2H, broad), 7.41 (2H, *J* = 9.0 Hz), 7.55 (2H, broad), 7.90 (2H, d, *J* = 6.9 Hz), 8.08–8.14 (2H, m) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$); 52.398, 56.432, 56.604, 111.033, 111.540, 113.681, 121.072, 122.037, 125.642, 128.950, 129.361, 129.523, 129.982, 131.799, 132.057, 132.420, 132.994, 142.086, 151.312, 156.131, 156.360, 166.877, 195.004, 195.951 ppm. HRMS (FAB; *m*-NBA) m/z: $[M+H]^+$: Calc. for $C_{28}H_{24}NO_6$, 470.1604 found, 470.1610.

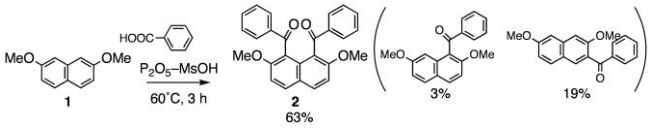
Synthesis of unsymmetric 1,8-diaroylated analogue 15

The unsymmetric methyl ester (**14**) (0.12 mmol, 54.6 mg), 2 M aqueous NaOH (1.0 mL), and methanol (1.0 mL) are placed in a 10 mL flask with a Dimorth condenser and heated with stirring up to 80 ˚C for 1 h. The reaction mixture was then cooled and conc. HCl was added to render the neutral (pH 7). The reaction mixture was extracted with chloroform (10 mL x 3). The combined organic layer thus obtained was dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give the cake. 1-(4-Aminobenzoyl)-8-(4-carboxy)-2,7-dimethoxynaphthalene (**15**) was isolated by preparative crystallization (Chloroform/methanol) as a yellow powdery solid. Yield: 75 %, m.p.: 545-547 K. IR (KBr): 3364 (O–H), 1653 (C=O), 1653, 1590, 1511 (Ar, naphthalene), 1262 (O-Me)cm^{-1}. ^1H NMR δ (300 MHz, DMSO-d_6): 3.59 (3H, s), 3.66 (3H, s), 5.98 (2H, s), 6.35 (2H, broad), 7.13 (2H, broad), 7.40 (2H, d, *J* = 9.0 Hz), 7.54 (2H, broad), 7.89 (2H, d, *J* = 6.6 Hz), 8.07-8.13 (2H, m) ppm. ^{13}C NMR δ (75 MHz, DMSO-d_6): 56.786, 56.834, 111.979, 112.295, 112.773, 120.622, 121.789, 125.383, 128.930, 129.303, 129.495, 130.432, 131.751,

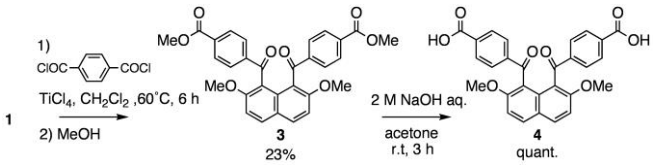
132.869, 141.694, 154.094, 155.872, 156.245, 167.756, 195.167, 197.069 ppm. HRMS (FAB; *m*-NBA) m/z: $[M+H]^+$: Calc. for $C_{27}H_{22}NO_6$, 456.1447, found 456.1455.

Results and Discussion

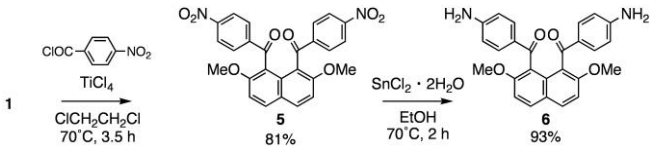
1,8-Dibenzoyl-2,7-dimethoxynaphthalene (**2**) was synthesized by a direct condensation of 2,7-dimethoxynaphthalene (**1**) with benzoic acid mediated by phosphorus pentoxide–methanesulfonic acid (P_2O_5–MsOH) (Scheme 1, *see* Experimental section). [24] Both the carboxy group-bearing analogue (**4**) and amino group-bearing one (**6**) were prepared via electrophilic aromatic aroylation at *peri*-positions of the naphthalene ring, followed by transformation reaction of the substituents in the aroyl groups (Schemes 2 and 3). Analogue (**3**) was isolated by quenching with methanol after diaroylation of substrate (**1**) with terephthaloyl chloride.



Scheme 1. Synthesis of 1,8-dibenzoyl-2,7-dimethoxynaphthalene (**2**) via P_2O_5–MsOH-mediated direct condensation.



Scheme 2. Synthesis of 1,8-dibenzoylnaphthalene analogue (**4**).



Scheme 3. Synthesis of 1,8-dibenzoylnaphthalene analogue (**6**).

The dynamic behaviour of the conformational exchange of analogues **2**, **4** and **6** in solution was analyzed by NMR measurement performed in DMSO-d_6 solution. Figure 1 shows the aromatic proton region of the ^{1}H NMR spectrum of 1,8-dibenzoylnaphthalene compound (**2**). Two signals at δ 8.16 ppm and 7.44 ppm are assigned to the protons at 4(5)- and 3(6)-positions of the naphthalene ring, respectively. The signal at δ 7.35 ppm (triplet) is assigned to the aromatic protons at *m*-positions of the benzoyl groups. The signals from δ 7.54 ppm to 7.42 ppm are assigned as the aromatic protons at *p*- and *o*-positions of the benzoyl groups. Figure 2 exhibits the ^{1}H NMR spectrum of 1,8-diaroylated naphthalene compound bearing carboxy groups (**4**). The signals at δ 8.20 ppm and 7.46 ppm are assigned to the protons at the 4(5)- and 3(6)-positions of the naphthalene ring, respectively. The signals at δ 7.91 ppm and 7.59 ppm are due to the protons at *o*- and *m*-positions of the benzene ring bearing the carboxy groups. Figure 3a displays the ^{1}H NMR spectrum of the amino group-bearing analogue (**6**). Two signals at δ 8.02 ppm and 7.35 ppm, and the signal at δ 5.89 ppm are assigned to the protons at 4(5)- and 3(6)-positions of the naphthalene ring, and the protons of the amino groups. The broad signals at δ 7.15 ppm and 6.40 ppm are assigned to the aromatic protons at *m*- and *o*-positions of the benzene ring bearing the amino group. The two broad signals of the aroyl groups become sharp at 150 ˚C as shown in Figure 3b.

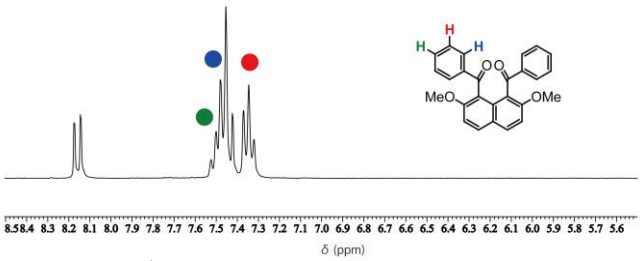


Figure 1. ^{1}H NMR spectrum of 1,8-dibenzoyl-2,7-dimethoxynaphthalene (**2**) in DMSO-d_6 (5.5–8.5 ppm).

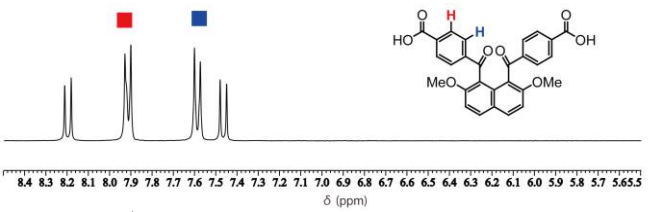


Figure 2. ^{1}H NMR spectrum of 1,8-dibenzoylnaphthalene analogue bearing *p*-carboxy group **4** in DMSO-d_6 (5.5–8.5 ppm).

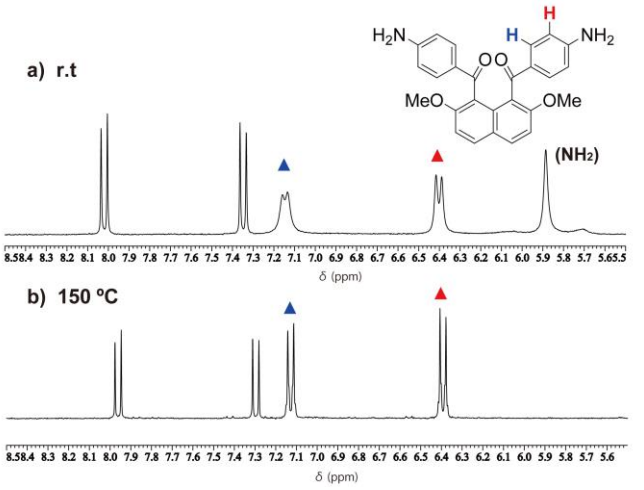
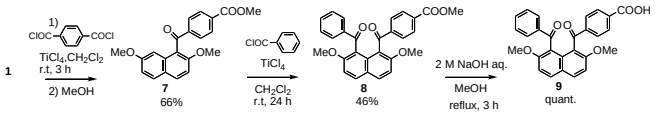


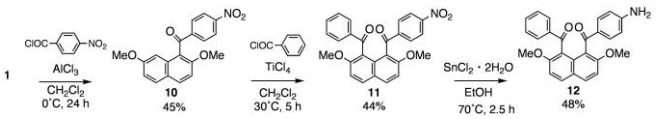
Figure 3. ^{1}H NMR spectra of 1,8-dibenzoylnaphthalene analogue bearing *p*-amino group (**6**) in DMSO-d_6 (5.5–8.5 ppm), (a) at room temperature, (b) at 150 ˚C.

The changes of the signal shape for the protons at *o*- and *m*-positions of the aroyl group in the amino group-bearing analogue (**6**) at room temperature and 150 ˚C suggest that C–C bond rotation between the carbonyl group and the naphthalene ring in the amino group-bearing analogue (**6**) is relatively slower than that in other 1,8-diaroylnaphthalene analogues **2** and **4** at room temperature. At 150 ˚C, the bond rotation is faster than room temperature, hence a magnetically equivalent environment is made on the benzene ring. As the result, the protons of the benzene rings are expressed as sharp signals.

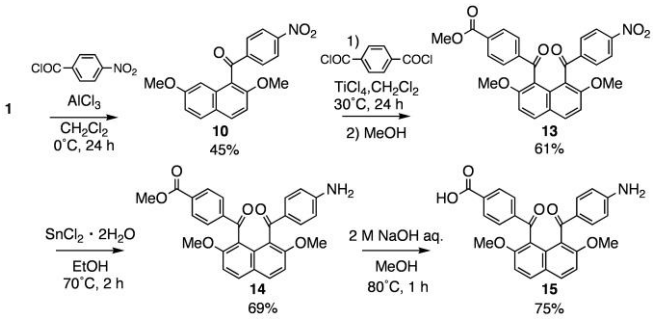
Unsymmetrically substituted 1,8-diaroylnaphthalene analogues in which one aroyl group has no substituent (i.e., benzoyl group) and the other aroyl group has a carboxyl group (**9**) or an amino one (**12**), or each aroyl group has a carboxy group and an amino one (**15**) were designed and successively synthesized by essentially the same procedure as described in Schemes 1, 2, and 3 (Schemes 4, 5, and 6; *see* Experimental section).



Scheme 4. Synthesis of unsymmetrically substituted 1,8-dibenzoylnaphthalene analogue bearing carboxy group **9.**



Scheme 5. Synthesis of unsymmetrically substituted 1,8-dibenzoylnaphthalene analogue bearing amino group **12.**



Scheme 6. Synthesis of unsymmetrically substituted 1,8-dibenzoylnaphthalene analogue **15.**

^{1}H NMR spectra of unsymmetrically substituted 1,8-diaroylnaphthalene analogues (**9**) and (**12**) are exhibited in Figures 4 and 5. In the case of unsymmetrically substituted analogue bearing carboxy group (**9**), the chemical shifts of the signals of the protons in two kinds of the aroyl groups are almost same with those of the corresponding symmetrically substituted analogues (**2**) and (**4**), i.e., δ 7.45 ppm (protons at *o*- and *p*-position for the benzoyl group), 7.35 ppm (protons at *m*-positions of the benzoyl group), 7.90 ppm (protons at *o*-positions to the carboxy group), and 7.55 ppm (protons at *m*-positions to the carboxy group). In a similar manner, the chemical shifts of the signals of the benzene rings in unsymmetrically substituted analogue bearing amino group (**12**) seem to the sum of the symmetrically substituted analogues (**2**) and (**6**). However, the shape of the signals assigned to the non-substituted aroyl group (from δ 7.39 to 7.52 ppm and from δ 7.22 to 7.38 ppm) are broadened in contrast to the sharp signals of the corresponding protons of the symmetric analogue (**2**) and the unsymmetric analogue (**9**). Similar behaviour is observed in unsymmetrically substituted 1,8-diaroylnaphthalene analogue bearing amino group and carboxy group (**15**) (Figure 6). Therefore, all of signals of the benzene rings are broadened if one aroyl group in the 1,8-diaroylated compound has an amino group.

NMR studies of unsymmetrically substituted 1,8-diaroylnaphthalene analogues, which have no substituent, a carboxy group, or an amino group in the aroyl groups, show that the (carbonyl)C–C(naphthalene) bond rotation behaviour of the aroyl groups in unsymmetrically substituted analogue coincides with that of the either of the symmetrically substituted analogue. (Carbonyl)C–C(naphthalene) bond rotation behaviour of one aroyl group follows that of the other aroyl group. In other words, the bond rotation of the neighbouring two aroyl groups in the 1,8-diaroylnaphthalene analogue does not occur independently with each other but cooperatively.

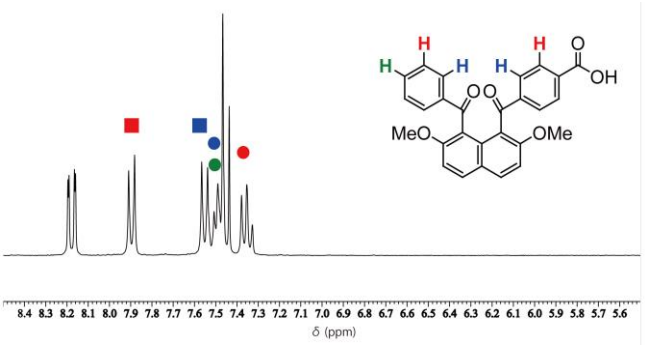


Figure 4. ^{1}H NMR spectra of unsymmetrically substituted 1,8-dibenzoylnaphthalene analogue bearing carboxy group **9** in DMSO-d_6 (5.5–8.5 ppm): $C_6\underline{\mathbf{H}}_5$ (●), *p*-COOH-$C_6\underline{\mathbf{H}}_4$ (■)

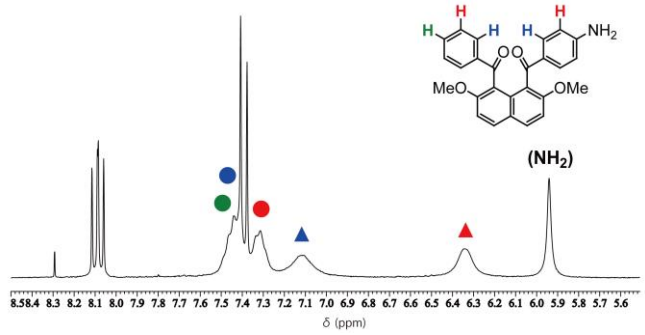


Figure 5. ^{1}H NMR spectra of unsymmetrically substituted 1,8-dibenzoylnaphthalene analogue bearing amino group **12** in DMSO-d_6 (5.5–8.5 ppm): $C_6\underline{\mathbf{H}}_5$ (●), *p*-NH_2-$C_6\underline{\mathbf{H}}_4$ (▲)

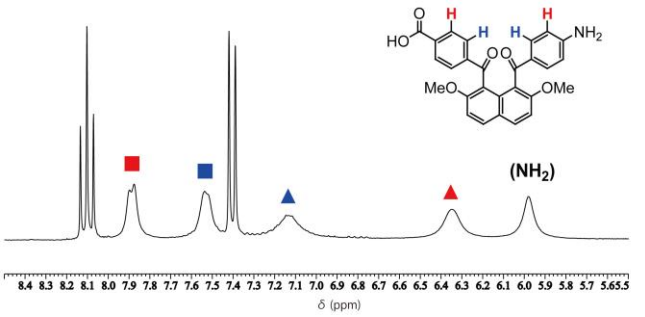


Figure 6. ^{1}H NMR spectra of unsymmetrically substituted 1,8-dibenzoylnaphthalene analogue bearing carboxy group and amino one **13** in DMSO-d_6 (5.5–8.5 ppm): *p*-COOH-$C_6\underline{\mathbf{H}}_4$ (■), *p*-NH_2-$C_6\underline{\mathbf{H}}_4$ (▲)

Plausible interconversion behaviour of 1,8-diaroylnaphthalene analogue is exhibited in Figure 7. If neighbouring two aroyl groups rotate independently, interconversion between *anti*-oriented conformers **I** and **I'** should proceed through unfavourable intermediate **IV** at least partially. Thus the neighbouring two aroyl groups rotate cooperatively with avoiding the intermediate **IV**. The interconversion process via cooperative (carbonyl)C–C(naphthalene) bond rotation of two aroyl groups presumably include *syn*-conformer **III**.

Recently, our group has reported intermolecularly connection reactions of aroyl groups in *peri*-aroylnaphthalene without high dilution conditions.[18]

According to X-ray crystal study of the bridged product, the two aroyl groups are oriented in a same direction. These results strongly indicate that two aroyl groups take *syn* fashion along with anti fashion in solution. However, *syn*-conformer would be unobservable independently on a time scale of ^{1}H NMR measurements at room temperature.

Conclusively, the aroyl groups of 1,8-bis(4-aminobenzoyl)-2,7-dimethoxynaphthalene rotate slower than other symmetric 1,8-diaroylnaphthalene analogues in solution. About the unsymmetrically substituted analogues, the bond rotation behaviour of the neighbouring two aroyl groups in 1,8-diaroyl-2,7-dimethoxynaphthalene, which one aroyl group rotates in conjunction with the other aroyl group, is demonstrated. These results strongly indicate that interconversion behaviour of 1,8-diaroyl-2,7-dimethoxynaphthalene analogue occurs through cooperative (carbonyl)C–C(naphthalene) bond rotation of the two aroyl groups at *peri*-positions of the naphthalene ring.

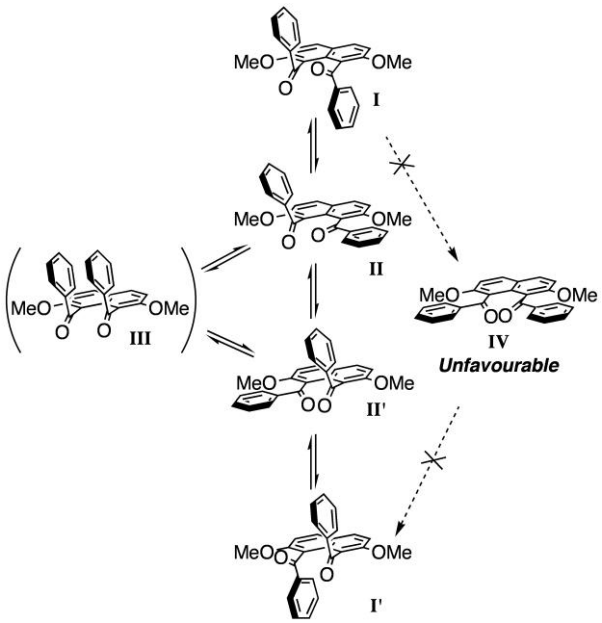


Figure 7. Plausible interconversion of 1,8-dibenzoylated naphthalene analogue with intermediates.

Acknowledgement

This work was partially supported by the Ogasawara Foundation for the Promotion of Science & Engineering, Tokyo, Japan.

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Received: 04.02.2015.
Accepted: 01.03.2015.